

CRITICAL THERAPEUTICS INC

Form 10-K

March 17, 2005

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**UNITED STATES SECURITIES AND EXCHANGE COMMISSION**  
**Washington, DC 20549**

**Form 10-K**  
**FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTION 13 OR 15(d)**  
**OF THE SECURITIES EXCHANGE ACT OF 1934**

(Mark One)

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2004**

**OR**

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the transition period from            to**

**Commission file number: 000-50767**

**CRITICAL THERAPEUTICS, INC.**

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

**Delaware**

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

**04-3523569**

*(IRS Employer  
Identification No.)*

**60 Westview Street**

**Lexington, Massachusetts**

*(Address of principal executive offices)*

**02421**

*(Zip Code)*

**Registrant's telephone number, including area code:**

**(781) 402-5700**

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

**None.**

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

**Common Stock, \$0.001 par value per share**

*(Title of Class)*

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of June 30, 2004, was approximately \$56,868,686, based on the price at which the registrant's common stock was last sold on that date.

As of March 15, 2005, the registrant had 24,097,624 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Specified portions of the registrant's proxy statement for the registrant's 2005 annual meeting of stockholders to be held on June 2, 2005, which are to be filed pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2004, are incorporated by reference into Part III of this report.

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ANNUAL REPORT  
ON FORM 10-K  
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**PART I**

**Cautionary Statement Regarding Forward-Looking Statements**

This annual report on Form 10-K includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For this purpose, any statements contained in this report regarding the progress and timing of our drug development programs and related trials; the timing of regulatory approvals and product launches; the efficacy of our drug candidates; our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management; and all other statements that are not purely historical in nature, constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words anticipate, believe, could, estimate, expect, intend, may, plan, project, should, will, would and similar expressions identify forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including our critical accounting estimates and risks relating to: conducting clinical trials including the timing and success of patient enrollment; the results of preclinical studies and clinical trials with respect to our products under development and whether such results will be indicative of results obtained in later clinical trials; the timing and success of submission, acceptance and approval of regulatory filings; our heavy dependence on the commercial success of ZYFLO® tablets and the controlled-release formulation of zileuton; our ability to obtain the substantial additional funding required to conduct our research, development and commercialization activities; our dependence on our strategic collaboration with MedImmune, Inc.; and our ability to obtain, maintain and enforce patent and other intellectual property protection for our discoveries and drug candidates. These and other risks are described in great detail below under the caption Factors That May Affect Future Results. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. In addition, any forward-looking statements in this annual report represent our views only as of the date of this annual report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, whether as a result of new information, future events or otherwise. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

**ITEM 1. BUSINESS**

**Overview**

Critical Therapeutics, Inc. is a biopharmaceutical company focused on the discovery, development and commercialization of products designed to treat respiratory, inflammatory and critical care diseases through the regulation of the body's inflammatory response. The inflammatory response occurs within the body's immune system following a stimulus such as infection or trauma. Our most advanced product is ZYFLO® Filmtab®, a tablet formulation of zileuton, which the U.S. Food and Drug Administration, or FDA, approved in 1996 for the prevention and chronic treatment of asthma. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO and other formulations of zileuton for multiple diseases and conditions. We are currently in the process of changing manufacturing sites for ZYFLO. Subject to FDA approval of these sites, we expect to begin selling ZYFLO in the United States in the second half of 2005.

We are also developing product candidates to regulate the excessive inflammatory response that can damage vital internal organs and, in the most severe cases, result in multiple organ failure and death.

*CTI-01.* We are developing a small molecule product candidate, CTI-01, that we believe may be effective in regulating the inflammatory response. Results from preclinical studies suggest that CTI-01

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inhibits the release of protein molecules called cytokines that are responsible for communication between cells in the body and are associated with conditions such as post-operative ileus, which is the loss of normal intestine movement following surgery, and the damage to vital organs that can occur in patients after cardiopulmonary bypass, a procedure commonly performed during heart surgery.

*HMGB1.* We believe that a cytokine called HMGB1, or high mobility group box protein 1, may be an important target for the development of products to treat inflammation-mediated diseases because of the timing and the duration of its release from cells into the bloodstream. We are currently collaborating with MedImmune, Inc. on preclinical development of our monoclonal antibodies directed towards HMGB1 in a number of animal models. In addition, we are currently collaborating with Beckman Coulter, Inc. on development of a diagnostic directed towards HMGB1.

*Cholinergic Anti-inflammatory Program.* We are developing small molecules designed to inhibit the body's inflammatory response by acting on the nicotinic  $\alpha$ -7 cholinergic target, which is a cell receptor associated with the production of the cytokines that play a fundamental role in the inflammatory response. We believe that successful development of a product candidate targeting the nicotinic  $\alpha$ -7 cholinergic receptor could lead to an oral anti-cytokine therapy for acute and chronic diseases. We are also exploring the development of a medical device, similar to those already marketed for the treatment of epileptic seizures, to stimulate the vagus nerve, a nerve that links the brain with the major organs of the body, and induce an anti-inflammatory response by acting on the  $\alpha$ -7 receptor.

We were incorporated in Delaware on July 14, 2000. Since our inception, we have incurred significant losses each year. As of December 31, 2004, we had an accumulated deficit of \$58.5 million. We expect to incur significant and growing losses for the foreseeable future. Although the size and timing of our future operating losses are subject to significant uncertainty, we expect our operating losses to continue to increase over the next several years as we continue to fund our development programs and prepare for potential commercial launch of our product candidates. We do not expect to achieve profitability in the foreseeable future; and we cannot assure you that we will achieve profitability at all. Since inception, we have raised proceeds to fund our operations through our initial public offering of common stock, private placements of equity securities, debt financings, the receipt of interest income and payments from our collaborators MedImmune and Beckman Coulter.

### **Our Strategy**

Our goal is to become a leading biopharmaceutical company focused on developing therapeutics to treat respiratory, inflammatory and critical care diseases through the regulation of the body's inflammatory response. The key elements of our strategy are to:

*Maximize the commercial potential of ZYFLO.* We are focused on successfully launching ZYFLO in the United States in the second half of 2005. We plan to build a marketing and sales infrastructure to promote ZYFLO and the controlled-release formulation of zileuton that we are developing for the treatment of asthma upon regulatory approval from the FDA. We believe that by targeting specialists rather than primary care physicians, we can successfully promote ZYFLO with an initial sales force of fewer than 100 sales representatives in the United States.

*Expand the potential applications of zileuton.* We believe that zileuton has potential therapeutic benefits in a range of diseases and conditions, such as acne, chronic obstructive pulmonary disease, or COPD, nasal polyposis and acute asthma exacerbations. We intend to expand the potential applications of zileuton through development of additional formulations, including controlled-release, intranasal and intravenous formulations.

*Advance and expand our portfolio of product candidates.* We intend to focus on developing products that address large unmet medical needs in the critical care market. We believe that our understanding of the cytokine cascade and its role in critical care diseases will enable us to continue



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to develop and discover drug candidates with novel mechanisms of action that may address some of the unmet medical needs in critical care medicine. We believe our focus on diseases associated with the severe inflammatory response will allow us to pursue drug development and discovery programs across a number of therapeutic areas in an efficient manner.

*Maximize the economic value of our product portfolio.* We believe we can maximize the potential economic benefit to us of our product candidates by retaining sole or shared ownership of our product development opportunities. We intend to undertake selected strategic collaborations, such as our collaborations with MedImmune and Beckman Coulter, to develop projects that may be beyond our internal resources, while seeking to retain co-promotion or commercial rights in any such collaborations.

*Strategically in-license or acquire attractive development candidates or approved products.* We intend to enhance our product pipeline and leverage the marketing and sales infrastructure that we are building through strategically in-licensing or acquiring product candidates or approved products for the critical care market. We believe our focus on critical care medicine and our targeted sales force will make us an attractive partner for companies seeking to out-license products or product candidates in our areas of focus.

**Our Product Pipeline**

The following table sets forth the current status of our product candidates in development and our research and development programs:

**Zileuton**

We have acquired from Abbott exclusive worldwide rights to develop and market ZYFLO and other formulations of zileuton for multiple diseases and conditions. ZYFLO, a tablet formulation of zileuton, is an FDA-approved product for the prevention and chronic treatment of asthma that was developed and previously sold by Abbott. We are required to submit a supplemental new drug application, or sNDA, for ZYFLO because we are changing the process for manufacturing and transferring the manufacturing of ZYFLO to new, third-party manufacturing sites. We intend to submit this sNDA to the FDA in late



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March 2005 shortly after completing the transfer of manufacturing, and, subject to regulatory approval, we expect to begin selling ZYFLO in the United States in the second half of 2005.

Zileuton blocks the activity of the 5-lipoxygenase enzyme, which is the main enzyme responsible for formation of a family of lipids known as leukotrienes. There are many different leukotrienes, and ZYFLO's mechanism of action blocks production of the entire leukotriene family. Leukotrienes are in part responsible for the inflammatory response associated with asthma and are known to cause many of the biological effects that contribute to inflammation, mucus production and closing of the lung airways of asthmatic patients. Leukotrienes are also implicated in the disturbance of normal lung airway function in certain other diseases, including COPD. ZYFLO is the only FDA-approved product that blocks the activity of the 5-lipoxygenase enzyme.

### ***Therapeutic Opportunity***

Asthma is a chronic respiratory disease that is characterized by the narrowing of the bronchi, or lung airways, that makes breathing difficult. An asthma attack leaves the victim gasping for breath as the airways become constricted, inflamed and clogged with thick, sticky secretions. Severe asthma attacks can be life threatening and, according to the American Lung Association, resulted in almost two million people visiting hospital emergency rooms in the United States in 2000. The Centers for Disease Control and Prevention estimate that 20.3 million people in the United States had asthma in 2001. The direct healthcare costs associated with treating asthma reached an estimated \$9.4 billion in 2001.

There is no one ideal treatment for asthma and there is no cure. Currently, patients are treated with a combination of products that are designed primarily to manage their disease symptoms by opening the airways in the lungs and reducing inflammation. Typical treatments include bronchodilatory drugs, such as Serevent®, leukotriene receptor antagonists, or LTRAs, such as Singulair®, inhaled corticosteroids, such as Flovent® and combination products such as Advair®, which is a combination of an inhaled corticosteroid and a bronchodilator. We believe many prescribing physicians are dissatisfied with the treatment options available for patients with uncontrolled or severe, persistent asthma due to the inability of these treatments to control symptoms reliably. As a result, these patients, who we believe constitute approximately 20% of the asthma population, often have severe asthma attacks requiring emergency room visits and, in many cases, further hospitalization to stabilize airway function. Despite the approval and launch in 2004 of Xolair® to treat severe allergic asthma, we believe patients with severe asthma remain underserved and in need of effective medication.

We believe that many patients with asthma may benefit from therapy with zileuton. Zileuton actively inhibits the main enzyme responsible for the production of a broad spectrum of lipids responsible for the symptoms associated with asthma, including all leukotrienes. We believe that this is an important distinction from Singulair®, the most frequently prescribed LTRA, which blocks only one of the two known receptors for a single leukotriene out of the many leukotrienes associated with asthma symptoms. We intend to market ZYLFO as a treatment for asthma patients who do not gain adequate symptomatic control from currently available medications.

### ***Zileuton Product Development***

#### ***ZYFLO: The Tablet Formulation of Zileuton***

ZYFLO is the only 5-lipoxygenase inhibitor drug to be approved for marketing by the FDA. In 1996, ZYFLO was approved by the FDA as an immediate-release, four-times-a-day tablet for the prevention and chronic treatment of asthma. ZYFLO was launched in the United States in 1997. We have completed the transfer of the manufacturing technology used in the production of the zileuton active pharmaceutical ingredient, or API, and for ZYFLO tablets from Abbott to contract manufacturing sites. We have completed manufacture of the tablets required for registration, and these tablets are currently undergoing stability testing. Once stability testing is completed, we expect to submit an sNDA, which FDA regulations require in connection with our changes in manufacturing process and manufacturing sites. We

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expect that the FDA's review of our sNDA will take approximately six months. If the FDA approves our sNDA within this timeframe, we would expect to begin marketing ZYFLO in the second half of 2005.

Dr. Paul Rubin, our President and Chief Executive Officer, led the development of ZYFLO while he was employed by Abbott. The full clinical development program for ZYFLO consisted of 21 safety and efficacy trials in an aggregate of approximately 3,000 patients with asthma. FDA approval was based on pivotal three-month and six-month safety and efficacy clinical trials in 774 asthma patients. The pivotal trials compared patients taking a combination of ZYFLO and their inhaled bronchodilators to patients taking a combination of placebo and inhaled bronchodilators. The results of the group taking ZYFLO and their inhaled bronchodilators showed:

rapid and sustained improvement for patients over a six-month period in objective and subjective measures of asthma control;

reduction of exacerbations and need for either bronchodilatory or steroid rescue medications; and

acute bronchodilatory effect two hours after the first dose.

Our post hoc analysis of the data suggested there was a greater airway response benefit in asthma patients with less than 50% of expected airway function, and a six-fold decrease in steroid rescues compared to placebo.

In these placebo-controlled clinical trials, 1.9% of patients taking ZYFLO experienced an increase in the liver enzyme alanine transaminase, or ALT, to greater than three times the level normally seen in the bloodstream compared to 0.2% of patients receiving placebo. These enzyme levels resolved or returned towards normal in both the patients who continued and those who discontinued the therapy.

In addition, prior to FDA approval, a long-term, safety surveillance trial was conducted in 2,947 patients. In this safety trial, 4.6% of patients taking ZYFLO experienced ALT levels greater than three times the level normally seen in the bloodstream compared to 1.1% of patients receiving placebo. In 61.0% of the patients with ALT levels greater than three times the level normally seen in the bloodstream, the elevation was seen in the first two months of dosing. After two months of treatment, the rate of ALT levels greater than three times the level normally seen in the bloodstream stabilized at an average of 0.3% per month for patients taking a combination of ZYFLO and their usual asthma medications compared to 0.11% per month for patients taking a combination of placebo and their usual asthma medications. This trial also demonstrated that ALT levels returned to below two times the level normally seen in the bloodstream in both the patients who continued and those who discontinued the therapy. The overall rate of patients with ALT levels greater than three times the level normally seen in the bloodstream was 3.2% in the approximately 5,000 patients who received ZYFLO in placebo-controlled and open-label trials combined. In these trials, one patient developed symptomatic hepatitis with jaundice, which resolved upon discontinuation of therapy, and three patients developed mild elevations in the protein bilirubin.

After reviewing the data from these trials, the FDA approved ZYFLO in 1996 on the basis of the data submitted and we are not aware of any reports of ZYFLO being directly associated with serious liver damage in patients treated with ZYFLO since its approval.

*Controlled-Release Formulation of Zileuton*

We believe that the controlled-release formulation of zileuton that we are developing will be more convenient for patients because of its twice-a-day dosing regimen, as compared to ZYFLO's current four-times-a-day dosing regimen, and may increase patient drug compliance. Abbott completed Phase III clinical trials for this formulation in asthma, but did not submit a new drug application, or NDA. Based upon data provided to us, we believe this decision was not based upon the clinical efficacy or safety data generated during the program. We expect to submit an NDA based on safety and efficacy data generated

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from the two completed Phase III clinical trials, a three-month efficacy trial and a six-month safety and efficacy trial. The results of these clinical trials were as follows:

The three-month pivotal efficacy trial, in which 409 patients received either the controlled-release formulation of zileuton or placebo, generated similar efficacy results to those seen in the ZYFLO pivotal trials. The trial demonstrated statistically significant improvements over placebo, in objective measures of asthma control, such as mean forced expiratory volume. The trial also showed a reduced need for bronchodilatory drugs as a rescue medication to alleviate uncontrolled symptoms;

The efficacy component of the six-month trial included 757 patients and generated similar efficacy results to those seen in the ZYFLO pivotal trials. The trial demonstrated statistically significant improvements over a combination of placebo and the patients' normal asthma therapies, in objective measures of asthma control, such as mean forced expiratory volume. In the trial, the controlled-release formulation of zileuton also showed a reduced need for bronchodilatory drugs as a rescue medication to alleviate uncontrolled symptoms; and

The safety data generated in a total of 1,335 patients from these two trials was comparable to safety data seen in the ZYFLO pivotal trials. The incidence of ALT levels greater than three times the level normally seen in the bloodstream in patients receiving zileuton was 2.1% and in all cases ALT levels resolved or returned towards normal in both the patients who continued and those who discontinued the therapy.

We believe that this clinical development package will be sufficient to support the submission in the fourth quarter of 2005 of an NDA for the controlled-release formulation of zileuton for asthma. However, before we can submit the NDA, we must receive satisfactory comparative bioavailability data from a clinical trial in healthy volunteers designed to show that our manufactured tablets behave similarly in the body to the tablets that had been manufactured by Abbott. At present, we are conducting production campaigns and assessing performance of the manufactured tablets, prior to initiation of the bioavailability study. We believe that any significant variability in product performance or delay in manufacturing could delay the submission of the NDA by up to six months.

*Intravenous Formulation of Zileuton*

We also commenced development in 2004 of a new intravenous formulation of zileuton for use in severe acute asthma attacks. In 2000, approximately two million hospital emergency room visits in the United States involved severe asthma attacks, of which approximately 465,000 resulted in hospitalization. Currently, most patients suffering severe asthma attacks are treated with bronchodilators inhaled via a nebulizer, typically for 20 minutes or more. Nebulizers attempt to restore airway function by delivering the bronchodilatory drug to the bloodstream via the lungs. However, the patient's ability to get the drug into his lungs may be impaired by his inability to breathe efficiently caused by the severe asthma attack. Clinical data demonstrate that zileuton exhibits its maximum effect on lung function when the blood drug concentration reaches its peak level and that the effect is achieved after a single dose of zileuton. We believe that an intravenous formulation of zileuton that would deliver zileuton directly to the bloodstream would have a rapid onset of action, reaching peak blood concentration within minutes of the injection. We believe that this rapid delivery of the drug to the patient's bloodstream may lead to more rapid symptom improvements, and potentially reduce the number of hospital admissions of patients arriving in the emergency room suffering from a severe asthma attack.

In 2004, we entered into an agreement with Baxter Healthcare Corporation to conduct feasibility studies to analyze the various properties of zileuton and determine the most suitable technologies for the development of an intravenous formulation of zileuton. As a result, we have produced, and are currently evaluating, two intravenous formulations of zileuton. Due to the large amount of available preclinical information on zileuton, we believe that the preclinical development requirements for the intravenous formulation will be restricted to limited exposure studies in animals designed to clarify the safety of the mode of administration. These studies are currently ongoing and as a result, we expect to begin Phase I clinical trials of a product candidate in the middle of 2005.

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***Commercialization Strategy***

We are developing a targeted marketing and sales infrastructure in connection with our anticipated launch of ZYFLO in the United States in the second half of 2005. We plan to build a marketing and sales force to promote ZYLFO and the controlled-release formulation of zileuton that we are developing for the treatment of asthma. We believe that by targeting specialists rather than primary care physicians, we can successfully promote ZYFLO with an initial sales force of fewer than 100 sales representatives in the United States.

We plan to utilize the knowledge we have obtained through review of recent ZYFLO prescription patterns, which demonstrate that, despite the lack of a sustained marketing effort, ZYFLO has developed an established prescriber base among specialists who treat asthma. Prescription data for the 12-month period ended September 30, 2003 revealed that approximately 1,700 physicians were prescribing the product. The top 20% of prescribing physicians accounted for 57% of all prescriptions and the top 25 prescribers averaged 79 prescriptions each. We believe these data suggest that physicians who are aware of zileuton prescribe the product in moderately high volumes.

We intend to position ZYFLO as a treatment for asthma patients who do not gain adequate control of their symptoms with other currently available medications. We expect that as part of our launch, we will promote ZYFLO to specialists who treat asthma and managed care decision makers. As part of our marketing strategy, we plan to educate key opinion leaders and physicians on the scientific data that differentiates ZYFLO's mechanism of action from other asthma treatments and emphasize clinical data that show safety and efficacy for ZYFLO in asthma at all levels of severity.

We also intend to maximize patient and physician access to ZYFLO by addressing ZYFLO's position on managed care formularies. We believe that in many managed care formularies, as a result of the lack of a sustained marketing effort, ZYFLO has been removed or relegated to third-tier status, which requires the highest co-pay for patients prescribed the product.

If we successfully complete the development of, and receive regulatory approval for, the controlled-release formulation of zileuton, we will seek to convert prescribing and usage of ZYFLO to this formulation.

We intend to explore the therapeutic benefits of zileuton in treating a range of diseases and conditions, including acne, COPD, nasal polyposis and mastocytosis. We are aware, for instance, of clinical data available in publications of clinical trials and individual patient case trials that indicate zileuton has shown efficacy in the treatment of nasal polyps and acne. We are currently conducting a Phase II clinical trial in patients with moderate to severe inflammatory acne and we expect to complete the trial by the end of the first half of 2005. In each case, if we develop zileuton for one of these diseases or conditions, we will need to commence clinical development programs to generate sufficient information to obtain a regulatory label. During the manufacturing transfer and regulatory review periods, we intend to conduct additional trials in specific asthma patient populations prior to commercial launch to aid in the successful repositioning of the product as well as to support the use of the product in the target markets.

**Critical Care: The Inflammatory Response**

We are developing product candidates directed towards the inflammatory response that we believe is responsible for the single or multiple organ failures often seen in patients admitted to the emergency room or the intensive care unit, or ICU. Our product development programs in this area center on cytokines and other inflammatory mediators that play a key role in regulating the body's immune system. We believe that the cytokine cascade is responsible for the severe inflammatory response seen in:

acute diseases and conditions that lead to admission to the ICU, such as sepsis, septic shock, post surgical ileus, the damage to vital organs resulting from cardiopulmonary bypass during surgery, trauma and burns; and

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acute exacerbations of chronic diseases that frequently lead to hospitalization, such as rheumatoid arthritis, Crohn's disease, acute pancreatitis and ulcerative colitis.

In the setting of severe infection, trauma, severe bleeding or a lack of oxygen to the major organs of the body, the overproduction of inflammatory mediators, including cytokines, can lead to organ failure, tissue destruction and, eventually, death. When cytokine levels become elevated, an excessive inflammatory response occurs that may potentially result in damage to vital internal organs and, in the most severe cases, may result in multiple organ failure and death. While TNF is the first cytokine released during the cytokine cascade, the transient nature of its release leaves only a short window of opportunity for therapy. Many previous therapies directed at TNF in acute diseases have failed in clinical development. The failure of such therapies may be a consequence of the fact that the cytokine cascade comprises many different cytokines, including HMGB1, which is believed to be released late in the inflammatory response and acts as the final common pathway to sickness and death.

Individual programs within our portfolio, while targeted toward the inflammatory response, exert their effects through different mechanisms of action. These programs include:

a CTI-01 program directed towards the development of a small molecule product candidate that directly affects the release of cytokines through a number of different mechanisms;

an HMGB1 program directed towards a newly-discovered pro-inflammatory cytokine, HMGB1; and

a cholinergic anti-inflammatory program directed towards a receptor that we believe regulates the release of the cytokines that play a fundamental role in the inflammatory response, including TNF, in response to an inflammatory stimulus.

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We believe the probability of success of any one of our programs is not directly dependent upon the success or failure of any of our other programs. We believe our therapeutic approaches provide multiple opportunities for success and may increase the productivity of our research and development efforts. The programs we currently have directed towards the inflammatory response are as follows:

***CTI-01 Program***

We are developing a small molecule, CTI-01, that we believe may be effective in regulating the inflammatory response in addition to its known antioxidant activity. We plan to develop CTI-01 for at least one disease or condition such as organ damage resulting from cardiopulmonary bypass or post-operative ileus. In animal studies, CTI-01 has improved organ function or survival in a number of models of critical illness. In these studies, CTI-01 was effective when the drug was administered after disease onset, as well as in preventative administration when the drug was administered before disease onset. CTI-01 has demonstrated positive responses in animal models of restricted blood supply to the intestines, severe bleeding, overwhelming bacterial infection and acute intestinal injury.

Scientific research suggests that CTI-01 inhibits the systemic release of a number of cytokines that play a fundamental role in the inflammatory response, including TNF and HMGB1. Many of these cytokines are responsible for the severe inflammatory response that contributes to organ damage. Research shows CTI-01 inhibits the activation of inflammatory signaling pathways, the activation of a number of pro-inflammatory genes and the release of the late-acting cytokine HMGB1, both *in vivo* and *in vitro*.

***Therapeutic Opportunity***

Our current formulation of CTI-01 is an intravenous infusion best administered in diseases and conditions that enable a central line to be utilized to deliver the drug to the patients' bloodstream via a large vein. We believe this product candidate to be best suited for diseases and conditions with the inflammatory response as the underlying complication and where patients already have central lines inserted for medical care. Potential opportunities for CTI-01 include:

damage to vital organs that can occur in patients after cardiopulmonary bypass, a procedure commonly performed during cardiothoracic surgery; and

post-operative ileus, which is the loss of normal contractile movement in the intestine due to inflammation of the muscle layers of the intestine after abdominal surgery, which is one of the major reasons why patients stay in the hospital after surgery.

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*Clinical Trials*

In 2003, we conducted a Phase I clinical trial of CTI-01 in healthy volunteers in the United Kingdom. The trial consisted of two phases, a phase designed to evaluate the highest dose that can be given before experiencing unwanted drug effects followed by an endotoxin challenge model designed to investigate whether CTI-01 would affect cytokine production. The results from the completed trial indicated:

a reduction in the TNF response to bacterial endotoxin challenge compared to placebo; and

a maximum tolerated dose of 160mg/kg infused over 12 hours.

