

Cardium Therapeutics, Inc.  
Form S-3  
March 29, 2007  
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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

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**FORM S-3**  
**REGISTRATION STATEMENT**

*UNDER*  
*THE SECURITIES ACT OF 1933*

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**CARDIUM THERAPEUTICS, INC.**

*(Exact name of registrant as specified in its charter)*

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**Delaware**  
*(State of incorporation)*

**27-0075787**  
*(IRS Employer Identification No.)*

**3611 Valley Centre Parkway, Suite 525**

**San Diego, California 92130**

**(858) 436-1000**

*(Address and telephone number of principal executive offices)*

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**Tyler M. Dylan**

**Chief Business Officer**

**3611 Valley Centre Parkway, Suite 525**

**San Diego, California 92130**

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(858) 436-1000

(Name, address and telephone number of agent for service)

Copy to:

David A. Fisher, Esq.

Fisher Thurber LLP

4225 Executive Square, Suite 1600, La Jolla, CA 92037

(858) 535-9400

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

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 of 1933, 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 of 1933, 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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act of 1933, check the following box:

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box:

**CALCULATION OF REGISTRATION FEE**

	Amount	Proposed maximum offering price	Proposed maximum aggregate	Amount of registration fee
Title of each class of securities to be registered	to be registered	per share	offering price	
Common Stock, \$0.001 par value per share	8,636,000	\$2.90 <sup>(1)</sup>	\$25,044,400 <sup>(1)</sup>	\$768.86
Common Stock, \$0.001 par value per share <sup>(2)</sup>	3,022,600	\$3.75 <sup>(3)</sup>	\$11,334,750 <sup>(3)</sup>	\$347.98
Common Stock, \$0.001 par value per share <sup>(2)</sup>	518,160	\$3.78 <sup>(3)</sup>	\$1,958,644 <sup>(3)</sup>	\$60.13
<b>TOTAL</b>	<b>12,176,760</b>			<b>\$1,176.97</b>

- (1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) of the Securities Act of 1993 and based upon the average high and low prices of the Registrant's common stock as reported on the OTC Bulletin Board on March 28, 2007.
- (2) Issuable upon exercise of warrants together with such indeterminate number of shares of common stock as may be issuable from time to time as a result of a stock split, stock dividend, recapitalization or other similar event.
- (3) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(g) of the Securities Act of 1993 and based upon the exercise price of the warrants.

**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 that 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 Securities and Exchange 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. Our selling stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities, and it is not soliciting offers to buy these securities in any state where the offer or sale is not permitted.**

**SUBJECT TO COMPLETION, DATED MARCH 29, 2007**

**12,176,760 Shares**  
**of**  
**Common Stock**

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This prospectus relates to resales of shares common stock and shares of common stock underlying warrants previously issued by Cardium Therapeutics, Inc. to the selling stockholders in connection with a private placement transaction that closed on March 9, 2007.

The selling stockholders identified in this prospectus, 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, at prices related to prevailing market prices or at privately negotiated prices. We will receive none of the proceeds from the sale of the shares by the selling stockholders. However, if the warrants are exercised, we will receive cash for the exercise price of the warrants.

The selling stockholders may resell the common stock to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions. The selling stockholders will bear all commissions and discounts, if any, attributable to the sales of shares. We will bear all costs, fees and expenses in connection with the registration of the shares.

Our common stock is quoted on the OTC Bulletin Board under the symbol CDTP . On March 28, 2007, the closing sale price of our common stock was \$3.00 per share. You are urged to obtain current market quotations for the common stock.

**An investment in our common stock involves a high degree of risk. Please carefully review the section titled Risk Factors beginning on page 3.**

The selling stockholders and any broker-dealer executing sell orders on behalf of the selling stockholders may be deemed to be underwriters within the meaning of the Securities Act of 1933 with respect to the shares sold by them. Commissions received by any broker-dealer may be deemed to be underwriting commissions under the Securities Act of 1933.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

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The date of this prospectus is \_\_\_\_\_, 2007

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You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone to provide you with information different from the information contained or incorporated by reference in this prospectus. This prospectus may only be used where it is legal to sell these securities. This prospectus is not an offer to sell, or a solicitation of an offer to buy, in any state where the offer or sale is prohibited. The information contained in this prospectus is accurate on the date of this prospectus and may become obsolete later. Neither the delivery of this prospectus, nor any sale made under this prospectus, will under any circumstances, imply that the information in this prospectus is correct as of any date after the date of this prospectus. References to Cardium, we, us or our refer to Cardium Therapeutics, Inc.

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**BUSINESS SUMMARY**

*This summary highlights certain information about Cardium and its business. This summary does not contain all of the information that is important to an investment decision. You should read the entire prospectus carefully, including Risk Factors beginning below on page 3, before deciding to invest in our common stock.*

**Our Business**

We are a medical technology company primarily focused on the development and commercialization of novel biologic therapeutics and medical devices for cardiovascular and ischemic disease. Since we were initially funded in October 2005, we have made three strategic acquisitions and assembled a portfolio of innovative late-stage cardiovascular and regenerative medicine product candidates, together with medical devices having U.S. Food and Drug Administration ( FDA ) clearances that are marketed and sold through our direct sales force. We have established a pipeline of innovative products that are divided into three operating units, Cardium Biologics, InnerCool Therapies, Inc. and the Tissue Repair Company.

As our current products and product candidates become successfully advanced, we intend to continue to pursue opportunistic acquisitions designed to enhance long-term stockholder value. At the same time, as technologies and product candidates are advanced and businesses are further developed, we may consider various corporate development transactions to enhance and monetize stockholder value such as corporate partnerings, spin-out transactions and equity distribution.

**Cardium Biologics**

The following describes the leading product candidates in Cardium Biologic s drug development pipeline:

***Generx<sup>TM</sup> (alferminogene tadenovec).*** Our lead product candidate, Generx, is a late-stage DNA-based growth factor therapeutic that is in a new class of cardiovascular biologics being developed to leverage the body s natural healing processes in response to repeated ischemic stress (insufficient blood flow and myocardial oxygen supply due to coronary heart disease). Generx is being developed as a one-time treatment to promote and stimulate the growth of collateral circulation in the hearts of patients with ischemic conditions such as recurrent angina. The natural biologic response to repeated transient ischemia is angiogenesis, the growth of new collateral blood vessels, which is orchestrated by a complex and not fully understood cascade involving many myocardial-derived growth factors. These newly formed vessels can effectively augment blood flow and oxygen delivery to parts of the patient s heart downstream from a blockage in a coronary artery. In many patients however, including those with recurrent angina, coronary collateral vessel formation is insufficient to meet the heart s needs during stress. Currently available anti-anginal drugs, which may provide symptomatic relief, are generally designed to alter the oxygen demand of the heart muscle or dilate vessels to temporarily relieve angina. Generx is an angiogenic therapeutic that is designed to promote the heart s natural response of collateral growth and to increase blood flow in the microcirculation. Generx is expected to commence a Phase 3 clinical study in the first half of 2007 that will be a randomized, placebo-controlled, double blind trial in approximately 300 women at multiple medical centers in the U.S. An additional follow-up study of Generx in men with recurrent angina due to myocardial ischemia is expected to commence later. Generx is the first and only DNA-based cardiovascular therapeutic to be advanced to Phase 3, and is believed to be the only current Phase 3 product candidate for the potential treatment of stable angina, a chronic medical condition affecting millions of patients in the U.S. and elsewhere.

***Corgentin [Ad5IGF-I].*** Corgentin, our lead pre-clinical product candidate, is a next-generation DNA-based therapeutic based on myocardial produced insulin-like growth factor-I (ad5IGF-I) which could be developed for administration in an acute care setting by interventional cardiologists as a treatment for heart attack patients immediately following percutaneous coronary intervention. Corgentin is designed to enhance myocardial healing in and around the infarct zone when used as an adjunct to existing vascular-directed pharmacologic and interventional therapies. To further confirm the utility of the Corgentin approach and establish its commercialization potential, we are planning additional pre-clinical studies in the porcine acute myocardial infarction model, closely mimicking the clinical setting. If confirmatory, we may seek to initiate clinical studies on our own or with a corporate development partner.

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***Genvascor [Ad5eNOS]***. Genvascor is a pre-clinical, DNA-based, endothelial nitric oxide synthase (eNOS) therapeutic. This product candidate is being designed to induce production of nitric oxide directed at mediating the effects of multiple growth factors to enhance neovascularization and increased blood flow for the treatment of patients with critical limb ischemia due to advanced peripheral vascular disease. We may seek to develop additional pre-clinical information through sponsored studies and, if confirmatory, we may consider the further development of Genvascor either alone or through a corporate collaboration.

### **Innercool Therapies**

Our InnerCool Therapies subsidiary is focused on the emerging field of temperature modulation or therapeutic hypothermia, which is designed to rapidly and controllably cool the body in order to reduce cell death and damage following acute ischemic events such as cardiac arrest or stroke, and to potentially lessen or prevent associated injuries such as adverse neurological outcomes. InnerCool's Celsius Control System has received FDA 510(k) clearance for use in inducing, maintaining and reversing mild hypothermia in neurosurgical patients, both in surgery and in recovery or intensive care. The system has also received FDA clearance for use in cardiac patients in order to achieve or maintain normal body temperatures during surgery and in recovery/intensive care, and as an adjunctive treatment for fever control in patients with cerebral infarction and intracerebral hemorrhage. InnerCool has also received a CE mark allowing the Celsius Control System to be marketed in the European Community, and a TGA approval allowing the system to be marketed in Australia.

Studies for additional indications with InnerCool's Celsius Control System are expected to be conducted in collaboration with the National Institutes of Health and other collaborating institutions. Potential future applications of the technology include endovascular cooling for cardiac arrest, acute ischemic stroke and myocardial infarction (heart attack), and acute traumatic injury. We plan to accelerate the commercialization of the Celsius Control System and broaden and expand its temperature modulation technology into other medical indications and applications. Since its acquisition by Cardium, InnerCool's sales force has been expanded, a new cGMP manufacturing facility has been secured to increase production capabilities, and a next-generation console for the Celsius Control System have been developed and a new external temperature modulation system are both being developed for planned launches in mid-2007. InnerCool is also in the process of finalizing a new external temperature modulation system, which is designed to provide a complementary tool for use in less-acute patients and in clinical settings that do not require very rapid cooling or re-warming, or which are best suited to prolonged temperature management. Both the new Celsius Control System and the new external temperature modulation system are expected to be launched in mid-2007.