At doses above the maximum tolerated dose, human volunteers in the trial experienced local irritation in the vein at the infusion site. In 2004, we conducted a second Phase I clinical trial in healthy volunteers in the United States. In this trial, in order to avoid the local venous irritation, CTI-01 was administered using a PICC line, or peripherally inserted central catheter line, positioned in a larger vein where faster bloodflow rates caused a more rapid dispersal of CTI-01 into the bloodstream. By overcoming the local irritation issue, we were able to deliver higher doses of CTI-01 to the volunteers. The results from the completed trial demonstrated that doses of up to 75 mg/kg could be infused over 30 minutes without significant side effects and enabled us to select a dose for use in a Phase II clinical trial.

In February 2005, we initiated a Phase II clinical trial to determine the safety and efficacy of CTI-01 in the prevention of organ damage in patients undergoing major cardiac surgery involving the use of cardiopulmonary bypass, such as coronary bypass graft and/or valve replacement or repair. This double-blind, randomized, placebo-controlled trial is being conducted at multiple centers in the United States, and we expect to complete enrollment by the end of 2005.

***HMGB1 Program***

We are evaluating mechanisms to prevent HMGB1 from effecting its role in inflammation-mediated diseases. HMGB1 has been identified as a potential late mediator of inflammation-induced tissue damage. Unlike other previously identified cytokines, such as interleukin-1 and TNF, HMGB1 is expressed much later in the inflammatory response and persists at elevated levels for a longer time period and we believe therefore is a unique target for the development of products to treat inflammation-mediated diseases.

In 2003, we entered into an exclusive license and collaboration agreement with MedImmune to jointly develop and commercialize products directed towards HMGB1. In January 2005, we entered into a collaboration with Beckman Coulter to develop a diagnostic that could be used to identify which patients have elevated levels of HMGB1 and would, therefore, be most likely to respond to anti-HMGB1 therapy.

Our internal research programs are currently aimed at generating antibodies that can neutralize circulating HMGB1 prior to it binding to its receptor. We have developed in our laboratories monoclonal antibodies directed towards HMGB1 that are currently in preclinical development. We intend to initiate small molecule programs directed towards HMGB1 once we are able to fully characterize its receptor.

*Therapeutic Opportunity*

We believe that HMGB1's delayed and prolonged expression offers a new target for the development of products with a significantly broader treatment window than TNF for acute diseases that can result in multiple organ failure, including sepsis and septic shock, and acute exacerbations of chronic diseases associated with the inflammatory response mediated by cytokines, such as rheumatoid arthritis.

Sepsis is the body's systemic inflammation response to infection or trauma. In animal models of septic shock, both polyclonal and monoclonal antibodies targeting HMGB1 were successful in significantly reducing the mortality rate associated with these models. To date, limited clinical investigations have identified that patients with sepsis have elevated levels of HMGB1 in their bloodstream, compared to normal individuals, who do not have detectable levels of HMGB1 in their bloodstream. The elevated HMGB1 levels appeared to be greatest in the patients who subsequently died as a result of their disease.

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Similar treatment opportunities also exist with other diseases that include an HMGB1 component, such as rheumatoid arthritis. Elevated levels of HMGB1 have been observed in the synovial fluid in the joints of rheumatoid arthritis patients, and positive symptom responses have been achieved in animal models of rheumatoid arthritis with anti-HMGB1 therapy.

### *Clinical Strategy*

We have generated a number of monoclonal antibodies that bind to HMGB1 and that are active *in vitro* and *in vivo*. A number of these antibodies have demonstrated a dose-dependent benefit on survival in a mouse model of overwhelming infection and a reduction in clinical arthritis symptoms in a mouse rheumatoid arthritis model. In both of these tests, the monoclonal antibodies were administered in a treatment model after disease onset, as opposed to the preventive model in which the drug is administered before disease onset.

We are currently collaborating with MedImmune in the further preclinical investigation of our monoclonal antibodies in a number of animal models. MedImmune is conducting programs necessary to advance potential product candidates into Phase I clinical trials of the lead product candidate. Together with MedImmune, we plan to develop product candidates in parallel for both acute and chronic diseases and conditions.

We are still investigating the receptor for HMGB1, and we plan to commence programs directed towards small molecules that block this receptor once we have isolated and fully characterized the receptor.

### ***Cholinergic Anti-inflammatory Program***

Stimulation of the vagus nerve, a nerve that links the brain with the major organs of the body, causes the release of a chemical neurotransmitter called acetylcholine. Acetylcholine has been shown to inhibit the release of cytokines that play a fundamental role in the inflammatory response, including TNF $\alpha$ . Research indicates that acetylcholine exerts anti-inflammatory activity by stimulating the nicotinic  $\alpha 7$  cholinergic receptor, or  $\alpha 7$  receptor, on the macrophage cell.

Historically, a number of companies have focused on the  $\alpha 7$  receptor target in the treatment of central nervous system, or CNS, diseases. We believe the discovery of the role of this receptor in inflammation has led to a new opportunity for the development of products to treat diseases in which inflammation plays a role. We are undertaking both a program to develop a small molecule product that inhibits the inflammatory response by acting on the  $\alpha 7$  receptor on human macrophage cells and a program to develop an electrical device to stimulate the vagus nerve to inhibit the release of proinflammatory cytokines.

### *Therapeutic Opportunity*

Our successful development of a product candidate targeting the  $\alpha 7$  receptor could lead to a novel treatment for severe acute inflammatory disease, as well as an oral anti-cytokine therapy that could be directed at chronic inflammatory diseases such as rheumatoid arthritis and Crohn's disease. We believe the previous work on this receptor will assist the discovery of new, peripherally acting drugs that stimulate the  $\alpha 7$  receptor. We believe a drug candidate taken orally could have a strong market position against current injectable anti-TNF $\alpha$  biological therapies, particularly if it avoids the potential immunological response to therapy, which is a known risk with antibody products.

### *Development Strategy*

**Small Molecule.** We are currently seeking to develop novel, small molecules directed towards the  $\alpha 7$  receptor. In September 2004, we licensed from the University of Florida access to a family of molecules known to be active against the  $\alpha 7$  receptor. We are currently conducting preclinical evaluation



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of these molecules in animal models of cytokine-mediated disease to determine the extent of their activity against this receptor.

*Electronic Vagal Stimulation.* We are also exploring the development of a medical device, similar to those already marketed for the treatment of epileptic seizures, to stimulate the vagus nerve, cause the release of acetylcholine and induce an anti-inflammatory response. We would develop this device only with a collaborator who has direct experience in device development and commercialization. Vagus nerve stimulators are currently approved and used for the treatment of epileptic seizures in the United States. Electronic vagal stimulation may provide a novel option for the treatment of acute exacerbations of rheumatoid arthritis, Crohn's disease, ulcerative colitis and pancreatitis.

## **Collaborations**

### ***MedImmune Collaboration***

In July 2003, we entered into an exclusive license and collaboration agreement with MedImmune to jointly develop products directed towards HMGB1. Under the terms of the agreement, we granted MedImmune an exclusive worldwide license, under patent rights and know-how controlled by us, to make, use and sell products, including small molecules and antibodies, that bind to, inhibit or inactivate HMGB1 and are used in the treatment or prevention, but not the diagnosis, of diseases, disorders and medical conditions.

We and MedImmune determine the extent of our collaboration on research and development matters each year upon the renewal of a rolling three-year research plan. We are currently working with MedImmune to evaluate the potential of a series of mouse monoclonal antibodies, discovered and cloned at our laboratories, as agents for development as therapeutic antibodies to enable them to enter clinical development. Under the terms of the agreement, MedImmune has agreed to fund and expend efforts to research and develop at least one HMGB1-inhibiting product for two indications through specified clinical phases.

Under the collaboration, MedImmune has paid us initial fees of \$12.5 million. We may also receive under the collaboration research and development payments from MedImmune, including a minimum of \$3.0 million of research and development payments for the first three years of the agreement, of which \$1.5 million had been paid by December 31, 2004. In addition, we may receive, subject to the terms and conditions of the agreement, other payments upon the achievement of research, development and commercialization milestones up to a maximum of \$124.0 million, after taking into account payments that we are obligated to make to North Shore-Long Island Jewish Research Institute on milestone payments we receive from MedImmune. MedImmune also has agreed to pay royalties to us based upon net sales by MedImmune of licensed products resulting from the collaboration. MedImmune's obligation to pay us royalties continues on a product-by-product and country-by-country basis until the later of ten years from the first commercial sale of a licensed product in each country and the expiration of the patent rights covering the product in that country. We are obligated to pay a portion of any milestone payments or royalties we receive from MedImmune to North Shore, which initially licensed to us patent rights and know-how related to HMGB1. In connection with entering into the collaboration agreement, an affiliate of MedImmune purchased an aggregate of \$15.0 million of our series B convertible preferred stock in October 2003 and March 2004, which converted into 2,857,142 shares of our common stock in June 2004 in connection with our initial public offering.

We have agreed to work exclusively with MedImmune in the research and development of HMGB1-inhibiting products. Under the terms of the agreement, MedImmune's license to commercialize HMGB1-inhibiting products generally excludes us from manufacturing, promoting or selling the licensed products. However, we have the option to co-promote in the United States the first product for the first indication approved in the United States, for which we must pay a portion of the ongoing development costs and will receive a proportion of the profits in lieu of royalties that would otherwise be owed to us.

MedImmune has the right to terminate the agreement at any time on six-months written notice. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the

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other party. Under specified conditions, we or MedImmune may have certain payment or royalty obligations after the termination of the agreement.

***Beckman Coulter Collaboration***

In January 2005, we entered into a license agreement with Beckman Coulter relating to the development of diagnostic products for measuring HMGB1. Under the terms of the agreement, we granted to Beckman Coulter and its affiliates an exclusive worldwide license, under patent rights and know-how controlled by us relating to the use of HMGB1 and its antibodies in diagnostics, to evaluate, develop, make, use and sell a kit or assemblage of reagents for measuring HMGB1 that utilizes one or more monoclonal antibodies to HMGB1 developed by us or on our behalf.

In consideration for the license, Beckman Coulter paid us a product evaluation license fee of \$250,000. Under the agreement, we may also receive additional aggregate license fees of up to \$850,000 upon the exercise by Beckman Coulter of its option to continue the license prior to a future date and the achievement of the first commercial sale of a licensed product. Beckman Coulter also agreed to pay us royalties based on net sales of licensed products by Beckman Coulter and its affiliates. Beckman Coulter has the right to grant sublicenses under the license, subject to our written consent, which we have agreed not to unreasonably withhold. In addition, Beckman Coulter agreed to pay us a percentage of any license fees, milestone payments or royalties actually received by Beckman Coulter from its sublicensees.

The license agreement will terminate if Beckman Coulter does not exercise its option to continue the license by a future date. In addition, Beckman Coulter has the right to terminate the license agreement at any time on 90-days written notice. Each party has the right to terminate the license agreement upon the occurrence of a material uncured breach by the other party.

**Research and Development**

We believe that our research and development capabilities and our sponsored research arrangements position us well to sustain our product pipeline. As of December 31, 2004, we had 34 employees engaged in research, development and regulatory affairs. Our research and development group seeks to identify the most promising development candidates and the most appropriate development pathways to maximize our chances of successful development. We also augment our internal research capabilities through sponsored research arrangements with academic and research institutions and individual academics, as well as in-licensed product candidates and technologies.

During the fiscal years ended December 31, 2002, 2003 and 2004, research and development expenses were \$3.3 million, \$17.5 million and \$25.6 million, respectively.

**Sales and Marketing**

We plan to develop a sales and marketing infrastructure to commercialize ZYFLO and the controlled-release formulation of zileuton in the United States. We believe that, by developing a sales and marketing infrastructure to commercialize zileuton, we will have a seasoned organization in place that we can leverage if and when we launch any future respiratory or critical care products. Accordingly, we have hired Frederick Finnegan as our Senior Vice President of Sales and Marketing, four regional sales directors and a national director for managed care to lead the development of this infrastructure. Mr. Finnegan has significant sales and marketing experience from previous roles at biotechnology and large and small pharmaceutical companies.

We intend to focus our sales and marketing efforts for zileuton on key opinion leaders and specialists who treat asthma, including allergists, pulmonologists and ENTs, or ear, nose and throat surgeons. Because we expect to target our marketing and sales efforts to the moderate to severe asthma market, we believe we can successfully focus our efforts with a relatively small sales force on the approximately 16,000 specialists who tend to treat the majority of these patients. These specialists include a top tier of 100 to 200 national or key opinion leaders who serve to influence the direction of the diagnosis and treatment of

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asthma through their research and publications, and a second tier of practice-based specialists who are responsible for treating the majority of patients.

Given the importance of these key opinion leaders, we plan to direct our scientific message and support to help educate and inform key opinion leaders regarding the scientific rationale and data that support our commercialization strategy. Initially, we will enter into consulting arrangements with approximately ten key opinion leaders who will comprise our expert panel. After our expert panel has been formed, we intend to expand our reach to 100 to 200 key opinion leaders through a group of medical liaisons who will be directed by our chief medical officer.

We plan to initiate contact with the second tier of practice-based specialists when we launch our sales force. In the first two years following the launch of our sales force, we do not expect to contact every practicing specialist who treats asthma. Instead, we expect to target the top 50% of specialists in terms of prescribing productivity within asthma and the top 400 to 500 physicians prescribing ZYFLO. As we expand our sales force, we expect to expand our reach to the top 70% to 80% of specialists who treat asthma.

Part of our overall strategy for zileuton also includes repositioning the product within the managed care market. We intend to position zileuton with managed care medical directors and pharmacists as a treatment alternative when medications have failed to provide adequate symptomatic control. As a result, in addition to the awareness provided by office-based representatives, we believe information regarding zileuton will reach potential prescribing physicians through managed care pharmacies communicating the product's modified formulary status.

We expect that our sales effort for zileuton will expand if we develop and obtain regulatory approval for the intravenous formulation of zileuton for urgent and inpatient treatment of acute exacerbations of asthma. We believe the launch of an intravenous formulation will increase awareness of zileuton among those primary care physicians, or PCPs, whose patients are prescribed zileuton after a visit to the emergency room due to an acute exacerbation of asthma. In addition, we intend to seek a co-promotion partner for the controlled-release and immediate-release formulations of zileuton who would take responsibility to promote zileuton to PCPs. We believe these efforts should enable us to migrate our sales and marketing focus and activities from solely office-based specialists to include the hospital products marketplace.

**Manufacturing**

We have no experience in, and we do not own any facilities for, manufacturing our product candidates. We currently outsource the manufacturing of our product candidates for use in clinical trials to qualified third parties and intend to continue to rely on contract manufacturing from third parties to supply products for both clinical use and commercial sale.

Prior to licensing zileuton to us, Abbott maintained its own manufacturing capabilities for ZYFLO. Under the terms of our license agreements, Abbott agreed to transfer its know-how and technology for the manufacture and validation of zileuton API and the immediate-release and controlled-release formulations of zileuton and the manufacturing process to us or a designated third party. We have established the following manufacturing arrangements for zileuton.

***Rhodia***

We have contracted with Rhodia Pharma Solutions Ltd. to establish and validate a manufacturing process for the API at sites operated by Rhodia. The technology transfer to Rhodia has been completed and Rhodia is validating the API manufacturing process and preparing to commence commercial production. In February 2005, we entered into a commercial supply agreement with Rhodia for the commercial production of the API. Under the commercial supply agreement, Rhodia has agreed to manufacture our commercial supplies of API, subject to specified limitations, through December 31, 2009. The agreement will automatically extend for successive one-year periods after December 31, 2009, unless

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Rhodia provides us with 18-months prior written notice of cancellation. We have the right to terminate the agreement upon 12-months prior written notice for any reason, provided that we may not cancel prior to January 1, 2008 for the purpose of retaining any other company to act as our exclusive supplier of the API. We also have the right to terminate the agreement upon six-months prior written notice if we terminate our plans to commercialize zileuton for all therapeutic indications. If we exercise our right to terminate the agreement prior to its scheduled expiration, we are obligated to reimburse Rhodia for specified raw material and out-of-pocket costs. In addition, if we exercise our right to terminate the agreement due to termination of our plans to commercialize zileuton for all therapeutic indications, then we are also obligated to pay Rhodia for all API manufactured by Rhodia through that date. Furthermore, each party has the right to immediately terminate the agreement for cause, including a material uncured default by the other party.

***Patheon***

We have contracted with Patheon Pharmaceuticals Inc. for the manufacture of ZYFLO for clinical trials and regulatory review. The agreement with Patheon has no specified term, and we can terminate the agreement at any time for any reason, subject to payment of fees and expenses incurred by Patheon through the date of termination. Patheon may deem the agreement to be terminated if any rescheduling of services requested by us results in a delay in Patheon's ability to provide services beyond 120 days. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party. In addition to this agreement, we have initiated discussions with Patheon for an agreement relating to the ongoing manufacture of commercial supplies of ZYFLO.

***SkyePharma***

We have contracted with SkyePharma PLC, through its subsidiary Jagotec AG, for the manufacture of the controlled-release tablet formulation of zileuton for clinical trials, regulatory review and commercial sale. SkyePharma has agreed to manufacture the commercial supplies of the controlled-release formulation of zileuton, upon FDA approval, under a manufacturing agreement that we would enter into with SkyePharma having a term of no less than five years. SkyePharma's current manufacturing obligations for the controlled-release formulation of zileuton are reflected in our license agreement relating to our use of SkyePharma's controlled-release patent rights and know-how. Both we and SkyePharma have the right to terminate that license agreement upon the occurrence of a material uncured breach by the other party. We have separately contracted with SkyePharma to help establish a manufacturing process for ZYFLO and, if needed, to manufacture ZYFLO for clinical trials and regulatory review. In consideration for SkyePharma's manufacturing and development services, we agreed to pay SkyePharma an upfront fee of \$250,000 and additional amounts on a time and materials basis. Both we and SkyePharma have the right to terminate the contract upon the occurrence of a material uncured breach by the other party, upon a change of control of the other party or, with the consent of the other party, if results achieved during testing or other technical, medical or scientific problems reasonably require termination. We also have the right to terminate the contract upon 120-days prior notice.

We expect to enter into manufacturing arrangements with third parties for the manufacture of our other product candidates for clinical use. For example, we will need to enter into arrangements for the manufacture of products for clinical trials in our cholinergic anti-inflammatory and CTI-01 programs. We believe that MedImmune will be responsible for manufacturing of any biologic products that result from our HMGB1 program.

**License and Royalty Agreements**

We have entered into a number of license agreements under which we have licensed intellectual property and other rights needed to develop our products, including the license agreements summarized below.

**Table of Contents*****Abbott***

In December 2003, we acquired an exclusive worldwide license, under patent rights and know-how controlled by Abbott, to develop, make, use and sell controlled-release and intravenous formulations of zileuton for all clinical indications, except for the treatment of children under age seven and use in cardiovascular and vascular devices. This license included an exclusive sublicense of Abbott's rights in proprietary controlled-release technology originally licensed to Abbott by Jagotec AG, a subsidiary of SkyePharma. In consideration for the license, we paid Abbott an initial \$1.5 million license fee and agreed to make aggregate milestone payments of up to \$13.0 million to Abbott upon the achievement of various development and commercialization milestones, including the completion of the technology transfer from Abbott to us, filing and approval of a product in the United States and specified minimum net sales of licensed products. In addition, we agreed to pay royalties to Abbott based on net sales of licensed products by us, our affiliates and sublicensees. Our obligation to pay royalties continues on a country-by-country basis for a period of ten years from the first commercial sale of a licensed product in each country. Upon the expiration of our obligation to pay royalties for licensed products in a given country, the license will become perpetual, irrevocable and fully paid up with respect to licensed products in that country. If we decide to sublicense rights under the license, we must first enter into good faith negotiations with Abbott for the commercialization rights to the licensed product. Each party has the right to terminate the license upon the occurrence of a material uncured breach by the other party. We also have the right to terminate the license at any time upon 60 days notice to Abbott and payment of a termination fee.

In March 2004, we acquired from Abbott the U.S. trademark ZYFLO® and an exclusive worldwide license, under patent rights and know-how controlled by Abbott, to develop, make, use and sell the immediate-release formulation of zileuton for all clinical indications. In consideration for the license and the trademark, we have agreed to pay Abbott an initial fee of \$500,000, a milestone payment of \$750,000 upon approval of the sNDA, and royalties based upon net sales of licensed products by us, our affiliates and sublicensees. Our obligation to pay royalties continues on a country-by-country basis for a period of ten years from the first commercial sale of a licensed product in each country. Upon the expiration of our obligation to pay royalties in a given country, the license will become perpetual, irrevocable and fully paid up with respect to licensed products in that country. Each party has the right to terminate the license upon the occurrence of a material uncured breach by the other party.

***SkyePharma***

In December 2003, we entered into an agreement with SkyePharma, through its subsidiary Jagotec, under which SkyePharma consented to Abbott's sublicense to us of rights to make, use and sell the controlled-release formulation of zileuton covered by SkyePharma's patent rights and know-how. Under the terms of the agreement, SkyePharma also agreed to manufacture the controlled-release formulation of zileuton for clinical trials, regulatory review and, subject to negotiation of a commercial manufacturing agreement, commercial sale. In consideration for SkyePharma's prior work associated with the licensed patent rights and know-how, we paid SkyePharma an upfront fee of \$750,000. We also agreed to make aggregate milestone payments to SkyePharma of up to \$6.6 million upon the achievement of various development and commercialization milestones. In addition, we agreed to pay royalties to SkyePharma based upon net sales of the product by us and our affiliates. We also agreed to pay royalties to SkyePharma under the license agreement between SkyePharma and Abbott based upon net sales of the product by us and our affiliates. We also agreed to pay SkyePharma fees if we sublicense our rights under the licensed patent rights and know-how. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party.

***North Shore***

In July 2001, we acquired from North Shore an exclusive worldwide license, under patent rights and know-how controlled by North Shore relating to HMGB1, to make, use and sell products covered by the licensed patent rights and know-how. North Shore retained the right to make and use the licensed products in its own laboratories solely for non-commercial, scientific purposes and non-commercial

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research. In consideration for the license, we paid an initial license fee of \$100,000. We also agreed to make milestone payments to North Shore of up to \$275,000 for the first product covered by the licensed patent rights and an additional \$100,000 for each additional distinguishable product covered by the licensed patent rights, up to \$137,500 for the first product covered by the licensed know-how and not the licensed patent rights and an additional \$50,000 for each additional distinguishable product covered by the licensed know-how and not the licensed patent rights, in each case upon the achievement of specified development and regulatory milestones for the applicable licensed product. In addition, we agreed to pay North Shore royalties based on net sales of licensed products by us and our affiliates until the later of ten years from the first commercial sale of each licensed product in a given country and the expiration of the patent rights covering the licensed product in that country. We agreed to pay minimum annual royalties to North Shore beginning in July 2007 regardless of whether we sell any licensed products. We also agreed to pay North Shore fees if we sublicense our rights under the licensed patent rights and know-how. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party.

We also have entered into two sponsored research and license agreements with North Shore. In July 2001, we entered into a sponsored research and license agreement with North Shore under which, as amended, we agreed to pay North Shore \$200,000 annually until June 2006 to sponsor research activities at North Shore to identify inhibitors and antagonists of HMGB1 and related proteins, including antibodies. In January 2003, we entered into a sponsored research and license agreement with North Shore under which we agreed to pay North Shore \$200,000 annually until January 2006 to sponsor research activities at North Shore in the field of cholinergic anti-inflammatory technology. Any future research terms under either of these agreements are subject to agreement between North Shore and us. Under the terms of these agreements, we acquired an exclusive worldwide license to make, use and sell products covered by the patent rights and know-how arising from the sponsored research. North Shore retained the right under each of these agreements to make and use the licensed products in its own laboratories solely for non-commercial, scientific purposes and non-commercial research.

In connection with the July 2001 sponsored research and license agreement, we issued North Shore 27,259 shares of our common stock and agreed to make milestone payments to North Shore of \$200,000 for the first product covered by the licensed patent rights, and an additional \$100,000 for each additional distinguishable product covered by the licensed patent rights, \$100,000 for the first product covered by the licensed know-how and not the licensed patent rights and an additional \$50,000 for each additional distinguishable product covered by the licensed know-how and not the licensed patent rights, in each case upon the achievement of specified development and regulatory approval milestones with respect to the applicable licensed product. In connection with the January 2003 sponsored research and license agreement, we paid North Shore an initial license fee of \$175,000 and agreed to pay additional amounts in connection with the filing of any U.S. patent application or issuance of a U.S. patent relating to the field of cholinergic anti-inflammatory technology. We also agreed to make aggregate milestone payments to North Shore of up to \$1.5 million in both cash and shares of our common stock upon the achievement of specified development and regulatory approval milestones with respect to any licensed product. In addition, under each of these agreements, we agreed to pay North Shore royalties based on net sales of a licensed product by us and our affiliates until the later of ten years from the first commercial sale of licensed products in a given country and the expiration of the patent rights covering the licensed product in that country. Under the January 2003 sponsored research and license agreement, we agreed to pay minimum annual royalties to North Shore beginning in the first year after termination of research activities regardless of whether we sell any licensed products. We also agreed to pay North Shore certain fees if we sublicense our rights under the licensed patent rights and know-how under either agreement. In connection with our sublicense to MedImmune of our rights with respect to HMGB1, we have paid North Shore \$2.0 million and issued to North Shore 66,666 shares of our common stock. Each party has the right to terminate each agreement upon the occurrence of a material uncured breach of that agreement by the other party.

**Table of Contents*****University of Florida***

In September 2004, we acquired from the University of Florida an exclusive worldwide license, under specified patent rights controlled by the University relating to a family of compounds known as cinnamylidene-anabaseines, to make, use and sell products covered by the licensed patent rights. These compounds target and stimulate the nicotinic alpha-7 cholinergic receptor. In consideration for the license, we agreed to pay an initial license fee and milestone payments upon the achievement of specified development and regulatory milestones for the licensed product. We also agreed to make certain minimum royalty payments during the term of the agreement and royalty payments based on net sales of a licensed product by us and our sublicensees. The University has the right to terminate the agreement upon our material uncured breach, including our failure to meet specified development and commercialization milestones for a licensed product. We may terminate the agreement upon 60-days notice to the University.