### **Tissue Repair Company**

Excellerate™ is the lead product candidate of the Tissue Repair Company, our wholly-owned subsidiary. Excellerate is a DNA-activated collagen gel for topical treatment formulated with an adenovector delivery carrier encoding human platelet-derived growth factor-B (PDGF-B) and is designed to stimulate angiogenesis and granulation tissue formation through the recruitment and proliferation of chemotactic cells such as monocytes and fibroblasts, which are necessary for the stimulation of a variety of wound healing processes. Excellerate is initially being developed as a single administration for the treatment of non-healing, neuropathic diabetic foot ulcers. Based on the prior pre-clinical and toxicology database, and results from the Phase 1/2 clinical study, we anticipate that Excellerate may be advanced into a randomized, double-blind, placebo-controlled, multi-center Phase 2b clinical study commencing in the second half of 2007.

Excellerate is based on Tissue Repair Company's Gene Activated Matrix™ technology, which is a technology designed to provide a therapeutic level of protein synthesis at a particular site in the body and can be used in soft tissue such as skin, ligament, tendons and cartilage, as well as hard tissue such as bone. The technology is distinctive in that it is an immobilized form of local gene delivery that allows for control of gene uptake. Gene Activated Matrix technology consists of a biocompatible matrix comprising a gene or DNA vector encoding a growth factor or other therapeutic protein. Other potential applications of Gene Activated Matrix technology include therapeutic angiogenesis (cardiovascular ischemia, peripheral arterial disease) and orthopedic products, including hard tissue (bone) and soft tissue (ligament, tendon, cartilage) repair.

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### **Corporate Information**

Our principal executive offices are located at 3611 Valley Centre Drive, Suite 525, San Diego, California 92130, and our telephone number is (858) 436-1000. Our website is located at [www.cardiumthx.com](http://www.cardiumthx.com). Information on our website is not part of this prospectus.

### **RISK FACTORS**

*You should carefully consider the risks described below, as well as the other information in this prospectus, when evaluating our business and future prospects. If any of the following risks actually occur, our business, financial condition and results of operations could be seriously harmed. In that event, the market price of our common stock could decline and you could lose all or a portion of the value of your investment in our common stock.*

#### ***Risks Related to Our Business and Industry***

***We are a development stage company formed in December 2003. We have incurred losses since inception and expect to incur significant net losses in the foreseeable future and may never become profitable.***

We have sustained operating losses to date and will likely continue to sustain losses as we seek to accelerate our product development efforts. We expect these losses to be substantial in the early years of our operations because our product development and other costs, including significant amounts we expect to spend on development activities and clinical trials for Generx , Excellerate and other product candidates, cannot be offset by our limited revenues during our development stage. As of December 31, 2006, our accumulated deficit was approximately \$24 million, and our cash equivalents were approximately \$5.9 million. To date, we have generated limited revenues, consisting of revenues from sales of our InnerCool Celsius Control System and associated disposables, as well as interest income. A large portion of our expenses are fixed, including expenses related to facilities, equipment, contractual commitments and personnel. As a result, we expect our net losses from operations to continue for at least the next five years. Our ability to generate additional revenues and potential to become profitable will depend largely on our ability, alone or with potential collaborators, to efficiently and successfully complete the development of our product candidates, successfully complete pre-clinical and clinical tests, obtain necessary regulatory approvals, and manufacture and market our products. There can be no assurance that any such events will occur or that we will ever become profitable. Even if we do achieve profitability, we cannot predict the level of such profitability. If we sustain losses over an extended period of time, we may be unable to continue our business.

***Our business prospects are difficult to evaluate because we are a new company and are developing complex and novel medical products.***

Since we have a short operating history and our product candidates rely on complex technologies, it may be difficult for you to assess our growth, partnering and earnings potential. It is likely we will face many of the difficulties that new technology companies often face. These include, among others: limited financial resources; developing, testing and marketing new products for which a market is not yet established and may never become established; challenges related to the development, approval and acceptance of a new technology or product; delays in reaching our goals; lack of substantial revenues and cash flow; high product development costs; competition from larger, more established companies; and difficulty recruiting qualified employees for management and other positions. We will likely face these and other difficulties in the future, some of which may be beyond our control. If we are unable to successfully address these difficulties as they arise, our future growth and earnings will be negatively affected. We cannot be certain that our business strategies will be successful or that we will successfully address any problems that may arise.



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***We will need substantial additional capital to develop our products and for our future operations. If we are unable to obtain such funds when needed, we may have to delay, scale back or terminate our product development or our business.***

Conducting the costly and time consuming research, pre-clinical and clinical testing necessary to obtain regulatory approvals and bring our products to market will require a commitment of substantial funds in excess of our current capital. Our future capital requirements will depend on many factors, including, among others: the progress of our current and new product development programs; the progress, scope and results of our pre-clinical and clinical testing; the time and cost involved in obtaining regulatory approvals; the cost of manufacturing our products and product candidates; the cost of prosecuting, enforcing and defending against patent claims and other intellectual property rights; competing technological and market developments; and our ability and costs to establish and maintain collaborative and other arrangements with third parties to assist in potentially bringing our products to market.

We will need to raise substantial additional capital to fund our future operations. We cannot be certain that additional financing will be available on acceptable terms, or at all. In recent years, it has been difficult for companies to raise capital due to a variety of factors, which may or may not continue. To the extent we raise additional capital through the sale of equity securities or we issue securities in connection with another transaction, the ownership position of existing stockholders could be substantially diluted. If additional funds are raised through the issuance of preferred stock or debt securities, these securities are likely to have rights, preferences and privileges senior to our common stock and may involve significant fees, interest expense, restrictive covenants and the granting of security interests in our assets. Fluctuating interest rates could also increase the costs of any debt financing we may obtain. Raising capital through a licensing or other transaction involving our intellectual property could require us to relinquish valuable intellectual property rights and thereby sacrifice long term value for short-term liquidity.

Our failure to successfully address ongoing liquidity requirements would have a substantially negative impact on our business. If we are unable to obtain additional capital on acceptable terms when needed, we may need to take actions that adversely affect our business, our stock price and our ability to achieve cash flow in the future, including possibly surrendering our rights to some technologies or product opportunities, delaying our clinical trials or curtailing or ceasing operations.

***We acquired the assets and business of InnerCool Therapies, Inc. in March 2006 and rights to develop the Excellerate product candidate of the Tissue Repair Company in August 2006 and may, in the future, pursue acquisitions of other companies or product rights that, if not successful, could adversely affect our business, financial condition and results of operations.***

On March 8, 2006, we completed our acquisition of the assets and business of InnerCool Therapies, Inc., a medical technology company focused on the emerging field of therapeutic hypothermia. On August 11, 2006, we acquired rights to develop the Excellerate product candidate of the Tissue Repair Company, a medical technology company focused on the development of growth factor therapeutics for the potential treatment of chronic wounds such as dermal ulcers. These businesses are subject to all of the operational risks that can affect medical technology companies, including those related to regulatory approvals and clinical studies, acceptance of technology, competing technology, intellectual property rights, profitability, suppliers and third party collaborators, adverse publicity, litigation, and retention of key personnel.

In the future, we may pursue additional acquisitions of other companies, technologies or products. Acquisitions of businesses or product rights, including the InnerCool and Tissue Repair Company transactions, involve numerous risks, including:

our limited experience in evaluating businesses and product opportunities and completing acquisitions;

the use of our existing cash reserves or the need to obtain additional financing to pay for all or a portion of the purchase price of such acquisitions and to support the ongoing operations of the businesses acquired;

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the potential need to issue convertible debt, equity securities, stock options and stock purchase warrants to complete an acquisition, which would dilute our stockholders and could adversely affect the market price of our common stock;

potential difficulties related to integrating the technology, products, personnel and operations of the acquired company;

requirements of significant capital infusions in circumstances under which the acquired business, its products and/or technologies may not generate sufficient revenue or any revenue to offset acquisition costs or ongoing expenses;

entering markets in which we have no or limited prior direct experience and where competitors have stronger market or intellectual property positions;

disruptions to our ongoing business, diversion of resources, increases in our expenses and distraction of management's attention from the normal daily operations of our business;

the potential to negatively impact our results of operations because an acquisition may require us to incur large one-time charges to earnings, amortize or write down amounts related to goodwill and other intangible assets, or incur or assume substantial debt or liabilities, or cause adverse tax consequences, substantial depreciation or deferred compensation charges;

an uncertain sales and earnings stream, or greater than expected liabilities and expenses, associated with the acquired company, product or product rights;

failure to operate effectively and efficiently as a combined organization utilizing common information and communication systems, operating procedures, financial controls and human resources practices;

potential loss of key employees of the acquired company; and

disruptions to our relationships with existing collaborators who could be competitive with the acquired business.

There can be no assurance that our InnerCool or Tissue Repair transactions, or other transactions that we may pursue, will ultimately prove successful. If we pursue an acquisition but are not successful in completing it, or if we complete an acquisition but are not successful in integrating the acquired company's employees, products or operations successfully, our business, financial condition or results of operations could be harmed.

***We are an early stage company and, other than InnerCool's Celsius Control System and related disposables that are approved for limited uses, we have no other products available for sale or use. Our product candidates require additional research, development, testing, and regulatory approvals before marketing. We may be unable to develop, obtain regulatory approval or market any of our product candidates or expand the market of our existing products and technology. If our product candidates are delayed or fail, our business and stockholder value will be negatively impacted, and we may have to curtail or cease our operations.***

We are in the early stage of product development and, other than InnerCool's Celsius Control System and related disposables that are approved only for limited uses, we currently do not sell any other products and may not have any other products commercially available for several years, if at all. Our product candidates, and the potential expansion of our therapeutic hypothermia products into other medical indications and applications, require additional research and development, clinical testing and regulatory clearances before we can market them. To our knowledge, the U.S. Food and Drug Administration, or FDA, has not yet approved any gene therapy or similar product and there can be no assurance that it will. There are many reasons that our products and product candidates may fail or not advance beyond clinical testing, including the possibility that:

our products and product candidates may be ineffective, unsafe or associated with unacceptable side effects;

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our product candidates may fail to receive necessary regulatory approvals or otherwise fail to meet applicable regulatory standards;

our product candidates may be too expensive to develop, manufacture or market;

physicians, patients, third-party payers or the medical community in general may not accept or use our products;

our potential collaborators may withdraw support for or otherwise impair the development and commercialization of our products or product candidates;

other parties may hold or acquire proprietary rights that could prevent us or our potential collaborators from developing or marketing our products or product candidates; or

others may develop equivalent, superior or less expensive products.

In addition, our product candidates are subject to the risks of failure inherent in the development of biologics, gene therapy and other products based on innovative technologies. As a result, we are not able to predict whether our research, development and testing activities will result in any commercially viable products or applications. If our product candidates are delayed or we fail to successfully develop and commercialize our product candidates, or if we are unable to expand the market of our existing products or related technology, our business, financial condition or results of operations will be negatively affected, and we may have to curtail or cease our operations.

***We may experience delays in our clinical trials that could adversely affect our business, financial results and commercial prospects.***

To obtain regulatory approvals for new products or to expand indications for existing ones, we must, among other things, initiate and successfully complete multiple clinical trials demonstrating to the satisfaction of the FDA that our product candidates are sufficiently safe and effective for a particular indication. We are in ongoing discussions with the FDA regarding clinical trials of our Generx product candidate, and expect to soon be in discussions regarding our recently acquired Excellerate product candidate. While we expect both product candidates to be in clinical trials in 2007, there is no assurance that they will be since the timing of clinical trials is dependent on, among other things, FDA reviews, clinical site approvals, successful manufacturing of clinical materials, sufficient funding and other factors outside of our control. Furthermore, there can be no assurance that our clinical trials will in fact demonstrate to the satisfaction of the FDA and others that our products are sufficiently safe or effective.

The FDA or we may also restrict or suspend our clinical trials at any time if either believes that we are exposing the subjects participating in the trials to unacceptable health risks. We expect to continue to rely on third party clinical investigators at medical institutions and healthcare facilities to conduct and monitor our clinical trials, and, as a result, we may face additional delaying factors outside of our control. Product development costs to us and our potential collaborators will increase, and our business may be negatively impacted, if we experience delays in testing or approvals or if we need to perform more or larger clinical trials than planned, for reasons such as the following:

the FDA or other health regulatory authorities, or institutional review boards, do not approve a clinical study protocol or place a clinical study on hold;

suitable patients do not enroll in a clinical study in sufficient numbers or at the expected rate, or data is adversely affected by trial conduct or patient drop out;

patients experience serious adverse events, including adverse side effects of our drug candidate or device;

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patients die during a clinical study for a variety of reasons that may or may not be related to our products, including the advanced stage of their disease and medical problems;

patients in the placebo or untreated control group exhibit greater than expected improvements or fewer than expected adverse events;

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third-party clinical investigators do not perform the clinical studies on the anticipated schedule or consistent with the clinical study protocol and good clinical practices, or other third-party organizations do not perform data collection and analysis in a timely or accurate manner;

service providers, collaborators or co-sponsors do not adequately perform their obligations in relation to the clinical study or cause the study to be delayed or terminated;

regulatory inspections of manufacturing facilities, which may, among other things, require us or a co-sponsor to undertake corrective action or suspend the clinical studies;

the interim results of the clinical study are inconclusive or negative;

the clinical study, although approved and completed, generates data that is not considered by the FDA or others to be sufficient to demonstrate safety and efficacy; and

changes in governmental regulations or administrative actions affect the conduct of the clinical trial or the interpretation of its results. Significant delays may adversely affect our financial results and the commercial prospects for our product candidates and delay our ability to become profitable.

***If we cannot successfully complete the clinical trial process for our product candidates, or products for which we seek expanded approvals, then we will not be able to market them. Even successful clinical trials may not result in a marketable product and may not be predictive of a product's safety or efficacy in a larger and more diverse patient population.***

Our Celsius Control System acquired from InnerCool Therapies has received FDA 510(k) clearance for certain specified indications but we may elect to pursue other indications, which would generally require that collaborators or we conduct additional clinical studies and/or testing. Our Generx and Excellerate product candidates are currently in the clinical stage. Other product candidates are in the pre-clinical stage and there can be no assurance they will ever advance to clinical trials. For product candidates that advance to clinical testing, we cannot be certain that a collaborator or we will successfully complete the clinical trials necessary to receive regulatory product approvals. This process is lengthy, unpredictable and expensive. To obtain regulatory approvals, a collaborative partner or we must ultimately demonstrate to the satisfaction of the FDA and others that our product candidates are sufficiently safe and effective for their proposed use.

Many factors, known and unknown, can adversely impact clinical trials and the ability to evaluate a product's safety and efficacy. Such factors may have a negative impact on our business by making it difficult to advance product candidates or by reducing or eliminating their potential or perceived value. Further, if we are forced to contribute greater financial and clinical resources to a study, valuable resources will be diverted from other areas of our business.

Clinical trials for products such as ours are often conducted with patients who have more advanced forms of a particular disease. For example, in clinical trials for our lead product candidate Generx, we expect to study patients who are not only suffering from severe forms of heart disease but are also older and much more likely to develop cancers and other serious adverse conditions. During the course of treatment, these patients could die or suffer other adverse events for reasons that may or may not be related to the proposed product being tested. Our clinical trials may also be adversely impacted by patient deaths or problems that occur in other trials. However, even if unrelated to our product, such events can nevertheless adversely impact our clinical trials. As a result, our business and ability to ultimately develop and market the products and obtain revenues would suffer.

Deaths and other adverse events that occur in the conduct of clinical trials may also result in an increase in governmental regulations or litigation, and could result in delays or halts being imposed upon clinical trials, including our own. In addition, patients involved in clinical trials such as ours often have unknown as well as known



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health risks and pre-existing conditions. An adverse event may therefore appear to have been caused or exacerbated by the administration of study product, even if it was not actually related. Such consequences can also increase the risk that any potential adverse event in our trial could give rise to claims for damages against us, or could cause further delays or halt our clinical trial, any of which results would negatively impact us. In addition, fears regarding the potential consequences of gene therapy trials or the conduct of such trials could dissuade investigators or patients from participating in our trials, which could substantially delay or prevent our product development efforts.

Even promising results in pre-clinical studies and initial clinical trials do not ensure successful results in later clinical trials, which test broader human use of our products. Many companies in our industry have suffered significant setbacks in advanced clinical trials, despite promising results in earlier trials. Even successful clinical trials may not result in a marketable product or be indicative of the efficacy or safety of a product in the broader patient population. Many factors or variables could affect the results of clinical trials and cause them to appear more promising than they may otherwise be. Product candidates that successfully complete clinical trials could ultimately be found to be unsafe or ineffective or to have poorer risk to benefit or cost to benefit profiles as compared to other potential products or therapies.

Our ability to complete clinical trials depends on many factors, including obtaining adequate clinical supplies and having a sufficient rate of patient recruitment. For example, patient recruitment is a function of many factors, including: the size of the patient population; the proximity of patients to clinical sites; the eligibility criteria for the trial; the perceptions of investigators and patients regarding safety; and the availability of other treatment options. Even if patients are successfully recruited, we cannot be sure they will complete the treatment process. Delays in patient enrollment or treatment in clinical trials may result in increased costs, program delays, or failure, any of which can substantially affect our business or perceived value.

In addition, DNA-based therapies such as those being developed by us are relatively new and are only beginning to be tested in humans. Regulatory authorities may require us or our potential collaborators to demonstrate that our products are improved treatments relative to other therapies or may significantly modify the requirements governing gene therapies, which could result in regulatory delays or rejections that negatively impact our business. Compliance with these regulatory requirements is also time consuming and expensive. If we fail to comply with regulatory requirements, either before approval or in marketing our products after approval, we could be subject to regulatory or judicial enforcement actions. These actions could result in withdrawal of existing approvals, product recalls, injunctions, civil penalties, criminal prosecution, and enhanced exposure to product liabilities.

Ethical, social and legal concerns about gene therapy and genetic research could also result in additional regulations restricting or prohibiting our products and processes we may use. More restrictive government regulations or negative public opinion may have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates.

With respect to markets in other countries, we or a partner will also be subject to regulatory requirements governing clinical trials in those countries. Even if we complete clinical trials, we may not be able to submit a marketing application. If we submit an application, the regulatory authorities may not review or approve it in a timely manner, if at all.

### ***Our technologies and product candidates may have unacceptable side effects that could delay or prevent product approval.***

Possible side effects of therapeutic technologies may be serious and life threatening. The occurrence of any unacceptable side effects during or after pre-clinical and clinical testing of our product candidates, or the perception or possibility that our products cause or could cause such side effects, could delay or prevent approval of our products and negatively impact our business. For example, possible serious side effects of viral vector-based gene transfer could potentially include viral or gene product toxicity resulting in inflammation or other injury to the heart or other parts of the body. In addition, the development or worsening of cancer in a patient could potentially be a perceived or actual side effect of gene therapy technologies such as our own. Furthermore, there is a possibility of side effects or decreased effectiveness associated with an immune response toward any viral vector or gene used in gene therapy. The possibility of such response may increase if there is a need to deliver the viral vector more than once.



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*Even if approved for marketing, our technologies and product candidates are relatively novel and unproven and they may fail to gain market acceptance.*

Our ongoing business and future depends on the success of our technologies and product candidates. Gene-based therapy and endovascular temperature control therapy are new and rapidly evolving medical approaches that have not been shown to be effective on a widespread basis. Biotechnology and pharmaceutical companies have successfully developed and commercialized only a limited number of biologic-based products to date and no gene therapy has yet been successfully commercialized. Our product candidates, and the technology underlying them, are new and unproven and there is no guarantee that health care providers or patients will be interested in our products even if they are approved for use. Our success will depend in part on our ability to demonstrate sufficient clinical benefits, reliability, safety and cost effectiveness of our product candidates and technology relative to other approaches, as well as on our ability to continue to develop our product candidates to respond to competitive and technological changes. If the market does not accept our products or product candidates, when and if we are able to commercialize them, then we may never become profitable. It is difficult to predict the future growth of our business, if any, and the size of the market for our product candidates because the market and technology are continually evolving. There can be no assurance that our technologies and product candidates will prove superior to technologies and products that may currently be available or may become available in the future or that our technologies or research and development activities will result in any commercially profitable products.