***University of Pittsburgh***

In November 2002, we acquired from the University of Pittsburgh an exclusive worldwide license, under specified patent rights controlled by the University relating to CTI-01, to make, use and sell products covered by the licensed patent rights. The University retained the right to use the licensed patent rights and products for its own non-commercial education and research purposes. In consideration for the license, we paid an initial license fee of \$35,000 and also agreed to pay the University annual maintenance fees until the first commercial sale of a licensed product. After the first commercial sale, we have agreed to pay the University royalties based on net sales of the licensed product by us and our sublicensees. The University has the right to terminate the agreement upon our material uncured breach, including our failure to meet specified development and commercialization milestones for a licensed product. We may terminate the agreement upon three-months notice to the University.

***Xanthus***

In December 2000, we acquired from Xanthus Life Sciences, formerly known as Phenome Sciences, an exclusive worldwide license, under specified patent rights and know-how controlled by Xanthus relating to CTI-01, to make, use and sell products covered by the licensed patent rights and know-how. Xanthus retained the right to use the licensed patent rights for non-commercial research purposes. In consideration for the license, we paid an initial license fee of \$103,000. We also agreed to use diligent efforts to achieve specified development and regulatory approval milestones and make aggregate milestone payments to Xanthus of up to \$2.0 million upon the achievement of those milestones. In addition, we agreed to pay Xanthus royalties based on net sales of licensed products by us and our sublicensees until the expiration of the patent rights covering the licensed product. We agreed to pay minimum annual royalties to Xanthus beginning in 2006 regardless of whether we sell any licensed products. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party. In specified circumstances, we may also terminate the agreement upon either three or twelve-months notice to Xanthus.

***Baxter***

In June 2004, we entered into an agreement with Baxter Healthcare Corporation to conduct feasibility studies to analyze the various properties of zileuton and determine the most suitable technologies for the development of an intravenous formulation of zileuton. In the event that we choose to pursue the commercialization of a specified intravenous formulation developed by Baxter that is based on the formulation technology of a third party, we have agreed to license that specified intravenous formulation and pay Baxter royalties based on net sales of that formulation.

**Proprietary Rights**

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our

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proprietary technology, inventions and improvements that are important to the development of our business and obtaining, where possible, assignment of invention agreements from employees and consultants. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We own or exclusively license a total of 22 issued U.S. patents, 42 issued foreign patents, 29 pending U.S. patent applications and 73 pending foreign patent applications consisting of:

	U.S.		Foreign		Program Total
	Issued	Pending	Issued	Pending	
Zileuton	15	1	36	9	61
HMGB1	3	13		27	43
CTI-01	1	6	1	24	32
Cholinergic anti-inflammatory	3	9	5	13	30
<b>Total</b>	<b>22</b>	<b>29</b>	<b>42</b>	<b>73</b>	<b>166</b>

The U.S. patent covering the composition of matter of zileuton that we licensed from Abbott expires in 2010, and the U.S. patent covering the controlled-release formulation of zileuton expires in 2012. The U.S. issued patents that we own or exclusively license covering our product candidates other than zileuton expire on various dates between 2017 and 2021.

The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. Our success depends, in part, on our ability to protect proprietary products, methods and technologies that we develop under the patent and other intellectual property laws of the United States and other countries, so that we can prevent others from using our inventions and proprietary information. If any parties should successfully claim that our proprietary products, methods and technologies infringe upon their intellectual property rights, we might be forced to pay damages, and a court could require us to stop the infringing activity. We do not know if our pending patent applications will result in issued patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. In addition, the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

***Trademarks, Trade Secrets and Other Proprietary Information***

We currently have filed trademark applications to register the Critical Therapeutics name and logo in both the United States and Europe. We have also filed trademark applications to register CT1 and CT2 in the United States. In March 2004, we acquired the U.S. trademark ZYFLO® from Abbott.

In addition, we depend upon trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, it is our general practice to enter into confidentiality agreements with our employees, consultants, strategic partners, outside scientific collaborators and sponsored researchers and other advisors. These agreements are designed to protect our proprietary information. These agreements are designed to deter, but may not prevent, unauthorized disclosure of our trade secrets, and any such unauthorized disclosure would have a material adverse effect on our business, for which monetary damages from the party making such unauthorized disclosure may not be adequate to compensate us.





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**Regulatory Matters**

The research, testing, manufacture and marketing of drug and biologic products and medical devices are extensively regulated in the United States and abroad. In the United States, drugs, biologics and medical devices are subject to rigorous regulation by the FDA. The Federal Food, Drug and Cosmetic Act and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, record keeping, packaging, labeling, advertising and promotion, marketing and distribution of pharmaceutical and biologic products and medical devices. The failure to comply with the applicable regulatory requirements may subject us to a variety of administrative or judicially imposed sanctions, including the FDA's refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

The steps ordinarily required before a new pharmaceutical or biologic product may be marketed in the United States include preclinical laboratory tests, animal tests and formulation studies, the submission to the FDA of an investigational new drug application, or IND, which must become effective prior to commencement of human clinical testing, and adequate and well-controlled clinical trials to establish that the product is safe and effective for the indication for which FDA approval is sought. Satisfaction of FDA approval requirements typically takes several years and the actual time taken may vary substantially depending upon the complexity of the product or disease. Government regulation may impose costly procedures on our activities, and may delay or prevent marketing of potential products for a considerable period of time or prevent such marketing entirely. Success in early stage clinical trials does not necessarily assure success in later stage clinical trials. Data obtained from clinical activities are not always conclusive and may be subject to alternative interpretations that could delay, limit or even prevent regulatory approval. Even if a product receives regulatory approval, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

Preclinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and efficacy of the product. The conduct of the preclinical tests and formulation of compounds for testing must comply with federal regulations and requirements. The results of preclinical testing are submitted to the FDA as part of an IND.

An IND must become effective prior to the commencement of clinical testing of a drug or biologic in humans. An IND will automatically become effective 30 days after receipt by the FDA if the FDA has not commented on or questioned the application during this 30-day waiting period. If the FDA has comments or questions, these must be resolved to the satisfaction of the FDA prior to commencement of clinical trials. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The IND process can result in substantial delay and expense.

Clinical trials involve the administration of the investigational new drug or biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and requirements, under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the safety and effectiveness criteria to be evaluated. Each protocol involving testing on subjects in the United States must be submitted to the FDA as part of the IND. The trial protocol and informed consent information for patients in clinical trials must be submitted to institutional review boards for approval.

Clinical trials to support new drug or biologic product applications for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the product into healthy human subjects or patients, the product is tested to assess metabolism, pharmacokinetics and pharmacological actions and safety, including side effects associated with increasing doses. Phase II usually involves trials in a limited patient population, to determine dosage tolerance and optimum dosage, identify possible adverse effects and safety risks, and provide preliminary support for the efficacy of the product in the indication being studied.

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If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase II evaluations, Phase III trials are undertaken to evaluate further clinical efficacy and to test further for safety within an expanded patient population, typically at geographically dispersed clinical trial sites. Phase I, Phase II or Phase III testing of any product candidates may not be completed successfully within any specified time period, if at all. Furthermore, the FDA, an institutional review board or we may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

After successful completion of the required clinical testing for a drug, generally an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of extensive clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of NDAs are additionally subject to substantial application user fees, currently exceeding \$600,000, the fee for submission of supplemental applications exceeds \$300,000 and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees, currently exceeding \$40,000 per product and \$200,000 per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. The FDA normally also will conduct a pre-approval inspection to ensure the manufacturing facility, methods and controls are adequate to preserve the drug's identity, strength, quality, purity and stability, and are in compliance with regulations governing current good manufacturing practices.

If the FDA's evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, an approvable letter followed by an approval letter. An approvable letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require post-approval testing and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling restrictions which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Supplemental applications must be filed for many post-approval changes, including changes in manufacturing facilities.

Some of our products may be regulated as biologics under the Public Health Service Act. Biologics must have a biologics license application, or BLA, approved prior to commercialization. Like NDAs, BLAs are subject to user fees. To obtain BLA approval, an applicant must provide preclinical and clinical evidence and other information to demonstrate that the biologic product is safe, pure and potent and that the facilities in which it is manufactured processed, packed or held meet standards, including good manufacturing practices and any additional standards in the license designed to ensure its continued safety, purity and potency. Biologics establishments are subject to preapproval inspections. The review process for BLAs is time consuming and uncertain, and BLA approval may be conditioned on post-approval testing and surveillance. Once granted, BLA approvals may be suspended or revoked under certain circumstances, such as if the product fails to conform to the standards established in the license.

Once the NDA or BLA is approved, a product will be subject to certain post-approval requirements, including requirements for adverse event reporting and submission of periodic reports. In addition, the

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FDA strictly regulates the promotional claims that may be made about prescription drug products and biologics. In particular, the FDA requires substantiation of any claims of superiority of one product over another, including that such claims be proven by adequate and well-controlled head-to-head clinical trials. To the extent that market acceptance of our products may depend on their superiority over existing therapies, any restriction on our ability to advertise or otherwise promote claims of superiority, or requirements to conduct additional expensive clinical trials to provide proof of such claims, could negatively affect the sales of our products or our costs.

We must also notify the FDA of any change in an approved product beyond variations already allowed in the approval. Certain changes to the product, its labeling or its manufacturing require prior FDA approval, including conduct of further clinical investigations to support the change. Major changes in manufacturing site require submission of an sNDA and approval by the FDA prior to distribution of the product using the change. Such supplements, referred to as Prior Approval Supplements, must contain information validating the effects of the change. An applicant may ask the FDA to expedite its review of such a supplement for public health reasons, such as a drug shortage. Approvals of labeling or manufacturing changes may be expensive and time-consuming and, if not approved, the product will not be allowed to be marketed as modified.

If the FDA's evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter. The not approvable letter outlines the deficiencies in the submission and often requires additional testing or information in order for the FDA to reconsider the application. Even after submitting this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. With limited exceptions, the FDA may withhold approval of an NDA regardless of prior advice it may have provided or commitments it may have made to the sponsor.

Once an NDA is approved, the product covered thereby becomes a listed drug that can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA. An abbreviated NDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. There is no requirement, other than the requirement for bioequivalence testing, for an abbreviated NDA applicant to conduct or submit results of preclinical or clinical tests to prove the safety or efficacy of its drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, are listed as such by the FDA, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor. During such three-year exclusivity period, the FDA cannot grant effective approval of an abbreviated NDA to commercially distribute a generic version of the drug based on that listed drug. However, the FDA can approve generic equivalents of that listed drug based on other listed drugs, such as a generic that is the same in every way but its indication for use, and thus the value of such exclusivity may be undermined. Federal law also provides a period of five years following approval of a drug containing no previously approved active ingredients. During such five-year period, abbreviated NDAs for generic versions of those drugs cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval. Additionally, in the event that the sponsor of the listed drug has properly informed the FDA of patents covering its listed drug, applicants submitting an abbreviated NDA referencing that drug are required to make one of four certifications, including certifying that it believes one or more listed patents are invalid or not infringed. If an applicant certifies invalidity or non-infringement, it is required to provide notice of its filing to the NDA sponsor and the patent holder. If the patent holder then initiates a suit for patent infringement against the abbreviated NDA sponsor within 45 days of receipt of the notice, the FDA cannot grant effective approval of the abbreviated NDA until either 30 months has passed or there has been a court decision holding that the patents in question are invalid or not infringed. If the NDA holder and patent owners do not begin an infringement action within

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45 days, the ANDA applicant may bring a declaratory judgment action to determine patent issues prior to marketing. If the abbreviated NDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then FDA cannot grant effective approval of the abbreviated NDA until those patents expire. If more than one applicant files a substantially complete ANDA on the same day for a previously unchallenged drug, each such first applicant will be entitled to share the 180-day exclusivity period, but there will only be one such period, beginning on the date of first marketing by any of the first applicants. The first abbreviated NDA submitting substantially complete applications certifying that listed patents for a particular product are invalid or not infringed may qualify for a period of 180 days after the first marketing of the generic product, during which subsequently submitted abbreviated NDAs cannot be granted effective approval.

We expect any devices that we develop for vagal nerve stimulation to be regulated as Class III medical devices subject to premarket approval, or PMA, requirements. Our diagnostic device could be subject to a PMA or to premarket 510(k) clearance. A PMA requires an applicant to prove the safety and effectiveness of a device to the FDA, and must contain clinical trial data. An investigational device exemption, or IDE, must become effective prior to commencement of clinical testing of a medical device in humans. An IDE will automatically become effective 30 days after receipt by the FDA if the FDA has not commented on or questioned the application during this 30-day period. If the FDA has comments or questions, these must be resolved to the satisfaction of the FDA prior to commencement of clinical trials. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The IDE process can result in substantial delay and expense.

After successful completion of the required clinical testing, the PMA or 510(k) is prepared and submitted to the FDA. The process of obtaining PMA approval is expensive and uncertain and includes the imposition of user fees, which currently exceed \$200,000. Among other things, PMAs must include preclinical and clinical data and manufacturing information. FDA approval of a PMA application can take years, and the agency may deny approval of an application. Any change affecting the safety or effectiveness of the device will require approval of a supplemental PMA. Premarket 510(k) clearance requires the submission to the FDA of a premarket notification, which may include clinical data. A premarket notification requires the applicant to establish that the device is substantially equivalent to a legally marketed device. The process of obtaining 510(k) clearance is expensive, uncertain and includes the imposition of user fees. 510(k) clearance is typically faster than approval of a PMA, but can take years. Any change that could significantly affect the safety or effectiveness of the device will require clearance of a new 510(k) submission. We cannot be sure that approval of a PMA or supplement or 510(k) clearance will be granted on a timely basis, if at all, or that FDA approval processes will not involve costs and delays that will adversely affect our ability to commercialize our products. We must also comply with pervasive regulation of any medical device after approval or clearance, including FDA regulation of our manufacturing practices and adverse event reporting activities. Violation of any FDA requirements could result in enforcement actions, such as withdrawal of approval, product recalls, product seizures, injunctions, total or partial suspension of production or distribution, fines, civil penalties and criminal prosecutions, which could have a material adverse effect on our business.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of drug products and medical devices. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of such changes, if any, may be.

***Foreign Regulation***

Approval of a product by comparable regulatory authorities may be necessary in foreign countries prior to the commencement of marketing of the product in those countries, whether or not FDA approval has been obtained. The approval procedure varies among countries and can involve requirements for

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additional testing. The time required may differ from that required for FDA approval. Although there are some procedures for unified filings for some European countries with the sponsorship of the country which first granted marketing approval, in general each country has its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

Under European Union regulatory systems, marketing authorization applications may be submitted at a centralized, a decentralized or a national level. The centralized procedure is mandatory for the approval of biotechnology products and provides for the grant of a single marketing authorization that is valid in all European Union member states. As of January 1995, a mutual recognition procedure is available at the request of the applicant for all medicinal products that are not subject to the centralized procedure. We will choose the appropriate route of European regulatory filing to accomplish the most rapid regulatory approvals. However, our chosen regulatory strategy may not secure regulatory approvals on a timely basis or at all.

### ***Hazardous Materials***

Our research and development processes involve the controlled use of hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. We do not expect the cost of complying with these laws and regulations to be material.

### **Competition**

The pharmaceutical and biotechnology industries in which we operate are characterized by rapidly advancing technologies and intense competition. Our competitors include pharmaceutical companies, biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. All of these competitors currently engage in or may engage in the future in the development, manufacture and commercialization of new pharmaceuticals, some of which may compete with our present or future products and product candidates. Many of our competitors have greater development, financial, manufacturing, marketing and sales experience and resources than we do, and they may develop new products or technologies that will render our products or technologies obsolete or noncompetitive. We cannot assure you that our products will compete successfully with these newly emerging technologies. In some cases, competitors will have greater name recognition and may offer discounts as a competitive tactic.

ZYFLO, our asthma product, and our controlled-release formulation of zileuton will face heavy competition in the asthma field. Many established therapies currently command large market shares in the mild to moderate asthma market. Merck's Singulair® and GlaxoSmithKline's Advair® are two widely-prescribed medicines for asthma in the United States. Singulair is a tablet taken once a day. Annual sales for Singulair in the United States are estimated to be over \$1.0 billion, and the majority of prescribing physicians are primary care physicians. Singulair costs approximately \$2.50 per day, which was approximately 10% to 12% less than the daily cost of ZYFLO when sold by Abbott. Singulair is also approved for pediatric asthma and allergic rhinitis. We believe that Singulair is prescribed less often for severe asthma patients and patients whose asthma is being managed by specialists.

Advair is an inhaled product taken twice a day that provides both bronchodilatory and anti-inflammatory benefits. Advair was launched in the United States in 2001, and annual sales are estimated to be over \$1.0 billion. The daily cost of Advair ranges from approximately \$3.50 to \$6.00 depending upon the strength of the dose. The daily costs of Advair at the lowest dose are approximately 20% more than daily cost of ZYFLO when sold by Abbott. When first launched, Advair was targeted to moderate to severe asthma where additional steroid use was often required, but is now targeted to mild to moderate asthma as well as COPD. Advair competes significantly with Singulair in the mild to moderate asthma market.

The severe asthma market, where we believe zileuton has great potential, is currently served by the therapies developed for mild to moderate asthma and oral, inhaled and injectable steroid treatments. One

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product, Xolair®, an anti-IgE antibody developed jointly by Novartis, Genentech and Tanox, recently gained approval for severe allergic asthma. Xolair is a monoclonal antibody delivered in a monthly or semi-monthly subcutaneous injection for the treatment of moderate to severe allergic asthma that acts by blocking the immunoglobulin E antibody that is an underlying cause of allergic asthma. The FDA approved the product in June 2003 and as of the end of 2004 was used to treat over 30,000 patients. Xolair is an injectable product, and the annual cost for treatment is approximately \$12,000 to \$20,000, depending on the dose. Xolair is targeted to patients with severe allergic asthma, particularly those patients who do not respond to therapies such as steroids. However, many managed care plans restrict its use through extensive prior authorization and step care requirements, such as a prior, failed course of therapy on Singulair, Accolade, Advair and/or in some cases ZYFLO, before Xolair can be considered.

If zileuton is developed as a treatment for COPD or acne, it will also face intense competition. COPD is a disease treated predominantly with asthma drugs and lung reduction surgery. Many physicians regard bronchodilators and inhaled steroids as effective in the treatment of mild to moderate COPD. Advair, which has a new approved indication for COPD, is also now being promoted as a treatment for COPD by GlaxoSmithKline. Spiriva®, a once-a-day muscarinic antagonist from Boehringer Ingelheim and Pfizer, already approved in Europe, is expected to be approved in the United States. Other novel approaches are also in the development process. GlaxoSmithKline is developing a neurokinin-3 receptor antagonist and an  $\alpha$ -4 integrin antagonist. Because both are in early development, their potential impact on the market is difficult to assess. Acne is a disease treated predominantly with antibiotics and, in the case of severe acne, retinoids. The leading branded retinoid is Roche Pharmaceutical's Accutane® (isotretinoin). Generic isotretinoin is now available from several manufacturers, and generic versions of the antibiotics used in mild to moderate forms of acne are common. Given the wide use of generic agents and the number of manufacturers competing in this category, penetration into this market will be difficult.

Our therapeutic programs directed toward the body's inflammatory response will compete predominantly with therapies that have been approved for diseases such as rheumatoid arthritis, like Amgen, Inc.'s Enbrel® and Johnson & Johnson's Remicade®, and diseases such as sepsis, such as Eli Lilly and Company's Xigris®. While non-steroidal, anti-inflammatory drugs like ibuprofen are often used for the treatment of rheumatoid arthritis and offer efficacy in reducing pain and inflammation, we believe that our cytokine-based therapeutic programs will compete predominantly with the anti-TNF $\alpha$  therapies that have been approved for diseases such as rheumatoid arthritis, like Enbrel® and Remicade®. Xigris®, a product developed by Eli Lilly for sepsis, has received regulatory approval for severe sepsis patients. Other than a wide range of anti-infective drugs, Xigris is one of the only drugs approved by the FDA for the treatment of sepsis. Other companies are developing therapies directed towards cytokines. We do not know whether any or all of these products under development will ever reach the market and if they do, whether they will do so before or after our products are approved.

**Employees**

As of December 31, 2004, we had 66 full-time employees, 34 of whom were engaged in research and development and 32 of whom were engaged in management, marketing, sales, administration and finance. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We have not experienced any work stoppages. We believe that relations with our employees are good.

**Available Information**

We maintain a web site with the address [www.crtx.com](http://www.crtx.com). We are not including the information contained on our web site as part of, or incorporating it by reference into, this annual report. We make available free of charge on or through our web site our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports as soon as practicable after such material is electronically filed with or furnished to the Securities and Exchange Commission. In addition, we intend to post on our web site all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or Nasdaq listing standards concerning any amendment to, or waiver from, our code of business conduct and ethics.

**Table of Contents****Factors That May Affect Future Results**

*If the market is not receptive to ZYFLO or the controlled-release formulation of zileuton upon their commercial introduction, we will be unable to generate significant revenues.*

The commercial success of ZYFLO and the controlled-release formulation of zileuton will depend upon the acceptance of these product candidates by the medical community, third-party payors and patients. Physicians will prescribe ZYFLO and the controlled-release formulation of zileuton only if they determine, based on experience, clinical data, side effect profiles or other factors, that these products either alone or in combination with other products are preferable to other available products or combinations of products.

Despite being approved by the FDA since 1997, ZYFLO has not achieved broad market acceptance. In the 12-month period ending September 2003, only 1,700 physicians prescribed the product. We may have difficulty expanding the prescriber and patient base for ZYFLO if physicians view the product as outdated or less effective than other products on the market. In addition, ZYFLO requires four-times-a-day dosing, which some physicians and patients may find inconvenient compared to other available asthma therapies that require dosing only once or twice daily.

Moreover, perceptions about the safety of ZYFLO could limit their market acceptance. In the placebo-controlled clinical trials that formed the basis for FDA approval of ZYFLO, 1.9% of patients taking ZYFLO experienced increased levels of a liver enzyme called alanine transaminase, or ALT, of over three times the levels normally seen in the bloodstream, compared to 0.2% of patients receiving placebo. In addition, prior to FDA approval, a long-term trial was conducted in 2,947 patients to evaluate the safety of ZYFLO, particularly in relation to liver enzyme effects. In this safety trial, 4.6% of the patients taking ZYFLO experienced increased levels of ALT of over three times the levels normally seen in the bloodstream, compared to 1.1% of patients receiving placebo. The overall percentage of patients that experienced increases in ALT of over three times the levels normally seen in the bloodstream was 3.2% in approximately 5,000 asthma patients who received ZYFLO in the clinical trials that were reviewed by the FDA prior to its approval of ZYFLO. In these trials, one patient developed symptomatic hepatitis with jaundice, which resolved upon discontinuation of therapy, and three patients developed mild elevations in bilirubin, a protein. Furthermore, because ZYFLO can elevate liver enzyme levels, periodic liver function tests are recommended for patients taking ZYFLO and may be advisable for patients taking our other zileuton product candidates. Some physicians and patients may perceive liver function tests as inconvenient or indicative of safety issues, which would make them reluctant to prescribe or accept ZYFLO and other zileuton product candidates. As a result, many physicians may have negative perceptions about the safety of ZYFLO and other zileuton product candidates, which could limit their commercial acceptance.

While we transfer manufacturing capabilities of ZYFLO from Abbott to our contract manufacturing sites and seek regulatory approval of our related sNDA, the product will not be commercially available. The absence of ZYFLO from the market could exacerbate any negative perceptions about ZYFLO if physicians believe the absence of ZYFLO from the market is related to safety or efficacy issues.

The position of ZYFLO in managed care formularies, which are lists of products approved by managed care organizations, may also make it difficult to expand the current market for this product. As a result of a lack of a sustained sales and marketing effort, ZYFLO has been removed from some formularies or relegated to third-tier status, which requires the highest co-pay for patients. In addition, ZYFLO may be removed from some managed care formularies as a result of the absence of ZYFLO from the market while we transfer manufacturing from Abbott to our contract manufacturing sites and seek regulatory approval of our related sNDA.

If we are unable to expand the use of ZYFLO and existing negative perceptions about ZYFLO persist, we will have difficulty achieving market acceptance for our other zileuton product candidates, such as the controlled-release formulation of zileuton. If we are unable to achieve market acceptance of ZYFLO or the controlled-release formulation of zileuton, we will not generate significant revenues unless we are able to successfully develop and commercialize other product candidates.



**Table of Contents*****Our business will depend heavily on the commercial success of ZYFLO and the controlled-release formulation of zileuton.***

Other than ZYFLO and the controlled-release formulation of zileuton, our product candidates are in early clinical, preclinical and research stages of development and are a number of years away from commercialization. As a result, if we obtain regulatory approval to market ZYFLO and the controlled-release formulation of zileuton, they will account for almost all of our revenues for the foreseeable future. Research and development of product candidates is a lengthy and expensive process. Our early-stage product candidates in particular will require substantial funding for us to complete preclinical testing and clinical trials and, if approved, for us to initiate manufacturing and commercialization. If ZYFLO and the controlled-release formulation of zileuton are not commercially successful, we may be forced to find additional sources of funding earlier than we anticipated. If we are not successful in obtaining additional funding on acceptable terms, we may be forced to significantly delay, limit or eliminate one or more of our research, development or commercialization programs. In addition, we may be forced to dismantle or redeploy the sales force that we are building in connection with the anticipated launch of these product candidates.