*We may not successfully establish and maintain collaborative and licensing arrangements, which could adversely affect our ability to develop and commercialize our product candidates.*

Our strategy for the development, testing, manufacturing and commercialization of our product candidates generally relies on establishing and maintaining collaborations with corporate partners, licensors and other third parties. For example, we have licenses from New York University and the University of California relating to the use and delivery of our Generx product candidates for the treatment of vascular disease, as well as a relationship with Schering AG Group (Germany) regarding the transfer of information about certain manufacturing and regulatory matters concerning our product candidates. We may not be able to maintain or expand these licenses and collaborations or establish additional licensing and collaboration arrangements necessary to develop and commercialize our product candidates. Even if we are able to maintain or establish licensing or collaboration arrangements, these arrangements may not be on favorable terms and may contain provisions that will restrict our ability to develop, test and market our product candidates. Any failure to maintain or establish licensing or collaboration arrangements on favorable terms could adversely affect our business prospects, financial condition or ability to develop and commercialize our product candidates.

We expect to rely at least in part on third party service providers and collaborators to perform a number of activities relating to the development and commercialization of our product candidates, including the manufacture of product materials, the design and conduct of clinical trials, and potentially the obtaining of regulatory approvals and the marketing and distribution of any successfully developed products. Our collaborative partners also may have or acquire rights to control aspects of our product development and clinical programs. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate. In addition, if any of these collaborative partners withdraw support for our programs or product candidates or otherwise impair their development, our business could be negatively affected. To the extent we undertake any of these activities internally, our expenses may increase.

Our success hinges on the proper and effective performance of our service providers and collaborators of their responsibilities under their arrangements with us. Our existing or potential collaborators may not perform their obligations in a timely fashion or in a manner satisfactory to us. We and our present and future collaborators may fail to develop or effectively commercialize products covered by our present and future collaborations if, among other things:

we do not achieve our objectives under our collaboration agreements;

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we or our collaborators are unable to obtain patent protection for the products or proprietary technologies we develop in our collaborations;

we are unable to manage multiple simultaneous product discovery and development collaborations;

our collaborators become competitors of ours or enter into agreements with our competitors;

we or our collaborators encounter regulatory hurdles that prevent commercialization of our products; or

we develop products and processes or enter into additional collaborations that conflict with the business objectives of our other collaborators.

In addition, conflicts may arise with our collaborators, such as conflicts concerning the interpretation of clinical data, the achievement of milestones, the interpretation of financial provisions or the ownership of intellectual property developed during the collaboration. If any conflicts arise with our existing or future collaborators, they may act in their self-interest, which may be adverse to our best interest. If we or our collaborators are unable to develop or commercialize products, or if conflicts arise with our collaborators, we will be delayed or prevented from developing and commercializing products, which will harm our business and financial results.

***We will rely on third parties to manufacture our product candidates. There can be no guarantee that we can obtain sufficient and acceptable quantities of our product candidates on acceptable terms, which may delay or impair our ability to develop, test and market such products.***

Our business strategy relies on third parties to manufacture and produce our products and product candidates and the catheters used to deliver the products in accordance with good manufacturing practices established by the FDA and other regulators. For example, we entered into a Production Service Agreement with Molecular Medicine Bioservices, Inc. pursuant to which Molecular Medicine agreed to manufacture our lead product candidate, Generx, for late-stage clinical development. These third party manufacturers are subject to extensive government regulation and must receive FDA approval before they can produce clinical material or commercial product.

Our products and product candidates may be in competition with other products for access to these facilities and may be subject to delays in manufacture if third parties give other products greater priority than our products. These third parties also may not deliver sufficient quantities of our products, manufacture our products in accordance with specifications, or comply with applicable government regulations. Successful large-scale manufacturing of gene-based therapy products has been accomplished by very few companies, and it is anticipated that significant process development changes will be necessary before commercializing and manufacturing any of our biologic product candidates. Additionally, if the manufactured products fail to perform as specified, our business and reputation could be severely impacted.

If any manufacturing agreement is terminated or any third party service provider or collaborator experiences a significant problem that could result in a delay or interruption in the supply of product materials to us, there are very few contract manufacturers who currently have the capability to produce our product candidates. There can be no assurance that manufacturers on whom we depend will be able to successfully produce our products or product candidates on acceptable terms, or on a timely or cost-effective basis, or in accordance with our product specifications and applicable FDA or other governmental regulations. We must have sufficient and acceptable quantities of our product materials to conduct our clinical trials and to market our product candidates, if and when such products have been approved by the FDA for marketing. If we are unable to obtain sufficient and acceptable quantities of our product material, we may be required to delay the clinical testing and marketing of our products, which would negatively impact our business.

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***If we do not comply with applicable regulatory requirements in the manufacture and distribution of our products and product candidates, we may incur penalties that may inhibit our ability to commercialize our products and adversely affect our financial condition and ability to become profitable.***

Our failure or the failure of our potential collaborators or third party manufacturers to comply with applicable FDA or other product-related regulatory requirements including manufacturing, quality control, labeling, safety surveillance, promoting and reporting may result in criminal prosecution, civil penalties, recall or seizure of our products, total or partial suspension of production or an injunction, as well as other regulatory action against our products, product candidates or us. Discovery of previously unknown problems with a product, supplier, manufacturer or facility may result in restrictions on the sale of our products, including a withdrawal of such products from the market. The occurrence of any of these events would negatively impact our business and results of operations.

***If we are unable to create and maintain sales, marketing and distribution capabilities or enter into agreements with third parties to perform those functions, we will not be able to commercialize our product candidates or market our products.***

We currently have limited sales, marketing and distribution capabilities in connection with our InnerCool products and none with respect to our other product candidates, which are not yet approved for marketing. To commercialize our other product candidates, if and when such products have been approved and are ready for marketing, we expect either to collaborate with third parties to perform these functions or develop them internally.

We have little experience in developing, training or managing a sales force and will incur substantial additional expenses for any products that we market directly. Developing a marketing and sales force is also time consuming and could delay the launch of new products or expansion of existing product sales. We expect that we will need to develop additional marketing and sales personnel, and/or work with outside providers, to achieve increased sales of our InnerCool products. In addition, we will compete with many companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts may be unable to compete successfully against these companies, in which event our business prospects may suffer.

***We face intense and increasing competition and must cope with rapid technological change, which may adversely affect our financial condition and/or our ability to successfully commercialize and/or market our products and product candidates.***

Our competitors and potential competitors include large pharmaceutical and medical device companies and more established biotechnology companies. These companies have significantly greater financial and other resources and greater expertise than us in research and development, manufacturing, pre-clinical and clinical testing, obtaining regulatory approvals and marketing. This may make it easier for them to respond more quickly than us to new or changing opportunities, technologies or market needs. Small companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical companies or through acquisition or development of intellectual property rights. Our larger competitors may be able to devote greater resources to research and development, marketing, distribution and other activities that could provide them with a competitive advantage. Many of these competitors operate large, well-funded research and development programs and have significant products approved or in development. Our potential competitors also include academic institutions, governmental agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for product and clinical development and marketing.

We are engaged in DNA-based therapies and temperature control therapy. Our industry is characterized by extensive research and development, rapid technological change, frequent innovations and new product introductions, and evolving industry standards. Existing products and therapies to treat vascular and cardiovascular disease, including drugs and surgical procedures, as well as competitive approaches to temperature control therapy such as those being developed by Alsius Corporation, Radiant Medical, Medivance, Gaymar Industries and Cincinnati Sub-Zero, will compete directly or indirectly with the products that we are seeking to develop and market. In addition, our competitors may develop more effective or more affordable products, or achieve earlier patent protection or product commercialization and market penetration than us. As these competitors develop their technologies, they may develop proprietary positions that prevent us from successfully commercializing our future products. To be successful, we must be able to adapt to rapidly changing technologies by continually enhancing our products and introducing new products. If we are unable to adapt, products and technologies developed by our competitors may render our products and product candidates uneconomical or obsolete, and we may not be successful in marketing

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our products and product candidates against competitors. We may never be able to capture and maintain the market share necessary for growth and profitability and there is no guarantee we will be able to compete successfully against current or future competitors.

***Changes and reforms in the health care system or reimbursement policies may adversely affect the sale of our products and future products or our ability to obtain an adequate level of reimbursement or acceptable prices for our products or future products.***

Other than InnerCool's Celsius Control System and associated disposables, we currently have no products approved for marketing. Our ability to earn sufficient returns on our products and future products, if and when such products are approved and ready for marketing, will depend in part on the extent to which reimbursement for our products and related treatments will be available from government health administration authorities, private health coverage insurers, managed care organizations and other third-party payers. If we fail to obtain appropriate reimbursement, it could prevent us from successfully commercializing and marketing our products and future products.

There have been and will continue to be efforts by governmental and third-party payers to contain or reduce the costs of health care through various means, including limiting coverage and the level of reimbursement. We expect that there will continue to be a number of legislative proposals to implement government controls and other reforms to limit coverage and reimbursement. Additionally, third-party payers, including Medicare, are increasingly challenging the price of medical products and services and are limiting the reimbursement levels offered to consumers for these medical products and services. If purchasers or users of our products or future products are not able to obtain adequate reimbursement from third-party payers for the cost of using the products, they may forego or reduce their use. Significant uncertainty exists as to the reimbursement status of newly approved health care products, including gene therapy and therapeutic hypothermia treatments, and whether adequate third-party coverage will be available. The announcement or considerations of these proposals or reforms could impair our ability to raise capital and negatively affect our business.

***If we are unable to attract and retain key personnel and advisors, it may adversely affect our ability to obtain financing, pursue collaborations or develop or market our products or product candidates.***

Our future success depends on our ability to attract, retain and motivate highly qualified management and scientific and regulatory personnel and advisors, as well as production, marketing and sales personnel in connection with our InnerCool products. The loss of any of our senior management team, in particular Christopher J. Reinhard, our Chairman of the Board, Chief Executive Officer, President and Treasurer, Tyler M. Dylan, our director, Chief Business Officer, General Counsel, Executive Vice President and Secretary, and Dennis M. Mulroy, our Chief Financial Officer, or our vice presidents, or the operating officers of our subsidiaries, could harm our business.