***If we do not successfully recruit and train qualified sales and marketing personnel and build a marketing and sales infrastructure, our ability to independently launch and market our product candidates, including ZYFLO, will be impaired. We will be required to incur significant costs and devote significant efforts to establish a direct sales force.***

We intend to independently launch and market ZYFLO, the controlled-release formulation of zileuton and other of our product candidates where we believe the target physician market can be effectively reached by our planned sales and marketing force. We intend to have a sales force of approximately 80 personnel by the time of our expected launch of ZYFLO in the second half of 2005. We believe that the aggregate sales and marketing costs to launch ZYFLO, including the cost of the sales force, will be approximately \$5.0 million. We currently have no distribution capabilities and have limited sales and marketing capabilities. We may not be able to attract, hire and train qualified sales and marketing personnel to build a significant or successful sales force. If we are not successful in our efforts to develop an internal sales force, our ability to independently launch and market our product candidates, including ZYFLO and the controlled-release formulation of zileuton, will be impaired.

We will have to invest significant amounts of money and management resources to develop internal sales and marketing capabilities. We intend to use a third party for distribution. Because we plan to minimize sales and marketing expenditures and activities, including the hiring and training of sales personnel, prior to obtaining the regulatory approval for ZYFLO, we may have insufficient time to build our sales and marketing capabilities in advance of the launch of ZYFLO. If we are not successful in building adequate sales and marketing capabilities in advance of the launch of ZYFLO, our ability to successfully commercialize the product may be impaired. If we develop these capabilities in advance of the launch of ZYFLO and approval of ZYFLO or the controlled-release formulation of zileuton is delayed substantially or not granted at all, we will have incurred significant unrecoverable expenses.

***If the market is not receptive to our other product candidates, we will be unable to generate revenues from sales of these products.***

The probability of commercial success of each of our product candidates is subject to significant uncertainty. Factors that we believe will materially affect market acceptance of our product candidates under development include:

the timing of our receipt of any marketing approvals, the terms of any approval and the countries in which approvals are obtained;

the safety, efficacy and ease of administration;

the therapeutic or other improvement over existing comparable products;

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pricing and cost effectiveness;

the ability to be produced in commercial quantities at acceptable costs; and

the extent and success of our sales and marketing efforts.

The failure of our product candidates other than ZYFLO and the controlled-release formulation of zileuton to achieve market acceptance would prevent us from ever generating meaningful revenues from sales of these product candidates.

***We may not be successful in our efforts to advance and expand our portfolio of product candidates.***

A key element of our strategy is to develop and commercialize product candidates that address large unmet medical needs in the critical care market. We seek to do so through:

internal research programs;

sponsored research programs with academic and other research institutions and individual doctors, chemists and researchers; and

in-licensing or acquisition of product candidates or approved products for the critical care market.

A significant portion of the research that we are conducting involves new and unproven technologies. Research programs to identify new product candidates, whether conducted by us or by academic or other research institutions under sponsored research agreements, require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a variety of reasons, including:

the research methodology used may not be successful in identifying potential product candidates; or

potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be effective products.

We may be unable to license or acquire suitable product candidates or products from third parties for a number of reasons. In particular, the licensing and acquisition of pharmaceutical products is competitive. A number of more established companies are also pursuing strategies to license or acquire products in the critical care market. These established companies may have a competitive advantage over us due to their size, cash resources or greater clinical development and commercialization capabilities. Other factors that may prevent us from licensing or otherwise acquiring suitable product candidates or approved products include the following:

we may be unable to license or acquire the relevant technology on terms that would allow us to make an appropriate return from the product;

companies that perceive us as a competitor may be unwilling to assign or license their product rights to us; or

we may be unable to identify suitable products or product candidates within our areas of expertise.

If we are unable to develop suitable potential product candidates through internal research programs, sponsored research programs or by obtaining rights from third parties, we will not be able to increase our revenues in future periods, which could result in significant harm to our financial position and adversely impact our stock price.

***We face substantial competition. If we are unable to compete effectively, our product candidates may be rendered noncompetitive or obsolete.***

The development and commercialization of new drugs is highly competitive. We will face competition with respect to the development of product candidates and for any products that we commercialize in the future from pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies, companies selling low-cost generic substitutes, academic institutions, government agencies or research

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institutions. A number of large pharmaceutical and biotechnology companies currently market and sell products to treat asthma that will compete with ZYFLO and the controlled-release formulation of zileuton, if approved. Many established therapies currently command large market shares in the mild to moderate asthma market, including Merck & Co., Inc.'s Singulair® and GlaxoSmithKline plc's Advair®. We will also face competition from other pharmaceutical companies seeking to develop drugs for the severe asthma market. The severe asthma market is currently served by the therapies developed for mild to moderate asthma and oral and injectable steroid treatments. One product, Xolair®, developed jointly by Novartis AG, Genentech, Inc. and Tanox, Inc., was approved in 2004 for severe allergic asthma and has established a strong sales base.

Zileuton will also face intense competition if we are able to develop it as a treatment for COPD or acne. COPD is a disease that is currently treated predominantly with asthma drugs and lung reduction surgery. Spiriva®, a once daily muscarinic antagonist from Boehringer Ingelheim GmbH and Pfizer, has been approved in Europe and the United States. Other novel approaches are also in the development process. Acne is a disease treated predominantly with antibiotics and, in the case of severe acne, retinoids. The leading branded retinoid is Roche Pharmaceutical's Accutane® (isotretinoin). Generic isotretinoin is now available from several manufacturers, and generic versions of the antibiotics used in mild to moderate forms of acne are common. Given the wide use of generic agents and the number of manufacturers competing in this category, penetration into this market will be difficult.

Our therapeutic programs directed toward the body's inflammatory response will compete predominantly with therapies that have been approved for diseases such as rheumatoid arthritis, like Amgen, Inc.'s Enbrel® and Johnson & Johnson's Remicade®, and diseases such as sepsis, like Eli Lilly and Company's Xigris®.

Our competitors' products may be more effective, or more effectively marketed and sold, than any of our products. Many of our competitors have:

- significantly greater financial, technical and human resources than we have and may be better equipped to discover, develop, manufacture and commercialize products;

- more extensive experience than we have in conducting preclinical studies and clinical trials, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products;

- competing products that have already received regulatory approval or are in late-stage development; and

- collaborative arrangements in our target markets with leading companies and research institutions.

We will face competition based on the safety and effectiveness of our products, the timing and scope of regulatory approvals, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. Our competitors may develop or commercialize more effective, safer or more affordable products, or obtain more effective patent protection, than we are able to. Accordingly, our competitors may commercialize products more rapidly or effectively than we are able to, which would adversely affect our competitive position, the likelihood that our product candidates will achieve initial market acceptance and our ability to generate meaningful revenues from our product candidates. Even if our product candidates achieve initial market acceptance, competitive products may render our products obsolete or noncompetitive. If our product candidates are rendered obsolete, we may not be able to recover the expenses of developing and commercializing those product candidates.

***As we evolve from a company primarily involved in discovery and development to one also involved in commercialization activities, we may encounter difficulties in managing our growth and expanding our operations successfully.***

In order to evolve from a company primarily engaged in research and development to one involved in the commercialization of product candidates, we will need to expand our administrative and operational infrastructure. As we advance our product candidates through clinical trials, we will need to expand our

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development, regulatory and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various collaborators, suppliers and other third parties. Our need to manage our operations and growth will require us to continue to improve our operational, financial and management controls, our reporting systems and our procedures in the United States and the other countries in which we operate. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner, or we may discover deficiencies in existing systems and controls that could expose us to an increased risk of incurring financial or accounting irregularities or fraud.

***If we are unable to retain key personnel and hire additional qualified scientific and other management personnel, we may not be able to successfully achieve our goals.***

We depend on the principal members of our scientific and management staff, including Paul Rubin, M.D., our president and chief executive officer, Walter Newman, Ph.D., our chief scientific officer and senior vice president of research and development, Trevor Phillips, Ph.D., our chief operating officer and senior vice president of operations, Frank Thomas, our chief financial officer, senior vice president of finance and treasurer, and Frederick Finnegan, our senior vice president of sales and marketing. The loss of any of these individuals' services would diminish the knowledge and experience that we, as an organization, possess and might significantly delay or prevent the achievement of our research, development or commercialization objectives and could cause us to incur additional costs to recruit replacement executive personnel. We do not maintain key person life insurance on any of these individuals. We are not aware of any present intention of any of these individuals to leave our company.

Our success depends in large part on our ability to attract and retain qualified scientific and management personnel such as these individuals. We expect that our potential expansion into areas and activities requiring additional expertise, such as clinical trials, governmental approvals, contract manufacturing and sales and marketing, will place additional requirements on our management, operational and financial resources. We expect these demands will require us to hire additional management and scientific personnel and will require our existing management personnel to develop additional expertise. We face intense competition for personnel. The failure to attract and retain personnel or to develop such expertise could delay or halt the research, development, regulatory approval and commercialization of our product candidates.

***Our corporate compliance program cannot guarantee that we are in compliance with all potentially applicable regulations.***

The development, manufacturing, pricing, sales and reimbursement of our product candidates, together with our general operations, are subject to extensive regulation by federal, state and other authorities within the United States and numerous entities outside of the United States. We are a relatively small company with 66 employees as of December 31, 2004, the majority of whom joined us in 2004. We rely heavily on third parties to conduct many important functions. Further, as a publicly traded company we are subject to significant legal and regulatory requirements, including the Sarbanes-Oxley Act of 2002 and regulations promulgated thereunder, some of which have either only recently been adopted or are subject to change. While we have developed and instituted a corporate compliance program based on what we believe are the current best practices and continue to update the program in response to newly implemented and changing regulatory requirements, it is possible that we may not be in compliance with all potentially applicable regulations. If we fail to comply with any of these regulations we could be subject to a range of regulatory actions, including significant fines, litigation, the suspension or termination of clinical trials, the failure to approve a product candidate, restrictions on our products or manufacturing processes, withdrawal of products from the market or other sanctions.

**Table of Contents*****The recent Medicare prescription drug coverage legislation and future legislative or regulatory reform of the health care system may affect our ability to sell our product candidates profitably.***

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies such as ours. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed in recent years. In addition, ongoing initiatives in the United States have and will continue to increase pressure on drug pricing. In some foreign countries, particularly countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In addition, as a result of the trend towards managed healthcare in the United States, as well as legislative proposals to constrain the growth of federal healthcare program expenditures, third-party payors are increasingly attempting to contain healthcare costs by demanding price discounts or rebates and limiting both coverage and the level of reimbursement of new drug products. Consequently, significant uncertainty exists as to the reimbursement status of newly approved healthcare products.

In particular, in December 2003, President Bush signed into law new Medicare prescription drug coverage legislation. The prescription drug program established by this legislation and future amendments or regulatory interpretations of the legislation could have the effect of reducing the prices that we are able to charge for any products we develop and sell through these plans. This prescription drug legislation and related amendments or regulations could also cause third-party payors other than the federal government, including the states under the Medicaid program, to discontinue coverage for any products we develop or to lower reimbursement amounts that they pay.

The Centers for Medicare and Medicaid Services, or CMS, the agency within the Department of Health and Human Services that administers Medicare and that may be responsible for setting reimbursement payment rates and coverage policies for any product candidates that we commercialize, has authority to decline to cover particular drugs if it determines that they are not reasonable and necessary for Medicare beneficiaries or to cover them at lower rates to reflect budgetary constraints or to match previously approved reimbursement rates for products that CMS considers to be therapeutically comparable. Furthermore, federal and state budgetary constraints may cause state Medicaid programs to restrict coverage or limit reimbursement rates for any product candidates that we may market. In addition, current U.S. laws and regulations restrict the importation of drugs from countries where they are sold at lower prices. Any future relaxation of these import restrictions could reduce the prices of drugs in the United States.

Further federal, state and foreign healthcare proposals and reforms are likely. While we cannot predict the legislative or regulatory proposals that will be adopted or what effect those proposals may have on our business, including the future reimbursement status of any of our product candidates, the announcement or adoption of such proposals could have an adverse effect on potential revenues from product candidates that we may successfully develop.

If we succeed in bringing any more of our product candidates to market, third-party payors may establish and maintain price levels insufficient for us to realize a sufficient return on our investment in product development. Significant changes in the healthcare system in the United States or elsewhere, including changes resulting from the implementation of the Medicare prescription drug coverage legislation and adverse trends in third-party reimbursement programs, would limit our ability to raise capital and successfully commercialize our product candidates.

***If we are subject to unfavorable pricing regulations or third-party reimbursement practices, we might not be able to recover the development and other costs of our product candidates.***

The regulations governing drug product licensing, pricing and reimbursement vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after

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initial approval is granted. Although we monitor these regulations, our product candidates other than ZYFLO and the controlled-release formulation of zileuton are currently in the development stage, and we will not be able to assess the impact of price regulations for at least several years. We may obtain regulatory approval for a product in a particular country but then be subject to price regulations, which may delay the commercial launch of the product and may negatively impact the revenues we are able to derive from our sales of the product in that country.

Successful commercialization of our product candidates will also depend in part on the extent to which reimbursement for our product candidates and related treatments will be available from government health administration authorities, private health insurers and other organizations. If we succeed in bringing one or more product candidates to the market, these product candidates may not be considered cost effective and reimbursement to the patient may not be available or sufficient to allow us to sell our product candidates on a competitive basis to a sufficient patient population. Because our product candidates other than ZYFLO and the controlled-release formulation of zileuton are in the development stage, we are unable at this time to determine the cost-effectiveness of these product candidates. We may need to conduct expensive pharmacoeconomic trials in order to demonstrate their cost-effectiveness. Sales of prescription drugs are highly dependent on the availability and level of reimbursement to the consumer from third-party payors, such as government and private insurance plans. These third-party payors frequently require that drug companies provide them with predetermined discounts or retroactive rebates from list prices, and third-party payors are increasingly challenging the prices charged for medical products. Because our product candidates other than ZYFLO and the controlled-release formulation of zileuton are in the development stage, we do not know the level of reimbursement, if any, we will receive for those product candidates if they are successfully developed. If the reimbursement we receive for any of our product candidates is inadequate in light of our development and other costs, our ability to realize profits from the affected product candidate would be limited.

***Our business has a substantial risk of product liability claims. If we are unable to obtain appropriate levels of insurance, a product liability claim against us could interfere with the development and commercialization of our product candidates or subject us to unanticipated damages or settlement amounts.***

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and marketing of drugs. If the use of one or more of our product candidates harms people, we may be subject to costly and damaging product liability claims. We currently have clinical trial insurance that covers our clinical trials up to a \$10.0 million annual aggregate limit and will seek to obtain product liability insurance prior to marketing ZYFLO, the controlled-release version of zileuton or any of our other product candidates. However, our insurance may not provide adequate coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain current amounts of insurance coverage, obtain additional insurance or obtain sufficient insurance at a reasonable cost to protect against losses that we have not anticipated in our business plans.

***We handle hazardous materials and must comply with laws and regulations, which can be expensive and restrict how we do business. If we are involved in a hazardous waste spill or other accident, we could be liable for damages, penalties or other forms of censure.***

Our research and development work involves, and any future manufacturing processes that we conduct may involve, the use of hazardous, controlled and radioactive materials. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials. Despite precautionary procedures that we implement for handling and disposing of these materials, we cannot eliminate the risk of accidental contamination or injury. In the event of a hazardous waste spill or other accident, we could be liable for damages, penalties or other forms of censure.

In addition, we may be required to incur significant costs to comply with laws and regulations in the future or we may be materially and adversely affected by current or future laws or regulations.

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While we have a property insurance policy that covers bio-contamination up to a \$25,000 per-occurrence limit and covers radioactive contamination up to a \$25,000 per-occurrence limit, this policy may not provide adequate coverage against potential losses, damages, penalties or costs relating to accidental contamination or injury as a result of hazardous, controlled or radioactive materials.

**Risks Relating to Development, Clinical Testing and Regulatory Approval of Our Product Candidates**

***If we do not obtain the regulatory approvals or clearances required to market and sell ZYFLO, the controlled-release formulation of zileuton or our other product candidates under development, our business will be unsuccessful.***

Neither we nor any of our collaborators may market any of our products in the United States, Europe or in any other country without marketing approval from the FDA or the equivalent foreign regulatory agency. Although ZYFLO has been approved by the FDA, we are required to submit an sNDA with the FDA for ZYFLO because we are changing the manufacturing process and transferring the manufacturing production for the active pharmaceutical ingredient, or API, of zileuton and the immediate-release ZYFLO finished product from Abbott to contract manufacturing sites. We expect to submit our sNDA for ZYFLO at the end of the first quarter of 2005. The FDA may not approve our sNDA on a timely basis or at all.

We expect to submit a new drug application, or NDA, to the FDA for the controlled-release formulation of zileuton in the fourth quarter of 2005. At present, we are conducting production campaigns and assessing performance of the manufactured tablets, prior to initiation of a bioavailability trial in healthy volunteers designed to confirm that our manufactured tablets behave similarly in the body to the tablets that had been manufactured by Abbott. We believe that any significant variability in product performance or delay in manufacturing could delay the submission of the NDA by up to six months. Abbott conducted all of the preclinical and clinical trials on the controlled-release formulation of zileuton before we in-licensed the product candidate. We intend to rely on the results of these prior clinical trials to support our NDA for this product candidate. If the FDA does not permit us to rely on the prior clinical data or if the data is not available at the clinical sites for required FDA audits, we would be required to repeat some or all of the clinical trials, which would lead to unanticipated costs and delays. Problems with the previous trials, such as incomplete, outdated or otherwise unacceptable data, could cause our NDA to be delayed or rejected.

The regulatory process to obtain market approval or clearance for a new drug, biologic or medical device takes many years, requires expenditures of substantial resources, is uncertain and is subject to unanticipated delays. We have had only limited experience in preparing applications and obtaining regulatory approvals and clearances. Adverse side effects of a product candidate or adverse device effects on subjects or patients in a clinical trial could result in the FDA or foreign regulatory authorities refusing to approve or clear a particular product candidate for any or all indications for use.

The FDA and foreign regulatory agencies have substantial discretion in the drug approval process and can deny, delay or limit approval of a product candidate for a variety of reasons. If we do not receive required regulatory approval or clearance to market ZYFLO, the controlled-release formulation of zileuton or any of our other product candidates under development, our ability to generate product revenue and achieve profitability, our reputation and our ability to raise additional capital will be materially impaired.

***If clinical trials for our product candidates are not successful, we may not be able to develop, obtain regulatory approval for and commercialize these product candidates successfully.***

All of our product candidates remain subject to regulatory approval or clearance, and all of our product candidates other than ZYFLO are still in development and remain subject to clinical testing. In order to obtain regulatory approvals or clearances for the commercial sale of our product candidates, we and our collaborators will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our product candidates. We may not be able to obtain authority from the FDA, institutional review boards or other regulatory agencies to commence or complete these clinical trials. If

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permitted, such clinical testing may not prove that our product candidates are safe and effective to the extent necessary to permit us to obtain marketing approvals or clearances from regulatory authorities. One or more of our product candidates may not exhibit the expected therapeutic results in humans, may cause harmful side effects or have other unexpected characteristics that may delay or preclude regulatory approval or clearance or limit commercial use if approved or cleared. Furthermore, we, one of our collaborators, institutional review boards, or regulatory agencies may hold, suspend or terminate clinical trials at any time if it is believed that the subjects or patients participating in such trials are being exposed to unacceptable health risks or for other reasons.

Preclinical testing and clinical trials of new drug, biologic and device candidates are lengthy and expensive and the historical failure rate for such candidates is high. We may not be able to advance any more product candidates into clinical trials. Even if we do successfully enter into clinical trials, the results from preclinical testing of a product candidate may not predict the results that will be obtained in human clinical trials. In addition, positive results demonstrated in preclinical studies and clinical trials that we complete may not be indicative of results obtained in later clinical trials. Clinical trials may take several years to complete, and failure can occur at any stage of testing.

Adverse or inconclusive clinical trial results concerning any of our product candidates could require us to conduct additional clinical trials, result in increased costs and significantly delay the submission for marketing approval or clearance for such product candidates with the FDA or other regulatory authorities or result in a submission or approval for a narrower indication. If clinical trials fail, our product candidates may not become commercially viable.

***If clinical trials for our product candidates are delayed, we would be unable to commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay the receipt of any revenues from product sales.***

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause regulatory authorities, institutional review boards or us to delay or suspend those clinical trials, or delay the analysis of data from our completed or ongoing clinical trials.

Any of the following could delay the completion of our ongoing and planned clinical trials:

ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;

delays or the inability to obtain required approvals from institutional review boards or other governing entities at clinical sites selected for participation in our clinical trials;

delays in enrolling patients and volunteers into clinical trials;

lower than anticipated retention rates of patients and volunteers in clinical trials;

the need to repeat clinical trials as a result of inconclusive or negative results or poorly executed testing;

insufficient supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials;

unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;

serious and unexpected drug-related side effects or adverse device effects experienced by participants in our clinical trials; or

the placement of a clinical hold on a trial.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis will be subject to a number of factors, including the size of the patient population, the nature of the protocol, the proximity of patients to



clinical sites, the availability of effective treatments for the relevant disease,

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competing trials with other drug candidates and the eligibility criteria for the clinical trial. Delays in patient enrollment can result in increased costs and longer development times. In addition, subjects may drop out of our clinical trials and thereby impair the validity or statistical significance of the trials.

We expect to rely on academic institutions and clinical research organizations to supervise or monitor some or all aspects of the clinical trials for the product candidates we advance into clinical testing. Accordingly, we have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own.

As a result of these factors, we or third parties on whom we rely may not successfully begin or complete our clinical trials in the time periods we have forecasted, if at all. If the results of our ongoing or planned clinical trials for our product candidates are not available when we expect or if we encounter any delay in the analysis of data from our preclinical studies and clinical trials, we may be unable to submit for regulatory approval or clearance or conduct additional clinical trials on the schedule we currently anticipate.

If clinical trials are delayed, the commercial viability of our product candidates may be reduced. If we incur costs and delays in our programs, or if we do not successfully develop and commercialize our products, our future operating and financial results will be materially affected.

***Even if we obtain regulatory approvals or clearances, our product candidates will be subject to ongoing regulatory review. If we fail to comply with continuing U.S. and applicable foreign regulations, we could lose those approvals and the sale of our product candidates could be suspended.***

Approvals and clearances of our product candidates are subject to continuing regulatory review, including the review of medical device reports, adverse drug or device experiences and clinical results from any post-market testing or vigilance required as a condition of approval that are reported after our product candidates become commercially available. The manufacturer and the manufacturing facilities we use to make any of our product candidates will also be subject to periodic review and inspection by the FDA. The subsequent discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer or facility, including withdrawal of the product from the market. Our product promotion and advertising will also be subject to regulatory requirements and continuing FDA review.

***If we or our third-party manufacturers or service providers fail to comply with regulatory laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to market and sell our product candidates and may harm our reputation.***

If we or our third-party manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our product candidates successfully and could harm our reputation and lead to less market acceptance of our product candidates. These enforcement actions include:

product seizures;

voluntary or mandatory recalls;

suspension of review or refusal to approve pending applications;

voluntary or mandatory patient or physician notification;

withdrawal of product approvals;

restrictions on, or prohibitions against, marketing our product candidates;

restrictions on applying for or obtaining government bids;

finances;

restrictions on importation of our product candidates;

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injunctions; and

civil and criminal penalties.

**Risks Relating to Our Dependence on Third Parties**

*We depend on MedImmune and Beckman Coulter and expect to depend on additional collaborators in the future for a significant portion of our revenues and to develop, conduct clinical trials with, obtain regulatory approvals for, and manufacture, market and sell some of our product candidates. These collaborations may not be successful.*

We are relying on MedImmune to fund the development of and to commercialize product candidates in our HMGB1 program. All of our revenues for the years ended December 31, 2003 and 2004 were derived from fees paid to us by MedImmune under our collaboration agreement. We are relying on Beckman Coulter to fund the development and to commercialize diagnostics in our HMGB1 program. We expect that until we generate revenue from the sale of ZYFLO, all of our revenues will continue to be derived from our collaboration agreements with MedImmune and Beckman Coulter. Additional payments due to us under the collaboration agreements with MedImmune and Beckman Coulter are generally based on our achievement of specific development and commercialization milestones that we may not meet. In addition, the collaboration agreements entitle us to royalty payments that are based on the sales of products developed and marketed through the collaborations. These future royalty payments may not materialize or may be less than expected if the related products are not successfully developed or marketed or if we are forced to license intellectual property from third parties. Accordingly, we cannot predict if our collaborations with MedImmune and Beckman Coulter will continue to generate revenues for us.

Our collaboration agreement with MedImmune generally is terminable by MedImmune at any time upon six-months notice to us or upon our material uncured breach of the agreement. Under the collaboration agreement, we are obligated to use commercially reasonable, good faith efforts to conduct the collaboration in accordance with rolling three-year research plans that describe and allocate between MedImmune and us responsibility for, among other things, the proposed research, preclinical studies, toxicology formulation activities and clinical studies for that time period. In addition, we and MedImmune agreed to work exclusively in the development and commercialization of HMGB1-inhibiting products for a period of four years, and, after such time, we have agreed to work exclusively with MedImmune in the development of HMGB1-inhibiting products for the remaining term of the agreement. If MedImmune were to terminate or breach our arrangement, and we were unable to enter into a similar collaboration agreement with another qualified third party in a timely manner or devote sufficient financial resources or capabilities to continue development and commercialization on our own, the development and commercialization of our HMGB1 program likely would be delayed, curtailed or terminated. The delay or termination of our HMGB1 program could significantly harm our future prospects. We intend to enter into collaboration agreements with other parties in the future that relate to other product candidates, and we are likely to have similar risks with regard to any such future collaborations.

Our license agreement with Beckman Coulter relating to the use of HMGB1 and its antibodies in diagnostics will terminate if Beckman Coulter does not exercise its option to continue the license by a future date. In addition, Beckman Coulter has the right to terminate the license agreement on 90-days written notice. Each party has the right to terminate the license agreement upon the occurrence of a material uncured breach by the other party. If Beckman Coulter were to terminate or breach our arrangement, and we were unable to enter into a similar agreement with another qualified third party in a timely manner or devote sufficient financial resources or capabilities to continue development and commercialization on our own, the development and commercialization of a diagnostic based on the use of HMGB1 and its antibodies likely would be delayed, curtailed or terminated.

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In addition, our collaborations with MedImmune and Beckman Coulter and any future collaborative arrangements that we enter into with third parties may not be scientifically or commercially successful. Factors that may affect the success of our collaborations include the following:

our collaborators may be pursuing alternative technologies or developing alternative products, either on their own or in collaboration with others, that may be competitive with the product on which they are collaborating with us or that could affect our collaborators' commitment to us;

reductions in marketing or sales efforts or a discontinuation of marketing or sales of our products by our collaborators would reduce our revenues, which we expect will be based on a percentage of net sales by collaborators;

our collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect how we are perceived in the business and financial communities;

our collaborators may not devote sufficient time and resources to any collaboration with us, which could prevent us from realizing the potential commercial benefits of that collaboration; and

our collaborators may pursue higher priority programs or change the focus of their development programs, which could affect their commitments to us.

***We have no manufacturing experience or resources and we must incur significant costs to develop this expertise or rely on third parties to manufacture our product candidates.***

We have no manufacturing experience. In order to continue to develop product candidates, apply for regulatory approvals and commercialize our product candidates, we will need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities. We currently rely on third parties for the production of our product candidates for preclinical and clinical testing purposes and we expect to continue to do so in the future. We have contracted with Rhodia Pharma Solutions to establish and validate a manufacturing process for the API and for commercial production of API, subject to specified limitations, through December 31, 2009. We have also contracted with SkyePharma PLC, through its subsidiary Jagotec AG, for the manufacture of tablets of the controlled-release formulation of zileuton for clinical trials, regulatory review and, subject to negotiation of a commercial manufacturing agreement, commercial sale. In addition, we have contracted with Patheon Pharmaceuticals to establish a manufacturing process for ZYFLO and to manufacture ZYFLO for clinical trials and regulatory review.

Only a limited number of manufacturers have the capability to supply us with zileuton, and we have not secured a long-term commercial supply arrangement for any of our product candidates, other than the controlled-release formulation of zileuton and the API. The manufacturing process for our product candidates is an element of the FDA approval process and we will need to contract with manufacturers who can meet the FDA requirements, including current Good Manufacturing Practices, on an ongoing basis. As part of obtaining regulatory approval for ZYFLO and the controlled-release formulation of zileuton, we are required to engage a commercial manufacturer to produce registration and validation batches of the drug consistent with regulatory approval requirements. Rhodia Pharma Solutions has produced the validation batches of API. We are dependent upon Rhodia Pharma Solutions, SkyePharma and Patheon, and will be dependent on any other third parties who manufacture our product candidates, to perform their obligations in a timely manner and in accordance with applicable government regulations. In addition, if we receive the necessary regulatory approval for our product candidates, we also expect to rely on third parties, including our collaborators, to produce materials required for commercial production. We may experience difficulty in obtaining adequate manufacturing capacity or timing for our needs. If we are unable to obtain or maintain contract manufacturing of these product candidates, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our product candidates.

The manufacturing process for the zileuton API involves an exothermic reaction that generates heat and, if not properly controlled by the safety and protection mechanisms in place at the manufacturing



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sites, could result in unintended combustion of the product. The manufacture of the API could be disrupted or delayed if a batch is destroyed or damaged or if local health and safety regulations require a third-party manufacturer to implement additional safety procedures or cease production.

We are and will continue to be dependent upon these third-party manufacturers to perform their obligations in a timely manner and consistent with regulatory requirements. If third-party manufacturers with whom we contract fail to perform their obligations, we may be adversely affected in a number of ways, including the following:

we may not be able to initiate or continue clinical trials of our product candidates that are under development;

we may be delayed in submitting applications for regulatory approvals or clearances for our product candidates;

we may be required to cease distribution or recall some or all batches of our product candidates; and

ultimately, we may not be able to meet commercial demands for our product candidates.

***If we are unable to enter into additional collaboration agreements, we may not be able to continue development of our product candidates.***

Our drug development programs and potential commercialization of our product candidates will require substantial additional cash to fund expenses to be incurred in connection with these activities. We may seek to enter into additional collaboration agreements with pharmaceutical companies to fund all or part of the costs of drug development and commercialization of product candidates. We may not be able to enter into future collaboration agreements, and the terms of the collaboration agreements, if any, may not be favorable to us. If we are not successful in efforts to enter into a collaboration arrangement with respect to a product candidate, we may not have sufficient funds to develop this or any other product candidate internally. If we do not have sufficient funds to develop our product candidates, we will not be able to bring these product candidates to market and generate revenue. In addition, our inability to enter into collaboration agreements could delay or preclude the development, manufacture and/or commercialization of a product candidate and could have a material adverse effect on our financial condition and results of operations because:

we may be required to expend our own funds to advance the product candidate to commercialization;

revenue from product sales could be delayed; or

we may elect not to commercialize the product candidate.

***We plan to rely significantly on third parties to market some product candidates and these third parties may not successfully commercialize these product candidates.***

For product candidates with large target physician markets, we plan to rely significantly on sales, marketing and distribution arrangements with third parties. For example, we plan to rely on MedImmune for the commercialization of any anti-HMGB1 products that we develop, and we plan to rely on Beckman Coulter for the commercialization of any diagnostic based on HMGB1 or its antibodies. We may not be successful in entering into additional marketing arrangements in the future and, even if successful, we may not be able to enter into these arrangements on terms that are favorable to us. In addition, we may have limited or no control over the sales, marketing and distribution activities of these third parties. If these third parties are not successful in commercializing the products covered by these arrangements, our future revenues may suffer.

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**Risks Relating to Intellectual Property and Licenses**

***If we are not able to obtain and enforce patent and other intellectual property protection for our discoveries, our ability to prevent third parties from using our inventions and proprietary information will be limited and we may not be able to operate our business profitably.***

Our success depends, in part, on our ability to protect proprietary products, methods and technologies that we invent and develop under the patent and other intellectual property laws of the United States and other countries, so that we can prevent others from using our inventions and proprietary information. Because certain U.S. patent applications are confidential until patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date that will not be filed in foreign countries and for which a request for non-publication is filed, third parties may have already filed patent applications for technology covered by our pending patent applications, and our patent applications may not have priority over any patent applications of others. There may also be prior art that may prevent allowance of our patent applications.

Our patent strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely or successful manner. Moreover, the mere issuance of a patent does not guarantee that it is valid or enforceable. As a result, even if we obtain patents, they may not be valid or enforceable against third parties.

Our pending patent applications may not result in issued patents. In addition, the patent positions of pharmaceutical or biotechnology companies, including ours, are generally uncertain and involve complex legal and factual considerations. The standards that the U.S. Patent and Trademark Office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical or biotechnology patents. Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims which will be allowed in any patents issued to us or to others with respect to our products in the future.

We also rely on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to, or independently developed by a competitor, any competitive advantage that we may have had in the development or commercialization of our product candidates would be minimized or eliminated.

***Litigation regarding patents, patent applications and other proprietary rights is expensive and time consuming. If we are unsuccessful in litigation concerning patents or patent applications owned or co-owned by us or licensed to us, we may not be able to protect our products from competition or we may be precluded from selling our products. If we are involved in such litigation, it could cause delays in, or prevent us from, bringing products to market and harm our ability to operate.***

Our success will depend in part on our ability to uphold and enforce the patents or patent applications owned or co-owned by us or licensed to us that cover our products and product candidates. Litigation, interferences or other adversarial proceedings relating to our patents or applications could take place in the United States in a federal court or in the U.S. Patent and Trademark Office or other administrative agencies. These proceedings could also take place in a foreign country, in either the court or the patent office of that country. Proceedings involving our patents or patent applications could result in adverse decisions regarding:

the patentability of our inventions, including those relating to our products; and/or

the enforceability, validity or scope of protection offered by our patents, including those relating to our products.



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These proceedings are costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. Even if we are successful in these proceedings, we may incur substantial cost and divert time and attention of our management and scientific personnel in pursuit of these proceedings, which could have a material adverse effect on our business.

Our success will also depend in part on our ability to avoid infringement of the patent rights of others. For example, we are aware of third-party patents and patent applications that relate to a class of chemicals known as pyruvates, of which CTI-01 is a member. We believe that our anticipated uses of CTI-01 do not infringe any valid third-party patents. If any use of CTI-01 that we pursue for a particular indication were found to infringe a valid third-party patent, we could be precluded from selling CTI-01 for that indication and be forced to pay damages.

If it is determined that we do infringe a patent right of another, we may be required to seek a license, defend an infringement action or challenge the validity of the patent in court. In addition, if we are not successful in infringement litigation brought against us and we do not license or develop non-infringing technology, we may:

incur substantial monetary damages, potentially including treble damages, if we are found to have willfully infringed on such parties' patent rights;

encounter significant delays in bringing our product candidates to market; or

be precluded from participating in the manufacture, use or sale of our products or methods of treatment.

If any parties should successfully claim that our creation or use of proprietary technologies infringes upon their intellectual property rights, we might be forced to pay damages. In addition to any damages we might have to pay, a court could require us to stop the infringing activity. Moreover, any legal action against us or our collaborators claiming damages and seeking to enjoin commercial activities relating to the affected products and processes could, in addition to subjecting us to potential liability for damages, require us or our collaborators to obtain a license in order to continue to manufacture or market the affected products and processes. Any such required license may not be made available on commercially acceptable terms, if at all. In addition, some licenses may be non-exclusive and, therefore, our competitors may have access to the same technology licensed to us.

If we fail to obtain a required license or are unable to design around a patent, we may be unable to effectively market some of our technology or products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, our MedImmune collaboration provides that a portion of the royalties payable to us by MedImmune for licenses to our intellectual property may be offset by amounts paid by MedImmune to third parties who have competing or superior intellectual property positions in the relevant fields, which could result in significant reductions in our revenues.

Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations.

***We in-license a significant portion of our principal proprietary technologies, and if we fail to comply with our obligations under any of the related agreements, we could lose license rights that are necessary to develop and market HMGB1 products and some of our other product candidates.***

We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary for our business. In fact, we acquired the rights to each of our product candidates under licenses with third parties. These licenses impose various development, commercialization, funding, royalty, diligence and other obligations on us. If we breach these obligations, our licensors may have the right to terminate the licenses or render the licenses non-exclusive, which would result in our being unable to

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develop, manufacture and sell products that are covered by the licensed technology, or at least to do so on an exclusive basis.

***Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.***

In order to protect our proprietary technology and processes, it is our general practice to enter into confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information and, in such cases, we could not assert any trade secret rights against such parties. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

**Risks Relating to Our Financial Results and Need for Additional Financing**

***We have incurred losses since inception and we anticipate that we will continue to incur losses for the foreseeable future. If we do not generate significant revenues, we will not be able to achieve profitability.***

We have experienced significant operating losses in each year since our inception in 2000. We had net losses of \$31.1 million in the year ended December 31, 2004 and \$20.1 million in the year ended December 31, 2003. As of December 31, 2004, we had an accumulated deficit of approximately \$58.5 million. We expect that we will continue to incur substantial losses for at least the next several years as we spend significant amounts to fund research, development and commercialization of our product candidates and to enhance our core technologies. We expect that the losses that we incur will fluctuate from quarter to quarter and that these fluctuations may be substantial. We will need to generate significant revenues to pay these costs and achieve profitability. Until we are able to generate such revenues, we will need to raise substantial additional capital to fund our operations.

***We will require substantial additional capital to fund our operations. If additional capital is not available, we may need to delay, limit or eliminate our development and commercialization processes.***

We expect to devote substantial resources to continue our research and development efforts, including preclinical testing and clinical trials, establish our sales and marketing infrastructure, achieve regulatory approvals and, subject to regulatory approval, commercially launch ZYFLO and the controlled-release formulation of zileuton and any future product candidates. Our funding requirements will depend on numerous factors, including:

the costs and timing of the commercial launch of ZYFLO, if and when it is approved by regulatory authorities;

the costs and timing of the development, regulatory submission and approval and the commercial launch of the controlled-release formulation of zileuton, if and when it is approved by regulatory authorities;

the scope and results of our clinical trials;

advancements of other product candidates into development;

potential acquisition or in-licensing of other products or technologies;

the time and costs involved in preparing, submitting and obtaining regulatory approvals;

the timing, receipt and amount of milestone and other payments, if any, from MedImmune or future collaborators;

the timing, receipt and amount of sales and royalties, if any, from our potential products;

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continued progress in our research and development programs, as well as the magnitude of these programs;

the cost of manufacturing, marketing and sales activities;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

the cost of obtaining and maintaining licenses to use patented technologies; and

our ability to establish and maintain additional collaborative arrangements.

We do not expect to generate significant additional funds from operations, other than payments that we receive from our collaboration with MedImmune or Beckman Coulter, until we successfully conduct clinical trials, achieve regulatory approvals and commercially launch ZYFLO and the controlled-release formulation of zileuton. In addition to the foregoing factors, we believe that our ability to access external funds will depend upon the success of our other preclinical and clinical development programs, the receptivity of the capital markets to financings by biopharmaceutical companies, our ability to enter into additional strategic collaborations with corporate and academic collaborators and the success of such collaborations.

The extent of our future capital requirements is difficult to assess and will depend largely on our ability to obtain regulatory approval for and successfully commercialize ZYFLO and the controlled-release formulation of zileuton. Based on our operating plans, we believe that our available cash and cash equivalents will be sufficient to fund anticipated levels of operations until the middle of 2006.

For the year ended December 31, 2004, our net cash used for operating activities was \$25.1 million and we had capital expenditures of \$2.0 million. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we will need to raise additional external funds through collaborative arrangements and public or private financings. Additional financing may not be available to us on acceptable terms or at all. In addition, the terms of the financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our then-existing stockholders will result. If we are unable to obtain funding on a timely basis, we may be required to significantly delay, limit or eliminate one or more of our research, development or commercialization programs, which could harm our financial condition and operating results. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products which we would otherwise pursue on our own.

***Changes in or interpretations of accounting rules and regulations, such as expensing of employee stock options, could result in unfavorable accounting charges or require us to change our compensation policies.***

Accounting methods and policies for business and market practices of biopharmaceutical companies are subject to review, interpretation and guidance from relevant accounting authorities, including the SEC. For example, a new accounting rule, which will become effective for us on July 1, 2005, requires us to record stock-based compensation expense for the fair value of stock options granted to employees. We rely heavily on stock options to compensate existing employees and attract new employees. Because we will be required to expense stock options, we may reduce our reliance on stock options as a compensation tool. If we reduce our reliance on stock options, it may be more difficult for us to attract and retain qualified employees. If we do not reduce our reliance on stock options, our reported losses would increase. Although we believe that our accounting practices are consistent with current accounting pronouncements, changes to or interpretations of accounting methods or policies in the future may require us to reclassify, restate or otherwise change or revise our financial statements.

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**Risks Relating to Our Common Stock**

***Our stock price is subject to fluctuation, which may cause an investment in our stock to suffer a decline in value.***

The market price of our common stock may fluctuate significantly in response to factors that are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of our common stock.

***If our quarterly results of operations fluctuate, this fluctuation may subject our stock price to volatility, which may cause an investment in our stock to suffer a decline in value.***

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. A number of factors, many of which are not within our control, could subject our operating results and stock price to volatility, including:

achievement of, or the failure to achieve, milestones under our development agreement with MedImmune, our license agreement with Beckman Coulter and, to the extent applicable, other licensing and collaboration agreements;

the results of ongoing and planned clinical trials of our product candidates;

production problems occurring at our third party manufacturers;

the results of regulatory reviews relating to the approval of our product candidates; and

general and industry-specific economic conditions that may affect our research and development expenditures.

Due to the possibility of significant fluctuations, we do not believe that quarterly comparisons of our operating results will necessarily be indicative of our future operating performance. If our quarterly operating results fail to meet the expectations of stock market analysts and investors, the price of our common stock may decline.

***If announcements of business developments by us or our competitors cause fluctuations in our stock price, an investment in our stock may suffer a decline in value.***

The market price of our common stock may be subject to substantial volatility as a result of announcements by us or other companies in our industry, including our collaborators. Announcements which may subject the price of our common stock to substantial volatility include announcements regarding:

our licensing and collaboration agreements and the products or product candidates that are the subject of those agreements;

the results of discovery, preclinical studies and clinical trials by us or our competitors;

the acquisition of technologies, product candidates or products by us or our competitors;

the development of new technologies, product candidates or products by us or our competitors;

regulatory actions with respect to our product candidates or products or those of our competitors; and

significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors.

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***Insiders have substantial control over us and could delay or prevent a change in corporate control, including a transaction in which our stockholders could sell or exchange their shares for a premium.***

As of February 28, 2005, our directors, executive officers and principal stockholders, together with their affiliates, beneficially owned, in the aggregate, approximately 67% of our outstanding common stock. As a result, our directors, executive officers and principal stockholders, together with their affiliates, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

delaying, deferring or preventing a change in control of our company;

impeding a merger, consolidation, takeover or other business combination involving our company; or

discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company.

***Anti-takeover provisions in our charter documents and under Delaware law could prevent or frustrate attempts by our stockholders to change our management and hinder efforts by a third party to acquire a controlling interest in us.***

We are incorporated in Delaware. Anti-takeover provisions of Delaware law and our charter documents may make a change in control more difficult, even if the stockholders desire a change in control. For example, our anti-takeover provisions include provisions in our by-laws providing that stockholders' meetings may be called only by the president or the majority of the board of directors and a provision in our certificate of incorporation providing that our stockholders may not take action by written consent.

Additionally, our board of directors has the authority to issue 5,000,000 shares of preferred stock and to determine the terms of those shares of stock without any further action by our stockholders. The rights of holders of our common stock are subject to the rights of the holders of any preferred stock that we issue. As a result, our issuance of preferred stock could cause the market value of our common stock to decline and could make it more difficult for a third party to acquire a majority of our outstanding voting stock.

Delaware law also prohibits a corporation from engaging in a business combination with any holder of 15% or more of its capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. The board may use this provision to prevent changes in our management. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future.

**ITEM 2. PROPERTIES**

We lease a facility that contains approximately 40,200 square feet of laboratory and office space in Lexington, Massachusetts, which we occupied and began leasing in March 2004. The lease expires on April 1, 2009. We believe our facilities are sufficient to meet our needs for the foreseeable future and, if needed, additional space will be available in the near term at a reasonable cost to us.

**ITEM 3. LEGAL PROCEEDINGS**

We are not currently a party to any material legal proceedings.

**ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

No matters were submitted to a vote of our security holders, through solicitation of proxies or otherwise, during the last quarter of the year ended December 31, 2004.

**Table of Contents****EXECUTIVE OFFICERS OF THE REGISTRANT**

Our executive officers, their ages and their positions as of February 28, 2005 are as follows:

<b>Name</b>	<b>Age</b>	<b>Position</b>
Paul D. Rubin, M.D.	51	President and Chief Executive Officer
Walter Newman, Ph.D.	59	Senior Vice President of Research and Discovery and Chief Scientific Officer
Trevor Phillips, Ph.D.	43	Senior Vice President of Operations and Chief Operating Officer
Frank E. Thomas	35	Senior Vice President of Finance, Chief Financial Officer and Treasurer
Frederick Finnegan	45	Senior Vice President of Sales and Marketing
Scott B. Townsend, J.D.	38	Vice President of Legal Affairs and Secretary

*Paul Rubin, M.D.* has served as our President and Chief Executive Officer since August 2002 and as a member of our board of directors since October 2002. From April 1996 to August 2002, Dr. Rubin served as Executive Vice President of Research and Development for Sepracor, Inc., a pharmaceutical company. From July 1993 to March 1996, Dr. Rubin served as Vice President and Worldwide Director Early Clinical Development and Clinical Pharmacology for GlaxoWellcome, Inc., a pharmaceutical company. From June 1987 to June 1993, Dr. Rubin served as Vice President of Immunology and Endocrine Development for Abbott Laboratories, a health care company. Dr. Rubin holds a B.S. in Biology from Occidental College and an M.D. from Rush Medical College.

*Walter Newman, Ph.D.* has served as our Chief Scientific Officer since May 2002, as our Senior Vice President of Research and Discovery since December 2004 and as our Vice President of Research and Discovery from May 2002 to December 2004. From October 2001 to May 2002, Dr. Newman served as an independent consultant to companies in the biotechnology industry. From January 2000 to September 2001, Dr. Newman served as Senior Vice President of Biotherapeutics for Millennium Pharmaceuticals, Inc., a pharmaceutical company. From April 1993 to December 1999, Dr. Newman served as Senior Vice President of Research for LeukoSite, Inc., a biotechnology company. Dr. Newman holds a B.S. in Chemistry and a Ph.D. in Immunochemistry from Columbia University.

*Trevor Phillips, Ph.D.* has served as our Chief Operating Officer since November 2003, as our Senior Vice President of Operations since December 2004, as our Secretary from March 2004 to September 2004, as our Treasurer from September 2003 to May 2004 and as our Vice President of Operations from October 2002 to December 2004. From November 2001 to September 2002, Dr. Phillips served as Senior Program Director for Sepracor, Inc., a pharmaceutical company. From October 1999 to November 2001, Dr. Phillips served as Director of Drug Development, Strategy and Planning for Scotia Holdings plc, a biotechnology company. From March 1997 to October 1999, Dr. Phillips served as a Senior Manager, Strategic Planning for Accenture Ltd. (formerly known as Andersen Consulting), a management consulting company. From March 1990 to March 1997, Dr. Phillips served in a variety of positions, including Director of Strategic Direction, for GlaxoWellcome plc, a pharmaceutical company. Dr. Phillips holds a B.Sc. in Microbiology from the University of Reading, a Ph.D. in Microbial Biochemistry from the University of Wales and an M.B.A from Henley Management College.

*Frank E. Thomas* has served as our Chief Financial Officer since April 2004, as our Treasurer since May 2004, as our Senior Vice President of Finance since December 2004 and as our Vice President of Finance from June 2004 to December 2004. From February 2000 to April 2004, Mr. Thomas served in a variety of finance positions with Esperion Therapeutics, Inc., a biopharmaceutical company, including most recently as Chief Financial Officer. Esperion was acquired by Pfizer Inc. in February 2004. From September 1997 to March 2000, Mr. Thomas served as Director of Finance and Corporate Controller for Mechanical Dynamics, Inc., a publicly-held software company. Prior to that, Mr. Thomas was a manager with Arthur Andersen LLP where he was a certified public accountant. Mr. Thomas holds a Bachelor in Business Administration from the University of Michigan.



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*Frederick Finnegan* has served as our Senior Vice President of Sales and Marketing since December 2004 and as our Vice President of Sales and Marketing from September 2003 to December 2004. From April 2001 to March 2003, Mr. Finnegan served as Vice President of New Products Marketing for Genzyme Corporation, a biotechnology company. From July 1990 to April 2001, Mr. Finnegan served in a number of marketing and sales assignments for Merck & Co., a pharmaceutical company, including most recently as Senior Director, New Products/ Anti-Infectives Worldwide Human Health Division, with responsibility for worldwide marketing of in-line and pre-launch products. Mr. Finnegan holds a B.S. in Business Administration and Pre-Medical Sciences from the University of New Hampshire and an M.S. in Management from the Massachusetts Institute of Technology's Sloan School of Management.

*Scott B. Townsend* has served as our Vice President of Legal Affairs since August 2004 and as our Secretary since September 2004. From August 2000 to August 2004, Mr. Townsend was employed by the law firm Wilmer Cutler Pickering Hale and Dorr LLP (formerly known as Hale and Dorr LLP) as a junior partner from May 2002 to August 2004 and as an associate from August 2000 to May 2002. Mr. Townsend was an associate with the law firm Kilpatrick Stockton LLP in Charlotte, NC from July 1999 to July 2000 and an associate with the law firm Goodwin Procter LLP in Boston, MA from September 1997 to July 1999. Mr. Townsend holds an A.B. in Economics and Government from Bowdoin College and a J.D. from The University of Virginia School of Law.

**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES****Market Price of and Dividends on Critical Therapeutics's Common Stock and Related Stockholder Matters**

Our common stock began trading on the Nasdaq National Market under the symbol CRTX on May 27, 2004. The following table sets forth, for the period indicated, the high and low sales closing prices of our common stock on the Nasdaq National Market.

<b>Year Ended December 31, 2004</b>	<b>High</b>	<b>Low</b>
Second Quarter (from May 27 to June 30)	\$ 7.65	\$ 6.71
Third Quarter (from July 1 to September 30)	\$ 7.05	\$ 4.74
Fourth Quarter (from October 1 to December 31)	\$ 8.49	\$ 5.25

On February 28, 2005, the closing price per share of our common stock was \$6.89, as reported on the Nasdaq National Market, and we had approximately 79 stockholders of record. This may not be an accurate indication of the total number of beneficial owners of our common stock as of February 28, 2005 because many shares are held by nominees in street name for beneficial owners.

We have never paid or declared any cash dividends on our common stock. We currently intend to retain earnings, if any, to finance the growth and development of our business, and we do not expect to pay any cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors. Pursuant to our credit agreement with Silicon Valley Bank, we are required to obtain Silicon Valley Bank's prior written consent before paying any dividends.

**Calculation of Aggregate Market Value of Non-Affiliate Shares**

For purposes of calculating the aggregate market value of shares of our common stock held by non-affiliates as set forth on the cover page of this Annual Report on Form 10-K, we have assumed that all outstanding shares are held by non-affiliates, except for shares held by each of our executive officers, directors and 5% or greater stockholders. However, this assumption should not be deemed to constitute an admission that all executive officers, directors and 5% or greater stockholders are, in fact, affiliates of our



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company, or that there are not other persons who may be deemed to be affiliates of our company. Further information concerning shareholdings of our officers, directors and principal stockholders is included or incorporated by reference in Part II, Item 12 of this Annual Report on Form 10-K.