To pursue our business strategy, we will need to hire or otherwise engage qualified scientific personnel and managers, including personnel with expertise in clinical trials, government regulation, manufacturing, marketing and other areas. Competition for qualified personnel is intense among companies, academic institutions and other organizations. If we are unable to attract and retain key personnel and advisors, it may negatively affect our ability to successfully develop, test, commercialize and market our products and product candidates.

***Our facilities are located in or near seismic zones, and an earthquake or other natural disaster or resource shortage could delay our research and development efforts and adversely affect our business.***

Our headquarters and research and development facilities in San Diego, California, and our third party manufacturing facilities in Carlsbad, California, are both located in or near seismic zones, and there is a constant possibility that an earthquake or other natural disaster or resource shortage could be disruptive to our operations and result in delays in our research and development efforts. In the event of a natural or other disaster such as earthquake, fire, flood or terrorist attack, if our facilities or the equipment in our facilities, or our clinical supplies, are significantly damaged or destroyed, we may not be able to rebuild or relocate our facility or replace any damaged equipment, records or clinical supplies in a timely manner and our business, financial condition and results of operations could be materially and adversely affected.

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*We will use hazardous and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.*

Our products and processes will involve the controlled storage, use and disposal of certain hazardous and biological materials and waste products. We and our suppliers and other collaborators are subject to federal, state and local regulations governing the use, manufacture, storage, handling and disposal of materials and waste products. Even if we and these suppliers and collaborators comply with the standards prescribed by law and regulation, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated. In the event of an accident, we could be held liable for any damages that result, and any liability could exceed the limits or fall outside the coverage of any insurance we may obtain and exceed our financial resources. We may not be able to maintain insurance on acceptable terms, or at all. We may incur significant costs to comply with current or future environmental laws and regulations.

*To the extent we enter markets outside the United States, our business will be subject to political, economic, legal and social risks in those markets, which could adversely affect our business.*

There are significant regulatory and legal barriers in markets outside the United States that we must overcome to the extent we enter or attempt to enter markets in countries other than the United States. We will be subject to the burden of complying with a wide variety of national and local laws, including multiple and possibly overlapping and conflicting laws. We also may experience difficulties adapting to new cultures, business customs and legal systems. Any sales and operations outside the United States, including those associated with our InnerCool products, would be subject to political, economic and social uncertainties including, among others:

changes and limits in import and export controls;

increases in custom duties and tariffs;

changes in currency exchange rates;

economic and political instability;

changes in government regulations and laws;

absence in some jurisdictions of effective laws to protect our intellectual property rights; and

currency transfer and other restrictions and regulations that may limit our ability to sell certain products or repatriate profits to the United States.

Any changes related to these and other factors could adversely affect our business to the extent we enter markets outside the United States.

### ***Risks Related to Our Intellectual Property and Potential Litigation***

***If our products and product candidates are not effectively protected by valid, issued patents or if we are not otherwise able to protect our proprietary information, or if our right to use intellectual property that we license from third parties is terminated or adversely affected, our financial condition, operations or ability to develop and commercialize our product candidates may be harmed.***

The success of our operations will depend in part on our ability and that of our licensors to: obtain patent protection for our gene therapy, therapeutic genes and/or gene-delivery methods, temperature control devices and procedures, and other methods or components on which we rely both in the United States and in other countries with substantial markets; defend patents once obtained; maintain trade secrets and operate without infringing upon the patents and proprietary rights of others; and obtain appropriate licenses upon reasonable terms to patents or

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proprietary rights held by others that are necessary or useful to us in commercializing our technology, both in the United States and in other countries with substantial markets.

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Our business substantially relies on our own or in-licensed intellectual property related to various technologies that are material to our products and processes. We depend on our and our licensors' abilities to successfully prosecute and enforce the patents, file patent applications and prevent infringement of those patents and patent applications. The licenses and other intellectual property rights we acquire may or may not provide us with exclusive rights. To the extent we do not have exclusive rights, others may license the same technology and may develop the technology more successfully or may develop products similar to ours and that compete with our products. Even if we are provided with exclusive rights, the scope of our rights under our licenses may be subject to dispute and termination or reduction by our licensors or third parties. Our licenses also contain milestones that we must meet and/or minimum royalty or other payments that we must make to maintain the licenses. There is no assurance that we will be able to meet such milestones and/or make such payments. Our licenses may be terminated if we fail to meet applicable milestones or make applicable payments.

***If we are not able to maintain adequate patent protection for our products and product candidates, we may be unable to prevent our competitors from using our technology or technology that we license.***

The patent positions of the technologies being developed by us and our collaborators involve complex legal and factual uncertainties. As a result, we cannot be certain that we or our collaborators will be able to obtain adequate patent protection for our products or product candidates. There can be no assurance that (i) any patents will be issued from any pending or future patent applications of ours or our collaborators; (ii) the scope of any patent protection will be sufficient to provide us with competitive advantages; (iii) any patents obtained by us or our collaborators will be held valid if subsequently challenged; or (iv) others will not claim rights in or ownership of the patents and other proprietary rights we or our collaborators may hold. Unauthorized parties may try to copy aspects of our products and technologies or obtain and use information we consider proprietary. Policing the unauthorized use of our proprietary rights is difficult. We cannot guarantee that no harm or threat will be made to our or our collaborators' intellectual property. In addition, changes in, or different interpretations of, patent laws in the United States and other countries may also adversely affect the scope of our patent protection and our competitive situation.

Due to the significant time lag between the filing of patent applications and the publication of such patents, we cannot be certain that our licensors were the first to file the patent applications we license or, even if they were the first to file, also were the first to invent, particularly with regards to patent rights in the United States. In addition, a number of pharmaceutical and biotechnology companies and research and academic institutions have developed technologies, filed patent applications or received patents on various technologies that may be related to our operations. Some of these technologies, applications or patents may conflict with our or our licensors' technologies or patent applications. A conflict could limit the scope of the patents, if any, that we or our licensors may be able to obtain or result in denial of our or our licensors' patent applications. If patents that cover our activities are issued to other companies, we may not be able to develop or obtain alternative technology.

Patents issued and patent applications filed internationally relating to gene therapy, temperature control therapy, and other of our technologies are numerous, and we cannot assure you that current and potential competitors or other third parties have not filed or received, or will not file or receive applications in the future for patents or obtain additional proprietary rights relating to products or processes used or proposed to be used by us.

Additionally, there is certain subject matter that is patentable in the United States but not generally patentable outside of the United States. Differences in what constitutes patentable subject matter in various countries may limit the protection we can obtain outside of the United States. For example, methods of treating humans are not patentable in many countries outside of the United States. These and other issues may prevent us from obtaining patent protection outside of the United States, which would have a material adverse effect on our business, financial condition and results of operations.

***We may be subject to costly claims, and, if we are unsuccessful in resolving conflicts regarding patent rights, we may be prevented from developing, commercializing or marketing our products and/ or product candidates.***

There has been, and will likely continue to be, substantial litigation regarding patent and other intellectual property rights in the biotechnology industry. As the biotechnology industry expands and more patents are issued, the risk increases that our processes, technology, products and product candidates may give rise to claims that they infringe

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on the patents of others. Others could bring legal actions against us claiming damages and seeking to stop clinical testing, manufacturing and marketing of the affected product or use of the affected process. Litigation may be necessary to enforce our or our licensors' proprietary rights or to determine the enforceability, scope and validity of the proprietary rights of others. If we become involved in litigation, it could be costly and divert our efforts and resources. In addition, if any of our competitors file patent applications in the United States claiming technology also invented by us or our licensors, we may need to participate in interference proceedings held by the U.S. Patent and Trademark Office to determine priority of invention and the right to a patent for the technology. Like litigation, interference proceedings can be lengthy and often result in substantial costs and diversion of resources.

For example, in connection with our exclusive license to the University of California's technology for cardiovascular gene therapy (filed by Hammond et al., an international application of which was published as WO96/26742), we and our predecessor in interest Collateral Therapeutics have assisted the University of California in an interference proceeding against a patent application filed by Jeffrey Leiden et al. (a U.S. counterpart of international application PCT/US93/11133, which published as WO94/11506). In the interference, which is essentially a contest to determine priority of invention, a panel of Administrative Patent Judges of the U.S. Board of Patent Appeals and Interferences or BPAI issued judgment against the Leiden applicants, ordering that the interference count, which represents the disputed subject matter, be awarded to Hammond, and that Leiden et al. be held not entitled to any patent containing claims corresponding to those in the interference. However, the patent applicant, Arch Development Corporation, which had licensed the technology to Boston Scientific Corporation, subsequently appealed the decision against them. In May 2006, the U.S. Court of Appeals for the Federal Circuit, which hears appeals in U.S. patent cases, refused requests by Arch and Boston Scientific to reverse the prior decision of the BPAI regarding priority of invention. The Federal Circuit also refused requests to remand the case for reconsideration of previously contested matters such as the novelty, nonobviousness or validity of the Hammond patents, and it summarily issued final judgment against the Leiden applicants. Appeals from decisions of the Federal Circuit to the U.S. Supreme Court are rarely granted under such circumstances and were not sought. In a related matter, Collateral Therapeutics, with our assistance, successfully opposed a European counterpart to the Leiden PCT application (EP-B-668913), which led to a decision to revoke the patent grant in Europe. Although the patentee, Arch Development Corporation, subsequently appealed the adverse decision, a ruling following appeal to the European Patent Office's Technical Board of Appeal has now been rendered and the European patent grant to Arch (which had been licensed to Boston Scientific) has now been revoked. If we do not continue to be successful in defending against these and any other adverse claims, we could be compelled to seek licenses from one or more third parties who could be direct or indirect competitors and who might not make licenses available on terms that we find commercially reasonable or at all. In addition, such proceedings, even if decided in our favor, involve lengthy processes, are subject to appeals, and typically result in substantial costs and diversion of resources.

As more potentially competing patent applications are filed, and as more patents are actually issued, in the fields of gene therapy, wound healing, adenoviral vectors or therapeutic hypothermia or in other fields in which we may become involved and with respect to component methods or compositions that we may employ, the risk increases that we or our licensors may be subjected to litigation or other proceedings that claim damages or seek to stop our manufacturing, marketing, product development or commercialization efforts. Even if such patent applications or patents are ultimately proven to be invalid, unenforceable or non-infringed, such proceedings are generally expensive and time consuming and could consume a significant portion of our resources and substantially impair our marketing and product development efforts.