**Recent Sales of Unregistered Securities; Uses of Proceeds From Registered Securities**

***Recent Sales of Unregistered Securities***

Not applicable.

***Use of Proceeds from Registered Securities***

In June 2004, we sold 6,110,000 shares of our common stock in our initial public offering, including 110,000 shares upon the exercise of an over-allotment option by the underwriters, pursuant to a registration statement on Form S-1 (File No. 333-113727), which was declared effective by the SEC on May 26, 2004. Our net proceeds from the offering equaled approximately \$37.8 million. Through December 31, 2004, we have not used any of the net proceeds from the offering. The net proceeds of the offering are invested in short-term, investment grade corporate and U.S. government securities. There has been no material change in our planned use of the net proceeds of the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act of 1933, as amended.

**ITEM 6. *SELECTED CONSOLIDATED FINANCIAL DATA***

This section presents our historical consolidated financial data. You should read carefully the following selected consolidated financial data together with our consolidated financial statements and the related notes included in this report, and the Management's Discussion and Analysis of Financial Condition and Results of Operations section of this report. The selected consolidated financial data in this section are not intended to replace our consolidated financial statements.

We derived the statements of operations data for the years ended December 31, 2004, 2003 and 2002 and the balance sheet data as of December 31, 2004 and 2003 from our audited consolidated financial statements, which are included at the end of this report. We derived the statements of operations data for the year ended December 31, 2001 and for the period from July 14, 2000 (inception) through December 31, 2000 and the balance sheet data as of December 31, 2002, 2001 and 2000 from our audited consolidated financial statements not included in this report. Historical results are not necessarily indicative of future results. You should read the notes to our consolidated financial statements for an explanation of the method used to determine the number of shares used in computing basic and diluted net loss per share.

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	Year Ended December 31,				July 14, 2000 (Inception) Through December 31, 2000
	2004	2003	2002	2001	
<b>(In thousands, except share and per share data)</b>					
<b>Statements of Operations</b>					
<b>Data:</b>					
Revenue under collaboration agreement	\$ 4,436	\$ 1,021	\$	\$	\$
Research and development expenses	25,578	17,458	3,284	957	25
General and administrative expenses	10,878	3,771	1,792	605	41
Total operating expenses	36,456	21,229	5,076	1,562	66
Loss from operations	(32,020)	(20,208)	(5,076)	(1,562)	(66)
Interest income	1,098	191	149	119	
Interest expense	(172)	(93)	(8)	(5)	
Net loss	(31,094)	(20,110)	(4,935)	(1,448)	(66)
Accretion of dividends and offering costs on preferred stock	(2,209)	(2,264)	(1,032)	(432)	
Net loss available to common stockholders	\$ (33,303)	\$ (22,374)	\$ (5,967)	\$ (1,880)	\$ (66)
Net loss per common share:					
Basic and diluted	\$ (2.28)	\$ (33.99)	\$ (23.74)	\$ (2.63)	\$ (0.05)
Weighted-average basic and diluted shares outstanding	14,631,371	658,204	251,346	714,820	1,226,664

**As of December 31,**

	2004	2003	2002	2001	2000
<b>(In thousands)</b>					
<b>Balance Sheet Data:</b>					
	\$ 78,829	\$ 40,078	\$ 13,539	\$ 8,580	\$

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Cash, cash equivalents and short-term investments

Working capital	64,357	25,218	13,017	8,501	(66)
Total assets	83,114	45,054	14,382	8,638	
Long term debt, net of current portion	1,367	720	202		
Redeemable convertible preferred stock		51,395	21,080	10,270	
Accumulated deficit	(58,527)	(27,433)	(7,323)	(1,517)	(69)
Total stockholders equity (deficit)	65,408	(24,851)	(7,554)	(1,750)	(66)

**Table of Contents****ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*You should read the following discussion and analysis of financial condition and results of operations together with the Selected Consolidated Financial Data section of this annual report on Form 10-K and our consolidated financial statements and accompanying notes appearing in this report. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results could differ materially from those anticipated by the forward-looking statements due to important factors including, but not limited to, those set forth under the caption Factors That May Affect Future Results in this report.*

**Financial Operations Overview**

We are a biopharmaceutical company and have devoted substantially all of our efforts since inception to the research and development and in-licensing of product candidates designed to treat respiratory, inflammatory and critical care diseases linked to the body's inflammatory response. We were incorporated in July 2000 as Medicept, Inc. and changed our name to Critical Therapeutics, Inc. in March 2001.

Since our inception, we have incurred significant losses each year. As of December 31, 2004, we had an accumulated deficit of \$58.5 million. We expect to incur significant and growing losses for the foreseeable future. Although the size and timing of our future operating losses are subject to significant uncertainty, we expect our operating losses to continue to increase as we continue to fund our development programs and prepare for potential commercial launch of our product candidates. Since inception, we have raised proceeds to fund our operations through our initial public offering of common stock, private placements of equity securities, debt financings, the receipt of interest income and payments from our collaborators MedImmune and Beckman Coulter.

In July 2003, we entered into an exclusive license and collaboration agreement with MedImmune for the discovery and development of novel drugs for the treatment of acute and chronic inflammatory diseases associated with HMGB1, a newly discovered cytokine. Under this collaboration, MedImmune paid us initial fees of \$12.5 million and an additional \$1.5 million during 2004 to fund certain research expenses incurred by us for the HMGB1 program. In addition, in connection with entering into this collaboration, an affiliate of MedImmune purchased \$15.0 million of our series B convertible preferred stock, which converted into 2,857,142 shares of common stock in June 2004 in connection with our initial public offering.

In June 2004, we sold 6,110,000 shares of our common stock in our initial public offering, including 110,000 shares pursuant to the underwriters' partial exercise of their over-allotment option. Our net proceeds from the offering were approximately \$37.8 million.

In January 2005, we entered into a license agreement with Beckman Coulter relating to the development of diagnostics for measuring HMGB1. In consideration for the license, Beckman Coulter paid us a product evaluation license fee of \$250,000 in February 2005.

*Revenue.* We have not generated any revenues from product sales since our inception on July 14, 2000, and do not expect to generate any revenues from product sales until at least the fourth quarter of 2005. All of our revenues to date have been derived from license fees, research and development payments and milestone payments that we received from MedImmune. In the future, we expect to generate revenues from a combination of product sales and payments under corporate collaborations.

*Research and Development Expenses.* Research and development expenses consist of expenses incurred in identifying, developing and testing product candidates. These expenses consist primarily of salaries and related expenses for personnel, fees paid to professional service providers for independently monitoring and analyzing clinical trials, costs of contract research and manufacturing and the cost of facilities. After FDA approval of a product candidate, manufacturing expenses associated with a product will be recorded as cost of sales rather than research and development expenses. We expense research and development costs and patent related costs as incurred. Because of our ability to utilize resources across

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several projects, many of our research and development costs are not tied to any particular project and are allocated among multiple projects. We record direct costs on a project-by-project basis. We record indirect costs in the aggregate in support of all research and development. Development costs for later stage programs such as CTI-01 tend to be higher than earlier stage programs such as our HMGB1 program, due to the costs associated with conducting clinical trials and larger scale manufacturing.

We expect that research and development expenses relating to our development portfolio will continue to increase for the foreseeable future. In particular, we expect to incur increased expenses over the next several years for clinical trials of our product development candidates, including all formulations of zileuton and CTI-01. We also expect manufacturing expenses included in research and development expenses to increase as we complete the technology transfer and scale-up relating to the manufacturing of ZYFLO and the controlled-release formulation of zileuton and produce inventory in preparation for the commercial launch of ZYFLO.

*General and Administrative Expenses.* General and administrative expenses consist primarily of salaries and other related costs for personnel in executive, finance, accounting, legal, business development, human resource and sales and marketing functions. Other costs reflected in general and administrative expenses include facility costs not otherwise included in research and development expenses and professional fees for legal and accounting services.

We anticipate that our general and administrative expenses will also increase as we expand our operations, facilities and other activities and as we continue operating as a publicly traded company. In addition, we expect to incur increased sales and marketing expenses as we commercialize ZYFLO and the controlled-release formulation of zileuton.

*Deferred Stock-Based Compensation Expense.* As discussed more fully in Note 6 to our consolidated financial statements included herein, in lieu of cash payments we granted 117,999 and 268,409 shares of common stock, restricted shares of our common stock and options to purchase common stock to non-employees during the year ended December 31, 2004 and 2003, respectively. We recorded these grants at fair value when granted. We periodically remeasure the fair value of the unvested portion of these grants, resulting in charges or credits to operations in periods when such remeasurement results in differences between the fair value of the underlying common stock and the exercise price of the options that is greater than or less than the differences, if any, between the fair value of the underlying common stock and the exercise price of the options at their respective previous measurement dates. We recorded stock-based compensation expense of \$1.8 million and \$4.9 million during the years ended December 31, 2004 and 2003, respectively, related to grants of common stock, restricted shares and stock options to non-employees.

As discussed more fully in Note 7 to our consolidated financial statements included herein we granted 2,855,288 and 1,165,027 stock options to employees during the years ended December 31, 2004 and 2003, respectively. Certain of the employee options granted during these periods were deemed for accounting purposes to have been granted with exercise prices below their then-current market value. We recorded the value of these differences as deferred stock-based compensation. We amortize the deferred amounts as charges to operations over the vesting periods of the grants, resulting in stock-based compensation expense. We recorded stock-based compensation expense of \$1.8 million and \$165,000 during the years ended December 31, 2004 and 2003, respectively, related to stock options granted to employees at exercise prices below their current market value on the date of grant. We anticipate recording additional stock-based compensation expense of \$1.8 million in 2005, \$1.8 million in 2006, \$1.6 million in 2007 and \$18,000 in 2008, less adjustment for forfeitures, relating to the amortization of employee deferred stock-based compensation recorded as of December 31, 2004.

**Critical Accounting Policies**

The discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires

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us to make estimates and judgments that affect our reported assets and liabilities, revenues and expenses, and other financial information. Actual results may differ significantly from these estimates under different assumptions and conditions. In addition, our reported financial condition and results of operations could vary due to a change in the application of a particular accounting standard.

We regard an accounting estimate or assumption underlying our financial statements as a critical accounting estimate where:

the nature of the estimate or assumption is material due to the level of subjectivity and judgment necessary to account for highly uncertain matters or the susceptibility of such matters to change; and

the impact of the estimates and assumptions on financial condition or operating performance is material.

Our significant accounting policies are more fully described in Note 2 to our consolidated financial statements included herein. Not all of these significant accounting policies, however, fit the definition of critical accounting estimates. We have discussed our accounting policies with the audit committee of our board of directors, and we believe that our estimates relating to revenue recognition, accrued expenses, stock-based compensation and income taxes described below fit the definition of critical accounting estimates.

*Revenue Recognition.* Under our collaboration agreements with MedImmune and Beckman Coulter, we are entitled to receive non-refundable license fees, milestone payments and other research and development payments. Payments received are initially deferred from revenue and subsequently recognized in our statement of operations when earned. We must make significant estimates in determining the performance period and periodically review these estimates, based on joint management committees and other information shared by our collaborators with us. We recognize these revenues over the estimated performance period as set forth in the contracts based on proportional performance and adjusted from time to time for any delays or acceleration in the development of the product. For example, a delay or acceleration of the performance period by our collaborator may result in further deferral of revenue or the acceleration of revenue previously deferred. Because MedImmune and Beckman Coulter can each cancel its agreement with us, we do not recognize revenues in excess of cumulative cash collections. It is difficult to estimate the impact of the adjustments on the results of our operations because, in each case, the amount of cash received would be a limiting factor in determining the adjustment.

*Accrued Expenses.* As part of the process of preparing our consolidated financial statements, we are required to estimate certain expenses. This process involves identifying services which have been performed on our behalf and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our consolidated financial statements. Examples of estimated expenses for which we accrue include professional service fees, such as fees paid to lawyers and accountants, contract service fees, such as amounts paid to clinical monitors, data management organizations and investigators in connection with clinical trials, and fees paid to contract manufacturers in connection with the production of clinical materials. In connection with service fees, our estimates are most affected by our understanding of the status and timing of services provided relative to the actual levels of services incurred by such service providers. The majority of our service providers invoice us monthly in arrears for services performed, however, certain service providers invoice us based upon milestones in the agreement. In the event that we do not identify certain costs which have begun to be incurred or we under- or over-estimate the level of services performed or the costs of such services, our reported expenses for such period would be too low or too high. The date on which certain services commence, the level of services performed on or before a given date and the cost of such services are often judgmental. We make these judgments based upon the facts and circumstances known to us in accordance with generally accepted accounting principles.

*Stock-Based Compensation.* To date, we have elected to follow Accounting Principles Board Opinion, or APB, No. 25, *Accounting for Stock Issued to Employees*, or APB 25, and related

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interpretations, in accounting for our stock-based compensation plans, rather than the alternative fair value accounting method provided for under Statement of Financial Accounting Standards, or SFAS, No. 123, *Accounting for Stock-Based Compensation Accounting Principles Board Opinion*, or SFAS 123. Accordingly, we have not recorded stock-based compensation expense for stock options issued to employees in fixed amounts with exercise prices at least equal to the fair value of the underlying common stock on the date of grant. In the notes to our consolidated financial statements included herein, we provide pro forma disclosures in accordance with SFAS 123 and related pronouncements. We account for transactions in which services are received in exchange for equity instruments based on the fair value of such services received from non-employees or of the equity instruments issued, whichever is more reliably measured, in accordance with SFAS 123 and Emerging Issues Task Force, or EITF, Issue No. 96-18, *Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, or EITF 96-18. The two factors which most affect charges or credits to operations related to stock-based compensation are the fair value of the common stock underlying stock options for which stock-based compensation is recorded and the volatility of such fair value. Accounting for equity instruments granted or sold by us under APB 25, SFAS 123 and EITF 96-18 requires fair value estimates of the equity instrument granted or sold. If our estimates of the fair value of these equity instruments are too high or too low, it would have the effect of overstating or understating expenses. When equity instruments are granted or sold in exchange for the receipt of goods or services and the value of those goods or services can be readily estimated, we use the value of such goods or services to determine the fair value of the equity instruments. When equity instruments are granted or sold in exchange for the receipt of goods or services and the value of those goods or services cannot be readily estimated, as is true in connection with most stock options and warrants granted to employees or non-employees, we estimate the fair value of the equity instruments based upon consideration of factors which we deem to be relevant at the time using cost, market or income approaches to such valuations. Because shares of our common stock have only recently become publicly traded, market factors historically considered in valuing stock and stock option grants include comparative values of public companies discounted for the risk and limited liquidity provided for in the shares we are issuing, pricing of private sales of our convertible preferred stock, prior valuations of stock grants and the effect of events that have occurred between the time of such grants, economic trends, perspective provided by investment banks and the comparative rights and preferences of the security being granted compared to the rights and preferences of our other outstanding equity.

*Income Taxes.* As part of the process of preparing our consolidated financial statements we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves us estimating our actual current tax exposure together with assessing temporary differences resulting from differing treatments of items for tax and accounting purposes. These differences result in deferred tax assets and liabilities. In addition, as of December 31, 2004, we had federal and state tax net operating loss carryforwards of \$38.8 million, which expire beginning in 2021 and 2006, respectively. We also have research and experimentation credit carryforwards of \$619,000, which expire beginning in 2021. We have recorded a valuation allowance of \$17.6 million as an offset against these otherwise recognizable net deferred tax assets due to the uncertainty surrounding the timing of the realization of the tax benefit. In the event that we determine in the future that we will be able to realize all or a portion of its net deferred tax benefit, an adjustment to deferred tax valuation allowance would increase net income in the period in which such a determination is made. The Tax Reform Act of 1986 contains provisions that may limit the utilization of net operating loss carryforwards and credits available to be used in any given year in the event of significant changes in ownership interest, as defined.

**Results of Operations*****Years Ended December 31, 2004 and 2003***

*Revenue Under Collaboration Agreement.* We recognized revenues of \$4.4 million in the year ended December 31, 2004 compared to \$1.0 million in the year ended December 31, 2003. These revenues represent the portion of the \$12.5 million of initial fees MedImmune paid us that we recognized in each

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year and a portion of the \$1.5 million billed to MedImmune in 2004 for development support that we recognized in 2004. We have reported the balance of the payments as deferred revenue and will recognize such amount over the initial estimated 41-month research term of our agreement with MedImmune based on the proportion of cumulative costs incurred as a percentage of the total costs estimated for the performance period. In September 2004, we revised our estimate of remaining total costs under the collaboration agreement with MedImmune, which resulted in an increase in revenue recognized of \$1.1 million in 2004. As of December 31, 2004, we had \$8.5 million in deferred revenue remaining to be recognized under the collaboration agreement with MedImmune.

*Research and Development Expenses.* Research and development expenses for the year ended December 31, 2004 were \$25.6 million compared to \$17.5 million for the year ended December 31, 2003. The \$8.1 million increase in 2004 was primarily attributable to \$1.8 million in increased clinical and preclinical activity for our CTI-01 program, and \$9.1 million of additional expense incurred in connection with our zileuton program, including expenses associated with initiating the transfer of Abbott's manufacturing technology to third parties and our up-front license fee paid to Abbott for the immediate-release formulation of zileuton. In addition, research and development expenses increased as a result of higher expenses associated with the growth in the number of employees performing research and development functions, and increased facilities, equipment and laboratory charges associated with our increased research and development activities during the year ended December 31, 2004. These increases were partially offset by a decrease of \$1.8 million in expense related to our HMGB1 program from \$3.5 million in 2003 to \$1.7 million in 2004 and a decrease of \$2.9 million in stock-based compensation expense from \$4.9 million in 2003 to \$2.0 million in 2004.

The following table summarizes the primary components of our direct research and development expenses for the years ended December 31, 2004 and 2003:

	<b>Year Ended December 31,</b>	
	<b>2004</b>	<b>2003</b>
	<b>(In thousands)</b>	
CTI-01	\$ 3,329	\$ 1,579
HMGB1	1,702	3,483
Cholinergic anti-inflammatory	1,533	630
Zileuton	12,369	3,269
General research and development expenses	4,637	3,589
Stock-based compensation expense	2,008	4,908
<b>Total research and development expenses</b>	<b>\$ 25,578</b>	<b>\$ 17,458</b>

Our general research and development expenses, which are not allocated to any specific program, increased by \$1.0 million in the year ended December 31, 2004 compared to the year ended December 31, 2003. This increase was primarily due to a \$667,000 increase in rent expense resulting from our move into a larger research facility and a \$653,000 increase in depreciation and amortization, partially offset by a \$242,000 reduction in allocated salaries and benefits of employees performing general research and development functions and a \$96,000 reduction in contract research expenses.

We anticipate that our research and development expenses will continue to increase as we further advance our research and development projects. The following summarizes the expenses associated with our primary research and development programs:



*Zileuton*. During the year ended December 31, 2004, we incurred substantial costs for the development and commercialization of both ZYFLO and the controlled-release formulation of zileuton, including costs associated with the technology transfer and scale-up of manufacturing of API and tablets for both formulations. Continuing throughout 2005, we expect our research and development expenses for zileuton will principally relate to the scale up and manufacture of registration batches of the controlled-release formulation of zileuton and the anticipated clinical

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trials of the controlled-release and intravenous formulations of zileuton. We are also pursuing development of zileuton for additional indications, including acne. We initiated a Phase II clinical trial in moderate to severe inflammatory acne patients during 2004 and expect to incur additional costs in conducting further development of zileuton for this indication in 2005. We believe that the aggregate technology transfer and validation costs associated with the change of manufacturing sites for ZYFLO and the controlled-release formulation of zileuton will be approximately \$10.5 million, of which \$7.2 million had been incurred through December 31, 2004. However, the actual costs and timing for the development and commercialization of our zileuton products are highly uncertain, subject to risk and will change depending upon the clinical indication developed and the development strategy adopted. As a result, we are unable to estimate the costs or the timing of advancing our zileuton products through clinical development and commercialization.

*CTI-01.* Expenses for CTI-01 increased in the year ended December 31, 2004 primarily due to costs associated with the completion of the first Phase I clinical trial that we initiated in 2003 and completed in 2004 in the United Kingdom and the costs of our second Phase I clinical trial that we initiated and completed in 2004 in the United States. In addition, we incurred costs in 2004 related to manufacturing of clinical supplies of CTI-01 in preparation for our Phase II clinical trial, which we initiated in February 2005. We expect our costs for this program will continue to increase in 2005 as we conduct our Phase II clinical trial of CTI-01, including the 150-patient trial in patients which we initiated in February 2005. These trials and the other development work required for this program will require significant expenditures before we can seek regulatory approval. We estimate that the total direct costs that we will need to incur to advance CTI-01 through clinical development will be at least \$25.0 million. However, the actual costs and timing of clinical trials and associated activities to enable a regulatory submission are highly uncertain, subject to risk and will change depending upon the clinical indication developed and the development strategy adopted. As a result, we believe that these estimated direct costs may change significantly as the product advances through clinical development.

*HMGB1.* Expenses for the research and development of HMGB1-inhibiting products decreased significantly in the year ended December 31, 2004 primarily due to the collaboration agreement entered into with MedImmune in the second half of 2003. As part of the agreement, MedImmune is funding a significant portion of the development costs including those incurred by us subject to certain annual limitations. We currently anticipate that most, if not all, research and development costs in 2005 will continue to be covered by MedImmune. However, we expect to undertake some internal research and preclinical testing, and we cannot be certain that the research payments received from MedImmune will fully cover the costs associated with these activities. Because our HMGB1 program is still in preclinical development, the actual costs and timing of preclinical development, clinical trials and associated activities are highly uncertain, subject to risk and will change depending upon the clinical indication developed and the development strategy adopted. As a result, we are not able to estimate the costs or the timing of advancing an HMGB1-inhibiting product or products through clinical development.

*Cholinergic anti-inflammatory.* Expenses for our cholinergic anti-inflammatory program increased in the year ended December 31, 2004 primarily due to costs associated with our efforts to develop small molecules and a medical device to stimulate the vagus nerve. We anticipate that significant additional expenditures will be required to advance any product candidate or device through preclinical and clinical development. However, because these projects are at a very early stage, the actual costs and timing of research, preclinical development, clinical trials and associated activities are highly uncertain, subject to risk and will change depending upon the project we choose to develop, the clinical indication developed and the development strategy adopted. As a result, we are unable to estimate the costs or the timing of advancing a small molecule or device from our cholinergic anti-inflammatory program through clinical development.

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*General and Administrative Expenses.* General and administrative expenses for the year ended December 31, 2004 were \$10.9 million compared to \$3.8 million for the year ended December 31, 2003. The \$7.1 million increase in 2004 was primarily attributable to the following:

a \$2.8 million increase in personnel costs primarily as a result of the increase in the number of employees performing general and administrative functions from nine employees at December 31, 2003 to thirty-two employees at December 31, 2004;

a \$349,000 increase in fees for professional services associated with our licensing and other corporate activity;

a \$415,000 increase in directors and officers insurance costs as a result of an increase in premiums following our initial public offering;

a \$1.7 million increase in facility and equipment costs as a result of our move in April 2004 to a larger facility;

a \$419,000 increase in cancellation of employee loans and gross-up payments for state and federal taxes; and

a \$1.4 million increase in stock-based compensation expense.

The increase in stock-based compensation expense was primarily attributable to the additional amortization on the issuance of certain employee stock options during 2003 and the first half of 2004 with an exercise price below the fair value at the date of grant prior to our initial public offering. This difference has been recorded as deferred stock-based compensation expense and is being amortized over the vesting period of the related stock awards. Therefore, the effect of such amortization, together with the effect of previously issued stock awards, resulted in an increase in stock-based compensation expense for the year ended December 31, 2004.

*Interest Income and Expense.* Interest income and interest expense amounted to \$1.1 million and \$172,000 respectively, for the year ended December 31, 2004, compared to \$191,000 and \$94,000, respectively, for the year ended December 31, 2003. The increase in interest income in 2004 was primarily attributable to interest earned on the \$56.2 million in gross proceeds from our series B preferred stock financing in October 2003 and March 2004 and the \$37.8 million in net proceeds from our initial public offering in June 2004. The increase in interest expense was primarily attributable to increased borrowings outstanding on our credit agreement in 2004 to finance capital purchases as compared to 2003.

*Accretion of Dividends and Offering Costs on Preferred Stock.* Accretion of dividends and offering costs on our convertible preferred stock for the year ended December 31, 2004 was \$2.2 million. Upon the completion of our initial public offering on June 2, 2004, our convertible preferred stock automatically converted into shares of common stock, and as a result there were no further accretion of dividends and offering costs on these shares for the periods subsequent to June 2, 2004.

***Years Ended December 31, 2003 and 2002***

*Revenue Under Collaboration Agreement.* We recognized revenues of \$1.0 million in the year ended December 31, 2003. These revenues represent the portion of the \$12.5 million MedImmune paid us under our collaboration with MedImmune that we recognized in 2003. We have recorded the balance of the payment as deferred revenue and will recognize such amount over the initial estimated 41-month research term of our agreement with MedImmune. The year ended December 31, 2003 was the first year in which we generated revenue.

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*Research and Development Expenses.* Research and development expenses for the year ended December 31, 2003 were \$17.5 million compared to \$3.3 million for the year ended December 31, 2002. The \$14.2 million increase in 2003 was attributable to \$3.1 million in increased research activity on our HMGB1 program, \$3.3 million incurred in connection with the commencement of our zileuton program, including expenses associated with initiating the transfer of Abbott's manufacturing technology, the initial \$1.5 million payable to Abbott in connection with our in-license of the controlled-release and intravenous formulations of zileuton, increased expenses associated with the increase in the number of employees performing research and development functions and increased facilities, equipment and laboratory charges associated with our increased research and development activities during 2003, and a \$4.8 million increase in stock-based compensation.