If there were an adverse outcome of any litigation or interference proceeding, we could have a potential liability for significant damages. In addition, we could be required to obtain a license to continue to make or market the affected product or use the affected process, or face an injunction to block our sale or marketing of affected products or use of the affected process. Costs of a license may be substantial and could include up-front payments as well as ongoing royalties. We may not be able to obtain such a license on acceptable terms, or at all, which could substantially impact our business.

***We may not have adequate protection for our unpatented proprietary information, which could adversely affect our competitive position.***

We also rely on trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. However, others may independently develop substantially equivalent



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proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. To protect our trade secrets, we may enter into confidentiality agreements with employees, consultants and potential collaborators. However, these agreements may not provide meaningful protection of our trade secrets or adequate remedies in the event of unauthorized use or disclosure of such information. Likewise, our trade secrets or know-how may become known through other means or be independently discovered by our competitors. Any of these events could prevent us from developing or commercializing our product candidates.

***We face the risk of product liability claims, which could adversely affect our business and financial condition.***

Our marketing and sale of therapeutic hypothermia products as well as our other operations will expose us to product liability risks that are inherent in the testing, manufacturing and marketing of biotechnology and medical device products. Failure to obtain or maintain sufficient product liability insurance or otherwise protect against product liability claims could prevent or delay the commercialization or marketing of our products or product candidates or expose us to substantial liabilities and diversions of resources, all of which can negatively impact our business. Regardless of the merit or eventual outcome, product liability claims may result in withdrawal of product candidates from clinical trials, costs of litigation, damage to our reputation, substantial monetary awards to plaintiffs and decreased demand for products.

Product liability may result from harm to patients using our products, such as a complication that was either not communicated as a potential side effect or was more extreme than communicated. We will require all patients enrolled in our clinical trials to sign consents, which explain various risks involved with participating in the trial. However, patient consents provide only a limited level of protection, and it may be alleged that the consent did not address or did not adequately address a risk that the patient suffered from. Additionally, we will generally be required to indemnify the clinical product manufacturers, clinical trial centers, medical professionals and other parties conducting related activities in connection with losses they may incur through their involvement in the clinical trials. We may not be able to obtain or maintain product liability insurance on acceptable terms or with adequate coverage against potential liabilities.

### ***Risks Related to Our Common Stock***

***The price of our common stock is expected to be volatile and an investment in our common stock could decline substantially in value.***

In light of our small size and limited resources, as well as the uncertainties and risks that can affect our business and industry, our stock price is expected to be highly volatile and can be subject to substantial drops, with or even in the absence of news affecting our business. The following factors, in addition to the other risk factors described in this prospectus, and the potentially low volume of trades in our common stock, may have a significant impact on the market price of our common stock, some of which are beyond our control:

anticipated or unanticipated changes in financial conditions, operating results or the perceived value of our business;

developments concerning any research and development, clinical trials, manufacturing, and marketing efforts or collaborations;

our announcement of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

announcements of technological innovations;

new products or services that we or our competitors offer;

the initiation, conduct and/or outcome of intellectual property and/or litigation matters;

changes in financial or other estimates by securities analysts or other reviewers or evaluators of our business;



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conditions or trends in bio-pharmaceutical or other healthcare industries;

regulatory developments in the United States and other countries;

changes in the economic performance and/or market valuations of other biotechnology and medical device companies;

additions or departures of key personnel;

sales or other transactions involving our common stock; and

global unrest, terrorist activities, and economic and other external factors.

The stock market in general has recently experienced relatively large price and volume fluctuations. In particular, the market prices of securities of smaller biotechnology and medical device companies have experienced dramatic fluctuations that often have been unrelated or disproportionate to the operating results of these companies. Continued market fluctuations could result in extreme volatility in the price of the common stock, which could cause a decline in the value of the common stock. You should also be aware that price volatility may be worse if the trading volume of the common stock remains limited or declines.

***We could be difficult to acquire due to anti-takeover provisions in our charter, our stockholder rights plan and Delaware law.***

Our board of directors has adopted a stockholder rights plan in which preferred stock purchase rights were distributed as a dividend. These provisions may make it more difficult for stockholders to take corporate actions and may have the effect of delaying or preventing a change in control. These provisions also could deter or prevent transactions that stockholders deem to be in their interests. In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. Subject to specified exceptions, this section provides that a corporation may not engage in any business combination with any interested stockholder during the three-year period following the time that such stockholder becomes an interested stockholder. This provision could have the effect of delaying or preventing a change of control of our company. The foregoing factors could reduce the price that investors or an acquirer might be willing to pay in the future for shares of our common stock.

***We have never paid cash dividends on our capital stock and we do not anticipate paying dividends in the foreseeable future.***

We have paid no cash dividends on any of our classes of capital stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any future debt or credit facility may preclude or limit our ability to pay any dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of potential gain for the foreseeable

**SPECIAL NOTE ABOUT FORWARD-LOOKING STATEMENTS**

Certain statements in this prospectus, including information incorporated by reference, are forward-looking statements within the meaning of Section 27A of the 33 Act, Section 21E of the Securities Exchange Act of 1934, as amended ( Exchange Act ), and the Private Securities Litigation Reform Act of 1995. Forward-looking statements reflect current views about future events and financial performance based on certain assumptions. They include opinions, forecasts, intentions, plans, goals, projections, guidance, expectations, beliefs or other statements that are not statements of historical fact. Words such as may, will, should, could, would, expects, plans, believes, anticipates, intends, approximates, predicts, or projects, or the negative or other variation of such words, and similar expressions may identify a statement as a forward-looking statement. Any statements that refer to projections of our future financial performance, our anticipated growth and trends in our business, our goals, strategies, focus and plans, and other characterizations of future events or circumstances, including statements expressing general optimism about future operating results, are forward-looking statements.

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The forward-looking statements in this prospectus speak only as of the date of this prospectus and caution should be taken not to place undue reliance on any such forward-looking statements. Forward-looking statements are subject to certain events, risks, and uncertainties that may be outside of our control. When considering forward-looking statements, you should carefully review the risks, uncertainties and other cautionary statements in this prospectus as they identify certain important factors that could cause actual results to differ materially from those expressed in or implied by the forward-looking statements. These factors include, among others, the risks described under **Risk Factors** and elsewhere in this prospectus, as well as in other reports and documents we file with the SEC.

### **USE OF PROCEEDS**

We will not receive any proceeds from the sale of share by the selling stockholders.

The selling stockholders will pay any discounts, commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in connection with the sale of the shares of our common stock offered by this prospectus. We will bear all other costs, fees and expenses incurred in connection with the registration of the shares of our common stock offered by this prospectus, including, without limitation, all registration and filing fees and fees and expenses of our legal counsel and auditors.

A portion of the shares of common stock covered by this prospectus are issuable upon exercise of warrants to purchase common stock. Upon any cash exercise of the warrants, the selling stockholders will pay us the exercise price of the warrants. Under certain circumstances, the holders of our warrants may exercise their warrants on a cashless basis. If all of the warrants are exercised at their initial exercise price, we would receive aggregate gross proceeds of approximately \$13,293,394. We expect to use any cash we receive upon the exercise of warrants for general corporate purposes.

### **SELLING STOCKHOLDERS**

The shares of common stock covered hereby consist of:

8,636,000 shares of our common stock that we issued to the selling stockholders in the private placement that closed on March 9, 2007;

3,022,600 shares of our common stock issuable upon exercise of warrants to purchase common stock. We issued these warrants to the selling stockholders who purchased shares common stock from us in the private placement; and

518,160 shares of our common stock issuable upon exercise of warrants to purchase common stock. We issued these warrants to the placement agent for the private placement.

In connection with the registration rights we granted to the selling stockholders, we filed with the Securities and Exchange Commission (SEC) a registration statement on Form S-3, of which this prospectus forms a part, with respect to the resale or other disposition of the shares of common stock offered by this prospectus or interests therein from time to time on publicly, in privately negotiated transactions or otherwise. We have also agreed to prepare and file amendments and supplements to the registration statement to the extent necessary to keep the registration statement effective for the period of time required under our agreement with the selling stockholders.

Beneficial ownership is determined in accordance with the rules of the SEC, and is based upon information provided by each respective selling stockholder, Forms 4, Schedules 13D and 13G and other public documents filed with the SEC. The number representing the number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes (i) all shares held by a selling stockholder prior to the private placement, plus (ii) all shares purchased by the selling stockholder pursuant to the private placement and being offered pursuant to the prospectus, as well as (iii) all options or other derivative securities which are exercisable within 60 days of March 28, 2007, including the warrants issued in the private placement. The percentages of shares owned after the offering are based on 40,914,425 shares of our common stock outstanding as of March 28, 2007, which includes the outstanding shares of common stock offered by this prospectus (but not the shares issuable upon exercise of the warrants issued in the private placement).



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Unless otherwise indicated below, to our knowledge, all persons named in this table have sole voting and investment power with respect to their shares of common stock, except to the extent authority is shared by spouses under applicable law. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for any person named below.

Except as noted in the footnotes below, none of the selling stockholders has held any position or office with us or our affiliates within the last three years or has had a material relationship with us or any of our predecessors or affiliates within the past three years, other than as a result of the ownership of our shares or other securities.

The selling stockholders may sell some, all or none of their shares of common stock offered by this prospectus. We do not know how long the selling stockholders will hold their shares of common stock before selling them. We currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares of common stock being offered hereunder other than the securities purchase agreement pursuant to which the selling stockholders purchased their shares of common stock from us. The shares offered by this prospectus may be offered from time to time by the selling stockholders, although the warrant shares will not be eligible to be offered pursuant to this prospectus until the related warrants are exercised. Accordingly, for purposes of this table, we have assumed that, after completion of the offering, the only shares that will continue to be held by the selling stockholders are those that were owned immediately prior to the private placement.

The selling stockholders may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act of 1933, as amended or the Securities Act, some or all of their shares of common stock since the date on which the information in the table below is presented. Information about the selling stockholders may change over time.

Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to Offering <sup>(1)</sup>	Number of Shares of Common Stock Being Offered	Number of Warrant Shares Being Offered	Number of Shares of Common Stock to Be Beneficially Owned After Offering	
				Number	Percentage
Andrew J. Kerkemeyer	138,500	100,000	35,000	3,500	*
Anthony and Mary Ellen Vassallo, JTWROS	173,734	104,000	36,400	33,334	*
Ari Abramowitz	48,600	36,000	12,600		*
Banca Partner S.p.A.	140,400	104,000	36,400	75,000	*
Block Family Trust	304,700	100,000	35,000	169,700	*
Byron and Marguerite Hestevold	182,790	104,000	36,400	42,390	*
C. LeAnn Elder Branzell	28,080	20,800	7,280		*
C. Louis Elder II	28,080	20,800	7,280		*
Calman J. Zamoiski, Jr.	183,600	136,000	47,600		*
Carton Permanent Trust of 1993, DTD 12/27/93	172,900	104,000	36,400	32,500	*
Castlerigg Master Investments, Ltd. <sup>(2)</sup>	1,620,000	1,200,000	420,000		*
Catherine J. Zamoiski	35,100	26,000	9,100		*
Charles E. Helsley	135,000	100,000	35,000		*
Charles N. Schumann	200,400	104,000	36,400	60,000	*
Clair Z. Segal	35,100	26,000	9,100		*
Clarence L. and Barbara K. Elder	504,900	374,000	130,900		*
Clayton J. Peters and Marty E. Peters JTWROS	28,080	20,800	7,280		*
Confederation, LLLP <sup>(3)</sup>	140,400	104,000	36,400		*

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Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to Offering <sup>(1)</sup>	Number of Shares of Common Stock Being Offered	Number of Warrant Shares Being Offered	Number of Shares of Common Stock to Be Beneficially Owned After Offering	
				Number	Percentage
David Berman	697,000	300,000	105,000	292,000	*
David Thoman and Christine Thoman	54,000	40,000	14,000		*
Dean A. Snyder Jr. and Robert E. Ireland, T.I.E.	340,400	104,000	36,400	200,000	*
Denis Fortin	412,000	120,000	42,000	250,000	*
DJB Holding Corporation ESOP, Daren J. Barone, Trustee	140,400	104,000	36,400		*
Dr. Harish H. Shah	151,667	100,000	35,000	16,667	*
Dudley Frank	262,000	120,000	42,000	100,000	*
Elijah Saunders	28,080	20,800	7,280		*
Elizabeth A. Bundy	28,080	20,800	7,280		*
Elizabeth Cohen and Maureen Skahan	28,080	20,800	7,280		*
Ellen L. Zamoiski	35,100	26,000	9,100		*
Enable Growth Partners LP <sup>(4)</sup>	1,377,000	1,020,000	357,000		*
Enable Opportunity Partners LP <sup>(5)</sup>	162,000	120,000	42,000		*
Fingestus S.A.	135,000	100,000	35,000		*
Howard Bergtraum	205,000	100,000	35,000	70,000	*
James A. Calkin, Jr.	89,000	40,000	14,000	35,000	*
James A. Lesley and Judy B. Lesley, Joint Tenants	104,500	40,000	14,000	50,500	*
James K. Hendren	260,000	100,000	35,000	125,000	*
Joanne Waeltermann, M.D.	10,530	7,800	2,730		*
John R. Costantino and Barbara Costantino JTWRS	27,000	20,000	7,000		*
Joseph I. DiMaria	150,000	100,000	35,000	15,000	*
Kristina K. Bundy	28,080	20,800	7,280		*
Larry R. Swanson	207,250 <sup>(6)</sup>	65,520	22,932	118,800 <sup>(7)</sup>	*
Lawrence F. and Sonja J. DeBaugh JTWROS	56,160	41,600	14,560		*
Lewis C. Solmon and Vicki R. Solmon					
JTWROS	28,080	20,800	7,280		*
Lisa M. Elder	28,080	20,800	7,280		*
Louis J. and Nancy S. Grasmick, Tenants by the Entirety	56,160	41,600	14,560		*
Martin s In <sup>(8)</sup>	56,160	41,600	14,560		*
Michael Kubersky	162,000	120,000	42,000		*
Murray Berman	178,667	120,000	42,000	16,667	*
National Securities, Inc. <sup>(9)</sup>	188,580		188,850		*
Nicholas Scott	79,000	40,000	14,000	25,000	*
Noel Krantz	140,400	104,000	36,400		*
Oppenheimer & Co. Inc. <sup>(10)</sup>	329,310		329,310		*
Peter G. and Georgia K. Angelos	2,080,000	208,000	72,800	1,800,000	4.4%
Peter M. Carton and Grace Melody Anne Carton	140,400	104,000	36,400		*

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Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to Offering <sup>(1)</sup>	Number of Shares of Common Stock Being Offered	Number of Warrant Shares Being Offered	Number of Shares of Common Stock to Be Beneficially Owned After Offering	
				Number	Percentage
Pierce Diversified Strategy Master Fund LLC, Ena <sup>(11)</sup>	81,000	60,000	21,000		*
Pinnacle Advertising <sup>(12)</sup>	141,000	100,000	35,000	6,000	*
Rachel Abramowitz	54,000	40,000	14,000		*
Rachel D. Zamoiski	35,100	26,000	9,100		*
Raymond A. Bartolacci, III	84,182	25,320	8,862	50,000	*
Richard D. Fitzgerald	154,000	40,000	14,000	100,000	*
Robert C. Anderson	140,400	104,000	36,400		*
Robert J. MacDaniels and Suzanne MacDaniels	56,160	41,600	14,560		*
Russell T. Bundy, Jr.	56,160	41,600	14,560		*
SF Capital Partners Ltd. <sup>(13)</sup>	1,620,000	1,200,000	420,000		*
Sidney W. Gilreath	192,000	120,000	42,000	30,000	*
SSE Taylor Partners, LLC	162,000	120,000	42,000		*
Star - Short Term Absolute Return (Star 1)	70,200	52,000	18,200		*
Star - Short Term Absolute Return (Star 4)	70,200	52,000	18,200		*
Stephen and Melinda Geppi JTWROS	209,116 <sup>(14)</sup>	56,160	19,656	133,300 <sup>(15)</sup>	*
Steve Wallitt	54,000	40,000	14,000		*
Tom Bullock and Tom Wellen	54,000	40,000	14,000		*
Transpro Property & Casualty Ins. Corp	162,000	120,000	42,000		*

\* Less than 1%

- (1) For each selling stockholder, amount listed includes the number of shares underlying the immediately exercisable warrants indicated for such stockholder in the column titled "Number of Warrant Shares Being Offered."
- (2) Sandell Asset Management Corp. ( "SAMC" ) is the investment manager of Castlerigg Master Investments Ltd. ( "Master" ). Thomas Sandell is the controlling person of SAMC and may be deemed to share beneficial ownership of the shares beneficially owned by Master. Castlerigg International Ltd. ( "Castlerigg International" ) is the controlling shareholder of Castlerigg International Holdings Limited ( "Holdings" ). Holdings is the controlling shareholder of Master. Each of Holdings and Castlerigg International may be deemed to share beneficial ownership of the shares beneficially owned by Castlerigg Master Investments Ltd.
- (3) Kerby E. Confer has investment and voting control over the shares held by Conferment, LLLP.
- (4) Enable Capital Management, LLC is the manager of Enable Growth Partners, LP and has voting control and investment discretion over the securities held by Enable Growth Partners, LP. Mitch Levine is the Managing Member of Enable Capital Management, LLC and, as such, has voting control and investment discretion over the securities held by Enable Growth Partners, LP.
- (5) Enable Capital Management, LLC is the manager of Enable Opportunity Partners, LP and has voting control and investment discretion over the securities held by Enable Opportunity Partners, LP. Mitch Levine is the Managing Member of Enable Capital Management, LLC and, as such, has voting control and investment discretion over the securities held by Enable Opportunity Partners, LP.
- (6) Includes an aggregate of 33,732 shares underlying warrants that are immediately exercisable.
- (7) Includes 10,800 shares underlying warrants that are immediately exercisable.
- (8) Joseph Mburu has investment and voting control over the shares held by Martin's Inc.
- (9) National Securities, Inc. acted as a soliciting dealer for our placement agent, Oppenheimer & Co. Inc., in connection with our private placement that closed March 9, 2007. As compensation for acting as a soliciting dealer, National received from Oppenheimer a reallowance of \$503,600 and warrants to



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- purchase an aggregate of 188,850 shares at an exercise price of \$3.78 per share. National acted as placement agent for our private placement that closed in October 2005. National is a broker-dealer. We do not have any arrangement with National for it to act as a broker-dealer for the sale of the shares included herein for the selling stockholders. National may be deemed to be an underwriter with respect to its respective sales of shares to be offered by National in this prospectus. Brian Friedman has investment and voting control over the shares held by National.
- (10) Oppenheimer & Co. Inc. acted as placement agent for our private placement that closed March 9, 2007. As compensation for its services as placement agent, Oppenheimer received a cash fee equal to approximately \$1,400,000, which represents 6.5% of the gross proceeds of the sale of the shares of common stock in the private placement, and warrants to purchase an aggregate of 518,160 shares at an exercise price of \$3.78 per share. National Securities, Inc. acted a soliciting dealer for Oppenheimer with respect to the private placement. As compensation for acting as a soliciting dealer, National received from Oppenheimer a reallowance of \$503,600 and warrants to purchase an aggregate of 188,850 shares at an exercise price of \$3.78 per share. Oppenheimer is a broker-dealer. We do not have any arrangement with Oppenheimer for it to act as a broker-dealer for the sale of the shares included herein for the selling stockholders. Oppenheimer may be deemed to be an underwriter with respect to its respective sales of shares to be offered by Oppenheimer in this prospectus. Each of Albert G. Lowenthal and Dennis McNamara has investment and voting control over the shares held by Oppenheimer.
- (11) Enable Capital Management, LLC is the manager of Pierce Diversified Master Strategy Fund, LLC Ena and has voting control and investment discretion over the securities held by Pierce Diversified Master Strategy Fund, LLC Ena. Mitch Levine is the Managing Member of Enable Capital Management, LLC and, as such, has voting control and investment discretion over the securities held by Pierce Diversified Master Strategy Fund, LLC Ena.
- (12) Michael Magnusson has investment and voting control over the shares held by Pinnacle Advertising.
- (13) The selling stockholder is or may be an affiliate of a registered broker-dealer. We have been informed by the selling stockholder that such selling stockholder acquired the securities offered by this prospectus for its own account in the ordinary course of business, and that at the time it acquired the securities, it had no agreements, plans or understandings, directly or indirectly, with any person to distribute the securities. Michael A. Roth and Brian J. Stark, in their capacities as managing members of Stark Offshore Investments, LLC, the investment manager to the selling stockholder, have voting and dispositive power with respect to the shares of this selling stockholder that are registered under this prospectus.
- (14) Includes an aggregate of 76,456 shares underlying warrants that are immediately exercisable.
- (15) Includes 56,800 shares underlying warrants that are immediately exercisable.