The following table summarizes the primary components of our research and development expenses for the years ended December 31, 2003 and 2002:

	<b>Year Ended December 31,</b>	
	<b>2003</b>	<b>2002</b>
	<b>(In thousands)</b>	
CTI-01	\$ 1,579	\$ 1,793
HMGB1	3,483	428
Cholinergic anti-inflammatory	630	62
Zileuton	3,269	
General research and development expenses	3,589	881
Stock-based compensation expense	4,908	120
<b>Total research and development expenses</b>	<b>\$ 17,458</b>	<b>\$ 3,284</b>

Our general research and development expenses, which are not allocated to any specific program, increased in 2003 due to a \$1.1 million increase in compensation expenses related to research and development employees, a \$440,000 increase in science services and a \$630,000 increase in expenses related to facilities and equipment.

Stock-based compensation expense, which is not allocated to any specific program, increased by \$4.8 million in 2003, primarily due to the effect of the increase in the value of our common stock on unvested non-employee options and restricted shares of common stock.

We anticipate that our research and development expenses will continue to increase as we further advance our research and development projects. The following summarizes the expenses associated with our primary research and development programs:

*Zileuton.* In 2003, we incurred costs with respect to the development of the controlled-release formulation of zileuton, including costs associated with the technology transfer relating to the manufacture of zileuton, including the API and the controlled-release tablets.

*CTI-01.* Expenses for CTI-01 increased in 2003 primarily due to costs associated with the Phase I clinical trial of CTI-01 that we conducted in 2003.

*HMGB1.* Expenses for HMGB1 increased significantly in 2003 primarily due to costs associated with the research and development of HMGB1-inhibiting products.

*Cholinergic Anti-inflammatory.* Expenses for our cholinergic anti-inflammatory program increased in 2003 primarily due to costs associated with our efforts to develop small molecules and a medical device to stimulate the vagus nerve.

*General and Administrative Expenses.* General and administrative expenses for the year ended December 31, 2003 were \$3.8 million compared to \$1.8 million for the year ended December 31, 2002. The \$2.0 million increase in 2003 was primarily attributable to a \$1.0 million increase in personnel costs relating to the increase in the number of employees performing general and administrative functions from

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five employees to nine employees, a \$535,000 increase in fees for professional services associated with our licensing transactions and other corporate activities, and a \$164,000 increase in stock-based compensation expense. The increase in stock-based compensation expense was primarily attributable to the effect of the increase of the value of our common stock on unvested employee options.

*Interest Income and Expense.* Interest income for the year ended December 31, 2003 was \$191,000 compared to \$149,000 for the year ended December 31, 2002. The \$42,000 increase in 2003 was primarily attributable to interest income received from the \$28.1 million in proceeds from our series B preferred stock financing in October 2003. Interest expense for the year ended December 31, 2003 was \$93,000 compared to \$8,000 for the year ended December 31, 2002. The \$85,000 increase was primarily attributable to an increase in borrowing to finance our equipment purchases.

*Accretion of Dividends and Offering Costs on Preferred Stock.* Accretion of dividends and offering costs on our convertible preferred stock for the year ended December 31, 2003 was \$2.3 million compared to \$1.0 million for the year ended December 31, 2002. The \$1.3 million increase in 2003 reflects the accretion of dividends on our series B convertible preferred stock issued in October 2003. Upon the closing of our initial public offering on June 2, 2004, our outstanding convertible preferred stock automatically converted into shares of common stock, and as a result, there were no further accretion of dividends and offering costs on these shares for the periods subsequent to June 2, 2004.

**Liquidity and Capital Resources***Sources of Liquidity*

Since our inception on July 14, 2000, we have raised proceeds to finance our operations through our initial public offering of common stock, private placements of equity securities, debt financings, the receipt of interest income, and payments from our collaborators MedImmune and Beckman Coulter. As of December 31, 2004, we had \$78.8 million in cash, cash equivalents and short-term investments.

In June 2004, we sold 6,110,000 shares of our common stock in our initial public offering, including 110,000 shares pursuant to the underwriters' partial exercise of their over-allotment option. Our net proceeds from the offering equaled approximately \$37.8 million. In March 2004, we issued and sold 20,055,160 shares of our series B convertible preferred stock, resulting in net proceeds of approximately \$28.1 million. All of our outstanding preferred stock was converted to common stock in connection with our initial public offering. We have invested the net proceeds from both financings in highly-liquid, interest-bearing, investment grade securities in accordance with our established corporate investment policy.

Under our collaboration with MedImmune, MedImmune paid us initial fees of \$12.5 million from August 2003 through January 2004. In connection with entering into this collaboration, an affiliate of MedImmune purchased \$15.0 million of our series B convertible preferred stock, which converted into 2,857,142 shares of our common stock upon the closing of our initial public offering. In addition, under our collaboration agreement with MedImmune, we may receive additional payments upon the achievement of research, development and commercialization milestones, up to a maximum of \$124.0 million, after taking into account payments we are obligated to make to North Shore-Long Island Jewish Research Institute on milestone payments we receive from MedImmune. We anticipate that we will receive \$2.0 million in aggregate milestone payments from MedImmune in 2005, after taking into account payments we are obligated to make to North Shore.

We finance the purchase of general purpose computer equipment, office equipment, fixtures and furnishings, test and laboratory equipment and software licenses and the completion of leasehold improvements through advances under our credit agreement with Silicon Valley Bank, which was most recently modified as of June 30, 2004. As of December 31, 2004, there was \$2.2 million in debt outstanding under our credit agreement, of which \$2.0 million was outstanding under equipment advances and \$155,000 was outstanding under leasehold advances.

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The equipment advances made prior to the modification of our credit agreement on June 30, 2004 accrue interest at an effective interest rate between 8.6% and 9.1% per year, and the leasehold advances made prior to June 30, 2004 accrue interest at an effective interest rate between 10.5% and 11.0% per year. We are required to make equal monthly payments of principal and interest with respect to each advance made prior to June 30, 2004. The total repayment term for equipment advances made prior to June 30, 2004 is 48 months. The total repayment term for leasehold advances made prior to June 30, 2004 is 24 months. Upon the maturity of any advance made prior to June 30, 2004, we are required to make a final payment to Silicon Valley Bank, in addition to the repayment of principal and interest, in an amount equal to a specified percentage of the original advance amount. The applicable percentage is 7.0% for advances to finance leasehold improvements and 8.5% for advances to finance equipment purchases. As of December 31, 2004, there was \$720,000 outstanding for advances made prior to June 30, 2004 bearing interest between 8.5% and 11%. Under the modification agreement signed as of June 30, 2004, we had the ability to borrow up to an additional \$3.0 million under our credit agreement from July 1, 2004 to December 31, 2004. Furthermore, we have additional borrowing capacity of up to \$1.3 million in 2005. Advances made under this modification agreement accrue interest at a rate equal to the prime rate plus 2% per year. Advances made under this modification agreement are required to be repaid in equal monthly installments of principal plus interest accrued through the date of repayment. The repayment term for advances made in 2004 is 42 months. The repayment term for advances made in 2005 is 36 months. Repayment begins the first day of the month following the advance. During the year ended December 31, 2004, we received \$1.6 million in advances under this modified credit agreement, of which \$1.5 million is outstanding as of December 31, 2004 bearing interest at the prime rate plus 2% per year.

We granted Silicon Valley Bank a first priority security interest in substantially all of our assets, excluding intellectual property, to secure our obligations under the credit agreement. In connection with entering into the original credit agreement in June 2002, we issued Silicon Valley Bank a warrant exercisable for 90,000 shares of our series A convertible preferred stock that became exercisable for 24,000 shares of our common stock upon the completion of our initial public offering. In November 2004, Silicon Valley Bank exercised its rights under the warrant through a cashless transaction that resulted in the issuance of 12,157 shares of common stock. As of December 31, 2004, there are no remaining warrants outstanding.

***Cash Flows***

For the year ended December 31, 2004, net cash used for operating activities was \$25.1 million compared to \$1.0 million net cash used for operating activities for the year ended December 31, 2003. The increase in cash used to fund operations resulted from lower cash received under our collaboration agreement with MedImmune and increased net losses from higher research and development activities on our zileuton, CTI-01 and cholinergic anti-inflammatory research and development programs. In 2003, we received \$10.0 million in up front fees from MedImmune compared to approximately \$4.0 million received in 2004 from additional up front license payments and funding to support our development costs on the HMGB1 program.

Net cash used in operations for the year ended December 31, 2004 consisted of a net loss of \$31.1 million and changes in working capital accounts resulting in \$28.1 million of cash used. These were partially offset by non-cash expenses of \$3.6 million in stock-based compensation and \$1.8 million in depreciation and amortization. Net cash used for investing activities for the year ended December 31, 2004 was \$70.0 million, including \$120.9 million used to purchase short-term investments and \$2.0 million used for the purchase of fixed assets. Short-term investments are defined as securities that have a maturity date greater than 90 days that can be sold within one year.

Net cash provided by financing activities for the year ended December 31, 2004 was \$67.0 million, relating principally to the proceeds from our initial public offering of our common stock in June 2004 and the issuance of our series B convertible preferred stock in March 2004. We sold 6,110,000 shares of our common stock in our initial public offering, including 110,000 shares pursuant to the underwriters' partial exercise of their over-allotment option. Our net proceeds from the offering equaled approximately

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\$37.8 million. Our net proceeds from the issuance of our series B convertible preferred stock in March 2004 equaled approximately \$28.1 million.

***Income Taxes***

We have accumulated net operating losses and tax credits available to offset future taxable income for federal and state income tax purposes as of December 31, 2004. If not utilized, federal and state net operating loss carryforwards will begin to expire in 2021 and 2006, respectively. The federal tax credits expire beginning in 2021. To date, we have not recognized the potential tax benefit of our net operating loss carryforwards or credits on our balance sheet or statements of operations. The future utilization of our net operating loss carryforwards may be limited based upon changes in ownership pursuant to regulations promulgated under the Internal Revenue Code.

***Funding Requirements***

We expect to devote substantial resources in 2005 to continue our research and development efforts, including preclinical testing and clinical trials, establish our sales and marketing infrastructure, achieve regulatory approvals and, subject to regulatory approval, commercially launch ZYFLO and the controlled-release formulation of zileuton and any future product candidates. We also expect to spend approximately \$2.5 million in capital expenditures in 2005 for the purchase of new equipment for our laboratories and software to support our growing infrastructure. Our funding requirements will depend on numerous factors, including:

the costs and timing of the commercial launch of ZYFLO, if and when it is approved by regulatory authorities;

the costs and timing of the development and the commercial launch of the controlled-release formulation of zileuton, if and when it is approved by regulatory authorities;

the scope and results of our clinical trials;

advancement of our other product candidates into development;

potential acquisition or in-licensing of other products or technologies;

the time and costs involved in obtaining regulatory approvals;

the timing, receipt and amount of milestone and other payments, if any, from MedImmune, Beckman Coulter or future collaborators;

the timing, receipt and amount of sales and royalties, if any, from our potential products;

continued progress in our research and development programs, as well as the magnitude of these programs;

the cost of manufacturing, marketing and sales activities;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

the cost of obtaining and maintaining licenses to use patented technologies; and

our ability to establish and maintain additional collaborative arrangements.

We do not expect to generate significant additional funds, other than payments that we receive under our collaboration with MedImmune or Beckman Coulter, until we successfully conduct clinical trials, achieve regulatory approvals and, subject to regulatory approval, commercially launch ZYFLO and the controlled-release formulation of zileuton. In addition to the foregoing factors, we believe that our ability to access external funds will depend upon the success of our other preclinical and clinical development programs, the receptivity of the capital markets to financings



by biopharmaceutical companies, our ability to enter into additional strategic collaborations with corporate and academic collaborators and the success of such collaborations.

Based on our operating plans, we believe that our available cash and cash equivalents will be sufficient to fund anticipated levels of operations until the middle of 2006.

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If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we will need to raise additional external funds through collaborative arrangements and public or private financings. Additional financing may not be available to us on acceptable terms or at all. In addition, the terms of the financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, dilution to our then-existing stockholders will result. If we are unable to obtain funding on a timely basis, we may be required to significantly delay, limit or eliminate one or more of our research, development or commercialization programs, which could harm our financial condition and operating results. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products which we would otherwise pursue on our own.

**Contractual Obligations**

We have summarized in the table below our fixed contractual obligations as of December 31, 2004.

**Payments Due by Period**

<b>Contractual Obligations</b>	<b>Total</b>	<b>Less than One Year</b>	<b>One to Three Years</b>	<b>Three to Five Years</b>	<b>After Five Years</b>
<b>(In thousands)</b>					
Short and long term debt	\$ 2,204	\$ 837	\$ 1,367	\$	\$
Research and license agreements	7,995	695	256	234	6,810
Consulting agreements	760	413	347		
Manufacturing and clinical trial agreements	7,317	6,443	874		
Operating lease obligations	5,622	1,503	2,613	1,506	
<b>Total contractual cash obligations</b>	<b>\$ 23,898</b>	<b>\$ 9,891</b>	<b>\$ 5,457</b>	<b>\$ 1,740</b>	<b>\$ 6,810</b>

The amounts listed for short and long term debt represent the principal amounts we owe under our credit agreement with Silicon Valley Bank.

The amounts listed for research and license agreements represent our fixed obligations payable to sponsor research and minimum royalty payments for licensed patents. These amounts do not include any additional amounts that we may be required to pay under our license agreements upon the achievement of scientific, regulatory and commercial milestones that may become payable depending on the progress of scientific development and regulatory approvals, including milestones such as the submission of an investigational new drug application to the FDA, similar submissions to foreign regulatory authorities and the first commercial sale of our products in various countries. In January 2005, we executed an exclusive license agreement with a third party. We are obligated to make a non-refundable license fee payment of approximately \$200,000 and up to an additional \$900,000 upon the achievement of future milestones. These amounts are not included in the table because the agreement was signed after December 31, 2004.

We are party to a number of agreements that require us to make milestone payments. In particular, under our license agreement with Abbott Laboratories for zileuton, we agreed to make aggregate milestone payments of up to \$13.0 million to Abbott upon the achievement of various development and commercialization milestones relating to zileuton, including the completion of the technology transfer from Abbott to us, filing and approval of a product in the United States and specified minimum net sales of licensed products. In addition, under our manufacturing agreement

with SkyePharma, through its subsidiary Jagotec, for the controlled-release version of zileuton, we agreed to make aggregate milestone payments of up to \$6.6 million upon the achievement of various development and commercialization milestones. We anticipate that, in addition to payments already made, we will pay approximately \$4.4 million in aggregate milestone payments related to zileuton by the end of 2005.

These amounts also do not include royalties on net sales of our products and payments on sublicense income that we may owe as a result of receiving payments under our collaboration agreement with

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MedImmune. Our license agreements are described more fully in Note 11 of our consolidated financial statements.

The amounts listed for consulting agreements are for fixed payments due to our scientific and business consultants. In early 2005, we executed agreements with third parties to provide business consulting services. We expect to pay approximately \$121,000 for these services over the next twelve months. These amounts are not included in the table because the agreements were signed after December 31, 2004.

The amounts listed for manufacturing and clinical trial agreements represent amounts due to third parties for manufacturing, clinical trials and pre-clinical studies. In early 2005, we executed agreements with third parties to provide research, manufacturing and support services for clinical trials of our zileuton program. We expect to pay approximately \$327,000 for these services over the next twelve months. These amounts are not included in the table because the agreements were signed after December 31, 2004.

We have contracted with Rhodia Pharma Solutions Ltd. to establish and validate a manufacturing process for the API at sites operated by Rhodia. The technology transfer to Rhodia has been completed and Rhodia is validating the zileuton manufacturing process and preparing to commence commercial production of the API. In February 2005, we entered into a commercial supply agreement with Rhodia for the commercial production of the API. Under the commercial supply agreement, Rhodia has agreed to manufacture our commercial supplies of API, subject to specified limitations, through December 31, 2009. The agreement will automatically extend for successive one-year periods after December 31, 2009, unless Rhodia provides us with 18-months prior written notice of cancellation. We have the right to terminate the agreement upon 12-months prior written notice for any reason, provided that we may not cancel prior to January 1, 2008 for the purpose of retaining any other company to act as our exclusive supplier of the API. We also have the right to terminate the agreement upon six-months prior written notice if we terminate our plans to commercialize zileuton for all therapeutic indications.

The amounts listed for research and license agreements, consulting agreements and manufacturing and clinical trial agreements include amounts that we owe under agreements that are subject to cancellation or termination by us under various circumstances, including a material uncured breach by the other party, minimum notice to the other party or payment of a termination fee.

The amounts listed for operating lease obligations represent the amount we owe under our office, vehicle and laboratory space lease agreements.

### **Effects of Inflation**

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

### **Recent Accounting Pronouncements**

In December 2004, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards No. 123R, *Share-Based Payment*, or SFAS No. 123R. This Statement is a revision of SFAS No. 123, *Accounting for Stock-Based Compensation*, and supersedes Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, and its related implementation guidance. SFAS No. 123R focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. The Statement requires entities to recognize stock compensation expense for awards of equity instruments to employees based on the grant-

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date fair value of those awards (with limited exceptions). SFAS No. 123R is effective for the first interim or annual reporting period that begins after June 15, 2005.

We are evaluating the two methods of adoption allowed by SFAS No. 123R: the modified-prospective transition method and the modified-retrospective transition method.

Adoption of SFAS No. 123R will significantly increase compensation expense. In addition, SFAS No. 123R requires that excess tax benefits related to stock compensation expense be reported as a financing cash inflow rather than as a reduction of taxes paid in cash flow from operations.

**ITEM 7A. *QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK***

We are exposed to market risk related to changes in interest rates. Our current investment policy is to maintain an investment portfolio consisting mainly of U.S. money market and corporate notes, directly or through managed funds, with maturities of two years or less. Our cash is deposited in and invested through highly rated financial institutions in North America. Our short-term investments are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 10% from levels at December 31, 2004, we estimate that the fair value of our investment portfolio would decline by approximately \$142,000. In addition, we could be exposed to losses related to these securities should one of our counterparties default. We attempt to mitigate this risk through credit monitoring procedures. We have the ability to hold our fixed income investments until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

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**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**  
**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**  
**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors of  
Critical Therapeutics, Inc.:

We have audited the accompanying consolidated balance sheets of Critical Therapeutics, Inc. and its subsidiary (the Company ) as of December 31, 2004 and 2003, and the related consolidated statements of operations, redeemable convertible preferred stock, stockholders' equity (deficit) and comprehensive loss, and cash flows for each of the three years in the period ended December 31, 2004. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required, nor have we been engaged to perform, an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Critical Therapeutics, Inc. and its subsidiary at December 31, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004 in conformity with accounting principles generally accepted in the United States of America.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts

March 14, 2005

**Table of Contents****CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
CONSOLIDATED BALANCE SHEETS**

	As of December 31,	
	2004	2003
	In thousands	
<b>ASSETS</b>		
<b>CURRENT ASSETS:</b>		
Cash and cash equivalents	\$ 11,980	\$ 40,078
Amount due under collaboration agreement	16	2,500
Short-term investments	66,849	
Prepaid expenses and other	1,851	430
<b>Total current assets</b>	<b>80,696</b>	<b>43,008</b>
<b>FIXED ASSETS, NET</b>	<b>2,205</b>	<b>1,556</b>
<b>NOTE RECEIVABLE FROM OFFICER</b>		<b>50</b>
<b>OTHER ASSETS</b>	<b>213</b>	<b>440</b>
<b>TOTAL</b>	<b>\$ 83,114</b>	<b>\$ 45,054</b>
<b>LIABILITIES AND STOCKHOLDERS EQUITY (DEFICIT)</b>		
<b>CURRENT LIABILITIES:</b>		
Current portion of long-term debt	\$ 837	\$ 552
Accounts payable	4,218	323
Accrued license fees		4,460
Accrued expenses	2,741	977
Revenue deferred under collaboration agreement	8,543	11,478
<b>Total current liabilities</b>	<b>16,339</b>	<b>17,790</b>
<b>COMMITMENTS (Note 12)</b>		
<b>LONG-TERM DEBT, less current portion</b>	<b>1,367</b>	<b>720</b>
<b>REDEEMABLE CONVERTIBLE PREFERRED STOCK</b>		
par value \$0.001; authorized 0 shares in 2004 and 70,000,000 shares in 2003; issued and outstanding 0 shares in 2004 and 40,355,167 shares in 2003		51,395
<b>STOCKHOLDERS EQUITY (DEFICIT):</b>		
Common stock, par value \$0.001; authorized 90,000,000 shares; issued and outstanding 24,085,481 shares in 2004 and 1,565,353 shares in 2003	24	2
Preferred stock, par value \$0.001; authorized 5,000,000 shares in 2004; no shares issued and outstanding in 2004		
Additional paid-in capital	130,374	11,156
Deferred stock-based compensation	(6,101)	(8,536)
Due from stockholders		(40)



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Accumulated deficit	(58,527)	(27,433)
Accumulated other comprehensive loss	(362)	
Total stockholders' equity (deficit)	65,408	(24,851)
<b>TOTAL</b>	<b>\$ 83,114</b>	<b>\$ 45,054</b>

The accompanying notes are an integral part of these consolidated financial statements.

**Table of Contents****CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
CONSOLIDATED STATEMENTS OF OPERATIONS**

	<b>Year Ended December 31,</b>		
	<b>2004</b>	<b>2003</b>	<b>2002</b>
	<b>In thousands, except share and per share data</b>		
REVENUE UNDER COLLABORATION AGREEMENT	\$ 4,436	\$ 1,021	\$
<b>OPERATING EXPENSES:</b>			
Research and development	25,578	17,458	3,284
General and administrative	10,878	3,771	1,792
Total operating expenses	36,456	21,229	5,076
LOSS FROM OPERATIONS	(32,020)	(20,208)	(5,076)
INTEREST INCOME	1,098	191	149
INTEREST EXPENSE	(172)	(93)	(8)
NET LOSS	(31,094)	(20,110)	(4,935)
ACCRETION OF DIVIDENDS AND OFFERING COSTS ON PREFERRED STOCK	(2,209)	(2,264)	(1,032)
NET LOSS AVAILABLE TO COMMON STOCKHOLDERS	\$ (33,303)	\$ (22,374)	\$ (5,967)
NET LOSS AVAILABLE TO COMMON STOCKHOLDERS PER SHARE Basic and diluted	\$ (2.28)	\$ (33.99)	\$ (23.74)
<b>WEIGHTED AVERAGE COMMON SHARES OUTSTANDING:</b>			
Basic and diluted	14,631,371	658,204	251,346

The accompanying notes are an integral part of these consolidated financial statements.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE  
PREFERRED STOCK, STOCKHOLDERS EQUITY (DEFICIT) AND COMPREHENSIVE LOSS  
YEARS ENDED DECEMBER 31, 2002, 2003 AND 2004**

	Redeemable Convertible Preferred Stock	Common Stock	Additional Paid-In Capital	Deferred Stock-Based Compensation	Due from Stockholders	Accumulated Deficit	Accumulated Comprehensive Loss	Total Stockholders Equity	Comprehensive Loss
<b>In thousands, except share data</b>									
<b>BALANCE</b>									
<b>January 1, 2002</b>									
	\$ 10,270	\$ 1	\$ 84	\$ (317)	\$ (1)	\$ (1,517)	\$	\$ (1,750)	
Issuance of 10,150,000 shares of Series A preferred stock for cash and note receivable	9,778								
Issuance of 43,998 shares of common stock to non-employees			16					16	
Issuance of 172,344 shares of common stock to employees			65		(40)			25	
Accretion of preferred stock dividends and issuance costs	1,032		(161)			(871)		(1,032)	

Amortization of deferred stock-based compensation				120			120	
Payment from stockholder					1		1	
Net loss						(4,935)	(4,935)	\$ (4,935)

**BALANCE  
December 31,  
2002**

	21,080	1	4	(197)	(40)	(7,323)	(7,555)	
Issuance of 20,055,167 shares of Series B preferred stock for cash	27,906							
Issuance of 16,980 shares of common stock, upon exercise of options under stock purchase plan		1	6				7	
Repurchase of 3,221 shares of common stock			(8)	7			(1)	
Deferred stock-based compensation to employees			6,673	(6,672)			1	
Deferred stock-based compensation to			6,745	(6,745)				

non-employees				
Accretion of preferred stock dividends and issuance costs	2,264	(2,264)	(2,264)	
Amortization of deferred stock-based compensation		5,071	5,071	
Payment from stockholder	145			
Net loss			(20,110)	\$ (20,110)

The accompanying notes are an integral part of these consolidated financial statements.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE  
PREFERRED STOCK, STOCKHOLDERS EQUITY (DEFICIT) AND COMPREHENSIVE  
LOSS (Continued)  
YEARS ENDED DECEMBER 31, 2002, 2003 AND 2004**

	Redeemable Convertible Preferred Stock	Common Stock	Additional Paid-In Capital	Deferred Stock-Based Compensation	Due from Stockholders	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholder Equity	Comprehensive Loss
In thousands except share data									
<b>BALANCE December 31, 2003</b>	\$ 51,395	\$ 2	\$ 11,156	\$ (8,536)	\$ (40)	\$ (27,433)		\$ (24,851)	
Issuance of 20,055,160 shares of Series B preferred stock for cash	28,050								
Issuance of 221,902 shares of common stock, upon exercise of options under stock purchase plan			175					175	
Issuance of 66,666 shares of common stock in connection with license agreement			485					485	
Deferred stock- based compensation to employees			523	(523)					
Deferred stock- based compensation to non-employees			348	(348)					
Accretion of preferred stock dividends and issuance costs	2,209		(2,209)					(2,209)	
Amortization of deferred				3,562				3,562	

stock-based compensation								
Reversal of deferred stock based compensation			(21)	21				
Forgiveness of officer notes	145				40			40
Issuance of 6,000,000 shares of common stock in initial public offering, net of \$2.0 million in offering costs		6	37,095					37,101
Conversion of 60,410,327 shares of preferred stock into 16,109,403 shares of common stock	(81,799)	16	81,783					81,799
Issuance of 110,000 shares of common stock for underwriters over- allotment			716					716
Issuance of 12,157 shares of common stock related to exercise of warrant			46					46
Grant of stock options to non-employees			277	(277)				
Net loss					(31,094)		(31,094)	\$ (31,094)
Unrealized loss on investments					(362)		(362)	(362)
Comprehensive loss								\$ (31,456)
<b>BALANCE</b>								
<b>December 31, 2004</b>	\$	\$ 24	\$ 130,374	\$ (6,101)	\$	\$ (58,527)	\$ (362)	\$ 65,408

The accompanying notes are an integral part of these consolidated financial statements.