**PLAN OF DISTRIBUTION**

We are registering the shares offered by this prospectus on behalf of the selling stockholders. The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. To the extent any of the selling stockholders gift, pledge or otherwise transfer the shares offered hereby, such transferees may offer and sell the shares from time to time under this prospectus, provided that this prospectus has been amended under Rule 424(b)(3) or other applicable provision of the Securities Act to include the name of such transferee in the list of selling stockholders under this prospectus.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

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block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales;

through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering. Upon any exercise of the warrants by payment of cash, however, we will receive the exercise price of the warrants.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act of 1933, provided that they meet the criteria and conform to the requirements of that rule.

The selling shareholders might be, and any broker-dealers that act in connection with the sale of securities will be, deemed to be underwriters within the meaning of Section 2(11) of the Securities Act, and any commissions received by such broker-dealers and any profit on the resale of the securities sold by them while acting as principals will be deemed to be underwriting discounts or commissions under the Securities Act.



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To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to keep the registration statement that includes this prospectus effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement or (2) the date on which the shares may be sold pursuant to Rule 144(k) of the Securities Act.

## **EXPERTS**

Marcum & Kliegman LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-KSB for the year ended December 31, 2006, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Marcum & Kliegman LLP's report, given on their authority as experts in accounting and auditing.

## **INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

The SEC allows us to incorporate by reference information that we file with the SEC, which means that we can disclose important information to you by referring you to those documents filed separately with the SEC. The information incorporated by reference is an important part of this prospectus, and information that we subsequently file will automatically update and supersede information in this prospectus and in our other filings with the SEC.

We incorporate by reference into this prospectus the documents listed below, which we have already filed with the SEC, and any future filings we make under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act, excluding any information in those documents that is deemed by the rules of the SEC to be furnished but not filed, until this offering is completed:

- (a) Our Annual Report on Form 10-KSB for the fiscal year ended December 31, 2006, filed with the SEC on March 15, 2007;
  - (b) Our Current Reports on Form 8-K, filed with the SEC on February 6, 2007, March 6, 2007, March 21, 2007 and March 23, 2007; and
  - (c) The description of our common stock contained in our registration statement on Form SB-2, filed with the SEC on January 18, 2006 (SEC File No. 333-131104), including all amendments or reports filed for the purpose of updating such description.
- We will provide without charge to each person to whom a copy of this prospectus is delivered, upon written or oral request of any such person, a copy of any or all of the foregoing documents incorporated by reference in this prospectus, including any exhibits that are specifically incorporated by reference in such documents. Requests should be made to:

Dennis M. Mulroy, Chief Financial Officer

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Cardium Therapeutics, Inc.

3611 Valley Centre Parkway, Suite 525

San Diego, California 92130

(858) 436-1000

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You should rely only on the information provided or incorporated by reference in this prospectus or any supplement to this prospectus. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front cover of the document.

**WHERE YOU CAN FIND MORE INFORMATION**

We file annual, quarterly and current reports, proxy statements and other documents with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Our SEC filings are also available to you on the SEC's Internet site at <http://www.sec.gov>. In addition, electronic copies of our most recently filed reports are available through our website at <http://www.cardiumthx.com>.

This prospectus is part of a registration statement that we filed with the SEC on Form S-3 relating to the common stock offered by this prospectus. This prospectus, which is a part of the registration statement, does not contain all of the information contained in the registration statement, including the exhibits to the registration statement. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet site.

**Table of Contents****Part II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution**

The following table sets forth the various expenses to be incurred in connection with the sale and distribution of the securities being registered hereby, all of which will be borne by Cardium Therapeutics, Inc. (except for any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares). All amounts shown are estimates except the SEC registration fee.

SEC registration fee	\$ 1,177
Legal fees and expenses	15,000
Printing and filing expenses	2,500
Accounting fees and expenses	3,500
Miscellaneous expenses	2,823
 Total	 \$ 25,000

**Item 15. Indemnification of Directors and Officers**

Cardium's certificate of incorporation provides that it may indemnify, to the full extent authorized or permitted by law, any person made, or threatened to be made, a defendant or witness to any action, suit or proceeding (whether civil or criminal or otherwise) by reason of the fact that he, his testator or intestate, is or was director or officer of Cardium or by reason of the fact that such director or officer, at the request of Cardium, is or was serving any other corporation, partnership, joint venture, employee benefit plan or other enterprise, in any capacity. Under Delaware law, a director or officer who has been successful on the merits or otherwise in defense of any action, suit or proceeding or in defense of any claim, issue or matter therein shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred. In other circumstances, a director, officer, employee or agent of Cardium may be indemnified against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interest of Cardium. The bylaws of Cardium provide that costs and expenses (including attorneys' fees) incurred by or on behalf of a director, officer, employee or agent of Cardium in defending or investigating any action, suit, proceeding or investigation shall be paid by Cardium in advance of the final disposition of such matter, if such director, officer, employee or agent undertakes in writing to repay any such advances if it is ultimately determined that he or she was not entitled to indemnification.

Cardium's certificate of incorporation further provides that Cardium may buy and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of Cardium, or is serving at the request of Cardium as a director, officer, employee or agent of any corporation, partnership, joint venture, trust, employee benefit plan or other enterprise against any liability asserted against him and incurred by him in any such capacity, or arising out of his status as such, whether or not Cardium would have the power to indemnify him against such liability under the provisions of the law. Cardium has in effect a directors and officers liability insurance policy protecting its directors and officers against liability by reason of their being or having been directors or officers of Cardium.

Under the terms of Cardium's charter, no director of Cardium shall be personally liable to Cardium or its stockholders for monetary damages for any breach of fiduciary duty by such a director as a director. Notwithstanding the foregoing, a director shall be liable to the extent provided by applicable law (i) for any breach of the director's duty of loyalty to Cardium or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) for any unlawful payment of dividends or unlawful stock purchase or redemption, or (iv) for any transaction from which such director derived an improper personal benefit.

Cardium has entered into indemnification agreements with each of its directors and anticipates that it will enter into similar arrangements with any future directors. Cardium may also enter into similar arrangements with certain of its officers who are not also directors. Generally, the indemnification agreements attempt to provide the maximum protection permitted by Delaware law with respect to indemnification of directors.

**Table of Contents****Item 16. Exhibits**

The following exhibit index shows those exhibits filed with this registration statement and those incorporated by reference:

<b>Exhibit Number</b>	<b>Description</b>	<b>Incorporated By Reference to</b>
4.1	Second Amended and Restated Certificate of Incorporation of the Registrant as filed with the Delaware Secretary of State on January 13, 2006	Exhibit 3(i) of the Registrant's Registration Statement on Form SB-2 (File No. 333-131104), filed with the SEC on January 18, 2006
4.2	Amended and Restated By-laws of the Registrant as adopted on January 12, 2006	Exhibit 3(i) of the Registrant's Registration Statement on Form SB-2 (File No. 333-131104), filed with the SEC on January 18, 2006
4.3	Form of the Registrant's Common Stock Certificate	Exhibit 4.5 of the Registrant's Annual Report on Form 10-KSB for the fiscal year ended December 31, 2005, filed with the SEC on March 31, 2006
4.4	Form of Warrant issued to purchasers in 2007 private financing	Exhibit 4.1 of the Registrant's Current Report on Form 8-K dated March 6, 2007, filed with the Commission on March 6, 2007
4.5	Form of Warrant issued to Oppenheimer & Co. Inc. as Placement Agent in 2007 financing	Exhibit 4.7 of the Registrant's Annual Report on Form 10-KSB for the fiscal year ended December 31, 2006, filed with the Commission on March 15, 2007
5.1	Opinion of Fisher Thurber LLP	Filed herewith
23.1	Consent of Marcum & Kliegman LLP	Filed herewith
23.2	Consent of Fisher Thurber LLP	Filed herewith (included in Exhibit 5.1)
24.1	Power of Attorney	Included on the signature page hereto

**Item 17. Undertakings**

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act");

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;



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*Provided, however,* that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the SEC by the Registrant pursuant to Section 13 or Section 15(d) of Securities Exchange Act of 1934, as amended (the Exchange Act ), that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(b) The Registrant hereby undertakes that, for the purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to Delaware law, the Registrant's charter, its bylaws, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on March 29, 2007.

CARDIUM THERAPEUTICS, INC.

By: */s/ Christopher J. Reinhard*  
Christopher J. Reinhard  
Chairman, Chief Executive Officer, President and Treasurer

**Table of Contents****POWER OF ATTORNEY**

Each person whose signature appears below constitutes and appoints Christopher J. Reinhard, his true and lawful attorney-in-fact and agent, acting alone, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and any registration statement of the same offering which is effective upon filing pursuant to Rule 462(b) under the Securities Act, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all said attorney-in-fact and agent, acting alone, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the date indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Christopher J. Reinhard Christopher J. Reinhard	Chairman, Chief Executive Officer, President and Treasurer	March 29, 2007
/s/ Dennis M. Mulroy Dennis M. Mulroy	Chief Financial Officer	March 29, 2007
/s/ Tyler M. Dylan Tyler M. Dylan	Director, Chief Business Officer, Executive Vice President, General Counsel and Secretary	March 29, 2007
/s/ Edward W. Gabrielson Edward W. Gabrielson	Director	March 29, 2007
/s/ Murray H. Hutchinson Murray H. Hutchinson	Director	March 29, 2007
/s/ Gerald J. Lewis Gerald J. Lewis	Director	March 29, 2007
/s/ Lon Edward Otremba Lon Edward Otremba	Director	March 29, 2007
/s/ Ronald I. Simon Ronald I. Simon	Director	March 29, 2007

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5.1	Opinion of Fisher Thurber LLP	Filed herewith
23.1	Consent of Marcum & Kliegman LLP	Filed herewith
23.2	Consent of Fisher Thurber LLP	Filed herewith (included in Exhibit 5.1)
24.1	Power of Attorney	Included on the signature page hereto