**Table of Contents****CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
CONSOLIDATED STATEMENTS OF CASH FLOWS****Year Ended December 31,**

	<b>2004</b>	<b>2003</b>	<b>2002</b>
<b>In thousands</b>			
<b>CASH FLOWS USED FOR OPERATING ACTIVITIES:</b>			
Net loss	\$ (31,094)	\$ (20,110)	\$ (4,935)
Adjustments to reconcile net loss to net cash used for operating activities:			
Depreciation and amortization	1,847	482	54
Stock-based compensation expense	3,562	5,072	120
Loss on disposal of fixed assets	278		
Loss on conversion of warrants	46		
Forgiveness of notes receivable	185		
Changes in assets and liabilities:			
Amount due under collaboration agreement	2,484	(2,500)	
Prepaid expenses and other	(1,421)	(622)	(259)
Other assets	277		
Accounts payable	3,895	(94)	367
Accrued license fees and other expenses	(2,211)	5,267	103
Revenue deferred under collaboration agreement	(2,935)	11,479	
Net cash used for operating activities	(25,087)	(1,026)	(4,550)
<b>CASH FLOWS USED FOR INVESTING ACTIVITIES:</b>			
Proceeds from sales and maturities of short-term investments	52,900		
Purchases of fixed assets	(2,019)	(1,492)	(581)
Purchases of short-term investments	(120,866)		
Net cash used for investing activities	(69,985)	(1,492)	(581)
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>			
Net proceeds from issuance of convertible preferred stock	28,050	27,906	9,778
Net proceeds from the initial public offering of common stock	37,817		
Proceeds from issuance of common stock	175	6	42
Proceeds from notes receivable		145	1
Repurchase of restricted common stock		(1)	
Proceeds from long-term debt	1,623	1,388	293
Repayments of long-term debt	(691)	(387)	(24)
Net cash provided by financing activities	66,974	29,057	10,090
<b>NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS</b>	<b>(28,098)</b>	<b>26,539</b>	<b>4,959</b>
	40,078	13,539	8,580



## CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD

CASH AND CASH EQUIVALENTS AT END OF PERIOD	\$ 11,980	\$ 40,078	\$ 13,539
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## SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:

## Cash paid during the period for:

Interest	\$ 126	\$ 94	\$ 7
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## SUPPLEMENTAL DISCLOSURE OF NONCASH INVESTING AND FINANCING ACTIVITIES:

Conversion of redeemable convertible preferred stock into common stock	\$ 81,799	\$	\$
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Accretion of dividends and offering costs on preferred stock	\$ 2,209	\$ 2,264	\$ 1,032
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Stock issued for stockholder receivables	\$	\$	\$ 330
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Dividends forfeited on preferred stock conversion into common stock	\$ 5,713	\$	\$
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Adjustment to deferred stock-based compensation for services to be performed	\$ 1,127	\$ 13,417	\$
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Settlement of accrued licensing fee with common stock	\$ 485	\$	\$
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Unrealized loss on investments	\$ 362	\$	\$
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The accompanying notes are an integral part of these consolidated financial statements.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**(1) Nature of Business**

Critical Therapeutics, Inc. (the Company) is a biopharmaceutical company focused on the discovery, development and commercialization of products for respiratory, inflammatory and critical care diseases.

The Company was incorporated in the state of Delaware on July 14, 2000 under the name Medicept, Inc. On March 12, 2001, the Company changed its name from Medicept, Inc. to Critical Therapeutics, Inc. The Company formed a wholly-owned subsidiary, CTI Securities Corporation, a Massachusetts corporation, in 2003.

The Company is subject to a number of risks similar to those of other companies in an early stage of development. Principal among these risks are dependence on key individuals, competition from substitute products and larger companies, the successful development and marketing of its products, and the need to obtain adequate additional financing necessary to fund future operations.

**(2) Summary of Significant Accounting Policies**

***Basis of Presentation***

The consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiary, CTI Securities Corporation. All intercompany balances and transactions have been eliminated.

***Use of Estimates***

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenue and expenses during the reporting period. Actual results could differ from those estimates.

***Research and Development***

Research and development expenses consist of expenses incurred in identifying, developing and testing product candidates. These expenses consist primarily of salaries and related expenses for personnel, fees paid to professional service providers for independently monitoring and analyzing clinical trials, costs of contract research and manufacturing and the cost of facilities. After regulatory approval of a product candidate, manufacturing expenses associated with a product will be recorded as cost of sales rather than research and development expenses. Research and development costs and patent related costs are expensed as incurred.

***Cash Equivalents and Short-Term Investments***

The Company considers all highly-liquid investments with original maturities of three months or less when purchased to be cash equivalents.

Short-term investments consist primarily of U.S. government treasury and agency notes, corporate debt obligations, municipal debt obligations, auction rate securities and money market funds, each of investment-grade quality, which have an original maturity date greater than 90 days that can be sold within one year. These securities are held until such time as the Company intends to use them to meet the ongoing liquidity needs to support its operations. These investments are recorded at fair value and accounted for as available-for-sale securities. The unrealized gain (loss) during the period is recorded as an adjustment to stockholders' equity. During the year ended December 31, 2004, the Company recorded an unrealized loss on investments of \$362,000. The original cost of debt securities is adjusted for

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

amortization of premiums and accretion of discounts to maturity. The amortization or accretion is included in interest income (expense) in the corresponding period.

On July 1, 2004, the Company adopted EITF Issue No. 03-1, *The Meaning of Other-Than-Temporary Impairment and its Application to Certain Investments* (EITF 03-1) as applicable to debt and equity securities that are within the scope of SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities* and equity securities that are accounted for using the cost method specified in APB Opinion No. 18, *The Equity Method of Accounting for Investments in Common Stock*, except for paragraphs 10-20 of this Issue regarding how to evaluate and recognize an impairment loss that is other-than-temporary, insofar as application of these paragraphs has been deferred. The Company has determined the unrealized gain (loss) on investments is temporary; therefore no impairment losses were recorded for the year ended December 31, 2004.

The unrealized losses as of December 31, 2004 were primarily caused by interest rate increases. The following table shows the gross unrealized losses and fair value of the Company's investments with unrealized losses that are not deemed to be other-than-temporarily impaired, aggregated by investment category:

	<b>As of December 31, 2004</b>			
	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized Losses</b>	<b>Fair Value</b>
<b>Cash and cash equivalents:</b>				
Cash	\$ 4,319	\$	\$	\$ 4,319
Commercial Paper	2,019			2,019
Money market mutual funds	5,642			5,642
<b>Cash and cash equivalents</b>	<b>11,980</b>			<b>11,980</b>
<b>Short-term investments:</b>				
U.S. government and agency securities	17,056		(42)	17,014
Corporate bonds	32,349		(316)	32,033
Municipal bonds	1,006		(4)	1,002
Auction rate securities	16,800			16,800
<b>Short-term investments</b>	<b>67,211</b>		<b>(362)</b>	<b>66,849</b>
<b>Cash and cash equivalents and short-term investments</b>	<b>\$ 79,191</b>	<b>\$</b>	<b>\$ (362)</b>	<b>\$ 78,829</b>

**Fixed Assets**

Fixed assets are stated at cost, net of accumulated depreciation and amortization. Depreciation is computed on a straight-line basis over estimated useful lives of three to seven years commencing upon the date the assets are placed in service. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in operating income. Repairs and maintenance costs are expensed as incurred.

**Impairment of Long-Lived Assets**

Long-lived assets and, if and when applicable, certain identifiable intangibles held and used are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be

recoverable. In performing the review for recoverability, the Company will estimate the future cash flows expected to result from the use of the asset and its eventual disposition. If the sum

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of the expected future cash flows (undiscounted and without interest charges) is less than the carrying amount of the asset, an impairment loss is recognized. Measurement of an impairment loss for long-lived assets and identifiable intangibles that the Company expects to hold and use is based on the fair value of the asset. No adjustments have been required to date.

***Revenue Recognition***

The Company recognizes revenue in accordance with the Securities and Exchange Commission's (SEC) Staff Accounting Bulletin No. 101, Revenue Recognition in Financial Statements (SAB 101), as amended by SEC Staff Accounting Bulletin No. 104 Revenue Recognition (SAB 104). Specifically, revenue is recognized when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable and collectibility is reasonably assured.

Revenue under the Company's collaboration agreement with MedImmune, Inc. as discussed in Note 3 is recognized over the estimated performance period based on a proportional performance model. Under the proportional performance model, performance is measured as the percentage of cost incurred to date compared to the total costs estimated for the performance period. The amount of revenue recognized during each period represents the cumulative performance percentage of amounts received and due to the Company under the agreement less amounts previously recognized. The Company periodically reviews the estimated performance period and total costs and, to the extent such estimates change, the impact of such change is recorded in operations at that time. Because the Company's collaborator has the right to cancel the agreement at any time, the Company does not recognize revenues in excess of cumulative cash collections. Deferred revenue consists of payments received in advance of revenue recognized under the agreement.

***Fair Value of Financial Instruments***

The carrying amounts of the Company's financial instruments, which include cash equivalents, short-term investments, accounts payable, accrued expenses, and long term obligations, approximate their fair values.

***Concentrations of Credit Risk and Limited Suppliers***

The financial instruments that potentially subject the Company to concentrations of credit risk are cash, cash equivalents and short-term investments. The Company's cash, cash equivalents and short-term investments are maintained with highly-rated commercial banks and are monitored against the Company's investment policy, which limits concentrations of investments in individual securities and issuers.

The Company relies on certain materials used in its development and manufacturing processes, some of which are procured from a single source. The failure of a supplier, including a subcontractor, to deliver on schedule could delay or interrupt the development or commercialization process and thereby adversely affect the Company's operating results.

***Income Taxes***

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have previously been included in either the Company's consolidated financial statements or

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
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tax returns. Deferred tax assets and liabilities are determined based on the differences between the financial accounting and tax bases of assets and liabilities using tax rates expected to be in effect for the year in which the differences are expected to reverse. A valuation allowance is provided against net deferred tax assets where management believes it is more likely than not that the asset will not be realized.

**Stock-Based Compensation**

The Company accounts for stock-based awards to employees using the intrinsic-value method as prescribed by Accounting Principles Board ( APB ) Opinion No. 25, Accounting for Stock Issued to Employees, and related interpretations. Accordingly, no compensation expense is recorded for options issued to employees in fixed amounts and with fixed exercise prices at least equal to the fair market value of the Company's common stock at the date of grant. Conversely, when the exercise price for accounting purposes is below fair value of the Company's common stock on the date of grant, a non-cash charge to compensation expense is recorded ratably over the term of the option vesting period in an amount equal to the difference between the value calculated using the exercise price and the fair value. All stock-based awards to non-employees are accounted for at their fair market value in accordance with Statement of Financial Accounts Standards ( SFAS ) No. 123 Accounting for Stock-Based Compensation, and Emerging Issues Task Force ( EITF ) No. 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.

The Company has adopted the provisions of SFAS No. 123, Accounting for Stock-Based Compensation, through disclosure only for options awarded to employees. SFAS No. 123 requires the disclosure of pro forma net loss as if the Company adopted the fair-value method of valuing its options. Under SFAS No. 123, the fair value of stock-based awards to employees is calculated through the use of option-pricing models.

Had employee compensation cost for the Company's stock plans been determined consistent with SFAS No. 123, the Company's proforma net loss and proforma net loss per share would have been as follows (in thousands, except loss per share data):

	<b>Year Ended December 31,</b>		
	<b>2004</b>	<b>2003</b>	<b>2002</b>
Net loss available to common stockholders as reported	\$ (33,303)	\$ (22,374)	\$ (5,967)
Add: Stock-based compensation expense included in reported net loss	1,784	165	
Deduct: Stock-based compensation expense determined under fair value method	(1,162)	(201)	(5)
Net loss available to common stockholders pro forma	\$ (32,681)	\$ (22,410)	\$ (5,972)
<b>Net loss per share (basic and diluted):</b>			
As reported	\$ (2.28)	\$ (33.99)	\$ (23.74)
Pro forma	\$ (2.23)	\$ (34.05)	\$ (23.76)

Option valuation models require the input of highly subjective assumptions. Because changes in subjective input assumptions can materially affect the fair value estimate, in management's opinion, the calculated fair value may not necessarily be indicative of the actual fair value of the stock options. The Company has computed the pro forma disclosures required under SFAS No. 123 for options granted using



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the Black-Scholes option-pricing model prescribed by SFAS No. 123. The assumptions used and weighted-average information are as follows:

	<b>December 31,</b>		
	<b>2004</b>	<b>2003</b>	<b>2002</b>
Risk free interest rate	3.3%	2.4%	2.3%
Expected dividend yield	0%	0%	0%
Expected lives	4 years	4 years	4 years
Expected volatility	100%	100%	100%
Weighted-average fair value of options granted equal to fair value	\$ 4.38	\$ 0.26	\$ 0.26
Weighted-average fair value of options granted below fair value	\$ 3.73	\$ 6.26	\$

In December 2004, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards No. 123R, *Share-Based Payment*, or SFAS No. 123R. This Statement is a revision of SFAS No. 123, *Accounting for Stock-Based Compensation*, and supersedes Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, and its related implementation guidance. SFAS No. 123R focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. The Statement requires entities to recognize stock compensation expense for awards (with limited exceptions). SFAS No. 123R is effective for the first interim or annual reporting period that begins after June 15, 2005.

The Company is evaluating the two methods of adoption allowed by SFAS No. 123R: the modified-prospective transition method and the modified-retrospective transition method.

Adoption of SFAS No. 123R will significantly increase compensation expense. In addition, SFAS No. 123R requires that excess tax benefits related to stock compensation expense be reported as a financing cash inflow rather than as a reduction of taxes paid in cash flow from operating activities in the consolidated statement of cash flows.

***Basic and Diluted Loss per Share***

Basic and diluted net loss per common share is calculated by dividing the net loss applicable to common stockholders by the weighted-average number of unrestricted common shares outstanding during the period. Diluted net loss per common share is the same as basic net loss per common share, since the effects of potentially dilutive securities are anti-dilutive for all periods presented. Anti-dilutive securities that are not included in the diluted net loss per share calculation aggregated 4,776,922, 42,928,818 and 21,910,577 as of December 31, 2004, 2003 and 2002, respectively. These anti-dilutive securities consist of outstanding stock options and unvested restricted common stock as of December 31, 2004, and outstanding redeemable convertible preferred stock, stock options, warrants and unvested restricted common stock as of December 31, 2003 and 2002.

The following table reconciles the weighted-average common shares outstanding to the shares used in the computation of basic and diluted weighted-average common shares outstanding:

	<b>Year Ended December 31,</b>		
	<b>2004</b>	<b>2003</b>	<b>2002</b>
Weighted-average common shares outstanding	15,077,169	1,553,309	1,430,910
Less: weighted-average restricted common shares outstanding	445,798	895,105	1,179,564



Basic and diluted weighted-average common shares outstanding	14,631,371	658,204	251,346
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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Accretion of Dividends and Offering Costs on Preferred Stock.***

Prior to the Company's initial public offering, holders of preferred stock had a right to receive dividends at a stated rate per share. The Company recorded accretion of these dividends as well as offering costs in order to arrive at the net loss available to common stockholders in the periods prior to the initial public offering. Upon conversion of the preferred stock into common stock, the holders of preferred stock, pursuant to the terms of the preferred stock, forfeited all cumulative accrued dividends. As of June 2, 2004, cumulative accrued dividends on the Company's preferred stock totaled \$5.7 million.

***Comprehensive Loss***

Comprehensive loss is the total of net loss and all other non-owner changes in equity. The difference between net loss, as reported in the accompanying condensed consolidated statements of operations for the year ended December 31, 2004, and comprehensive loss is the unrealized gain (loss) on short-term investments for the period. There were no items affecting comprehensive loss for the years ended December 31, 2003 and 2002. Total comprehensive loss was \$31.5 million for the year ended December 31, 2004. The unrealized loss on investments is the only component of accumulated other comprehensive loss in the accompanying condensed consolidated balance sheet as of December 31, 2004.

***Disclosure About Segments of an Enterprise***

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker, or decision-making group, in making decisions regarding resource allocation and assessing performance. To date, the Company has viewed its operations and manages its business as principally one operating segment.

**(3) Collaboration Agreement**

On July 30, 2003, the Company entered into an exclusive license and collaboration agreement with MedImmune to jointly develop therapeutic products. Under the agreement, the Company has granted MedImmune an exclusive, worldwide royalty bearing license in exchange for a license fee, research funding, research and development milestone payments and royalties on product sales. The Company is required to perform certain research activities under an agreed upon research plan covering a period of 41 months which began on July 30, 2003. During the 41-month research plan, the Company may receive additional research funding from MedImmune based on the number of full time equivalents employed by the Company for the purposes of executing the research plan. No performance is required of the Company subsequent to the research period. MedImmune will be responsible for subsequent product development and commercialization. All payments made to the Company under the agreement are non-refundable.

During 2003, the Company was scheduled to receive \$12.5 million in up front license fees and research funding. As of December 31, 2003, the Company had received a total of \$10.0 million, with the balance of \$2.5 million received in January 2004. In addition, the Company received approximately \$1.5 million in research funding from MedImmune in 2004. As described in Note 1, revenue under this arrangement is being recognized under a proportional performance model. During 2004 and 2003, the Company recognized revenue of approximately \$4.4 million and \$1.0 million, respectively, under this agreement. As of December 31, 2004, deferred revenue of approximately \$8.5 million consists of up-front payments and research funding received in advance of revenue recognized under the agreement. As of December 31, 2003, deferred revenue of approximately \$11.5 million consists of up-front payments received in advance of revenue recognized.

In the event that specified research and development and commercialization milestones are achieved, MedImmune will be obligated to make further payments to the Company. MedImmune has agreed to

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

make royalty payments to the Company upon sale by MedImmune of any products resulting from the collaboration.

MedImmune Ventures, an affiliate of MedImmune, participated in the Company's private placement of Series B Preferred Stock and purchased 5,357,143 shares for \$7.5 million on October 3, 2003 and an additional 5,357,143 shares for \$7.5 million on March 5, 2004 (see Note 6). The purchase price paid by MedImmune for these shares was the same as that paid by the other participants.

**(4) Fixed Assets**

Fixed assets consisted of the following at December 31:

	<b>2004</b>	<b>2003</b>
Laboratory equipment	\$ 1,591	\$ 967
Computer and office equipment	580	207
Furniture and fixtures	471	43
Leasehold improvements	203	870
<b>Total</b>	<b>2,845</b>	<b>2,087</b>
Less accumulated depreciation and amortization	(640)	(531)
<b>Fixed assets net</b>	<b>\$ 2,205</b>	<b>\$ 1,556</b>

Depreciation and amortization expense on fixed assets for the years ended December 31, 2004, 2003 and 2002 was \$1.1 million, \$482,000 and \$54,000, respectively.

**(5) Long Term Debt**

On June 28, 2002, the Company entered into a loan and security agreement (the Agreement) with a lender that allows the Company to borrow up to \$2,250,000 to finance the purchase of equipment and \$750,000 to finance leasehold improvements through June 30, 2003. In connection with the Agreement, the Company issued 90,000 warrants to purchase Series A Redeemable Convertible Preferred Stock. The warrants are exercisable at the option of the holder at \$1.00 per share and expire 10 years from the date of issuance. Using the Black-Scholes option-pricing model, the value assigned to the warrants was deemed to be de minimus. The warrants were valued using the following assumptions: no volatility, 4.93% risk-free interest rate, 8% dividend yield, and a 10-year contractual life. During 2004, the holder exercised the warrants issued under the Agreement.

Effective June 30, 2004, the Company entered into a modification to its existing loan and security agreement. The modification gave the Company the ability to borrow up to an additional \$3.0 million under a credit agreement from July 1, 2004 to December 31, 2004. From January 1, 2005 to December 31, 2005, the Company has additional borrowing capacity up to an amount equal to the lesser of (i) \$3.0 million minus the principal amount of advances made in 2004 or (ii) \$1.3 million. Advances made under this modification accrue interest at a rate equal to the prime rate plus 2% per year and are required to be repaid in equal monthly installments of principal plus interest accrued through the date of repayment. The repayment term for advances made under this modification are 42 and 36 months, respectively. In connection with the original loan and security agreement, the Company granted the lender a first priority security interest in substantially all of the Company's assets, excluding intellectual property, to secure the Company's obligations under the credit agreement. During the year ended December 31, 2004, the Company borrowed \$1.6 million under the modified credit agreement.

As of December 31, 2004, amounts outstanding under the equipment loans total approximately \$2.0 million and bear interest at per annum effective interest rates between 8.6% and 9.1%. Principal and



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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

interest are payable in 48 equal monthly installments from the loan date. In addition to any interest and principal paid on each borrowing, the Company is required to pay an additional 8.5% of the original advance amount on the final payment as additional interest. The Company is accreting the interest expense related to the final payment using the effective interest rate method.

As of December 31, 2004, amounts outstanding under loans for leasehold improvements total \$155,000 and bear interest at per annum effective interest rates between 10.5% and 11.0%. Principal and interest are payable in 24 equal monthly installments beginning the month following loan date. In addition to any interest and principal paid on each borrowing, the Company is required to pay an additional 7.0% of the original advance amount on the final payment as additional interest. The Company is accreting the interest expense related to the final payment using the effective interest rate method.

In connection with the Agreement, the Company granted the lender a security interest in certain assets of the Company.

The loans mature through 2008 as follows:

2005	\$ 837
2006	698
2007	577
2008	92
	\$ 2,204

**(6) Redeemable Convertible Preferred Stock and Stockholders Equity (Deficit)**

***Initial Public Offering of Common Stock***

On June 2, 2004, the Company sold 6,000,000 shares of its common stock in its initial public offering at a price to the public of \$7.00 per share. On June 30, 2004, the Company sold an additional 110,000 shares at a price to the public of \$7.00 per share pursuant to the partial exercise of the underwriters' over-allotment option. The Company received gross proceeds of \$42.8 million, of which \$3.0 million was paid as an underwriting discount. Expenses related to the offering totaled approximately \$2.0 million. The Company has invested the net proceeds in highly liquid, interest-bearing, investment grade securities.

***Reverse Stock Split***

The Company effected a 1-for-3.75 reverse stock split of all outstanding common stock and stock options effective as of May 20, 2004. All references to the number of common shares and per share amounts have been retroactively restated for all periods presented to reflect this reverse stock split including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

***Authorized Capital***

As of December 31, 2004, the authorized capital stock of the Company consists of 90,000,000 shares of voting common stock (common stock) with a par value of \$0.001 per share, and 5,000,000 shares of undesignated preferred stock (preferred stock) with a par value of \$0.001 per share. The common stock holders are entitled to one vote per share. The rights and preferences of the preferred stock may be established from time to time by the Company's Board of Directors.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Restricted Common Stock Issuances to Non-Employees***

On July 14, 2000, the Company issued 1,226,664 shares of \$0.001 par value common stock to its founders, who are non-employees, for \$900, which was paid in September 2001. On July 6, 2001, and in connection with the sale of Series A Preferred Stock to investors, the Company entered into a restricted stock agreement with each of its founders imposing certain restrictions on these shares. The restricted stock provides for a repurchase feature at the original purchase price whereby the restriction lapses as follows: 109,332 shares immediately (July 6, 2001), 164,000 shares on July 6, 2002, 820,000 shares ratably on the last day of each month over the 36 months subsequent to July 6, 2002, and the remaining 133,332 shares upon the completion of certain performance milestones.

During 2002, the Company amended the restricted stock agreements to provide for the vesting of 39,999 shares in December 2002, which were previously included in the 133,332 shares subject to vesting upon completion of certain performance milestones. During 2003, the Company amended the restricted stock agreements to provide for the vesting of the remaining 93,333 shares in December 2003.

During 2002, the Company issued an additional 43,998 shares of common stock subject to restriction to its founders for proceeds of \$16,500. The shares vest as follows: 10,999 of the shares vested in October 2003, with the remaining 32,999 shares vesting monthly from November 2003 through October 2006.

On July 1, 2001, the Company issued 27,259 shares of common stock subject to restrictions and vesting, as partial consideration for a sponsored research and licensing agreement with North Shore (see Note 11). 25% of the shares vested immediately, 25% vested in 2001, 25% will vest on July 1, 2006, and 25% will vest on July 1, 2007.

During 2001, the Company issued 46,663 shares of its common stock, subject to restricted stock agreements, to consultants to the Company for proceeds of \$17,500. Approximately 25% of these shares vested in 2002 and the remaining shares vest monthly through September 2005.

Compensation to date associated with the restricted stock issued to non-employees has been measured as the difference between the fair value of the shares and the amount paid by the holder. Final measurement occurs when performance is complete which is assumed to be when the restrictions lapse. The Company recorded deferred compensation of \$0, \$4,921,991 and \$0 in 2004, 2003 and 2002, respectively, and stock-based compensation expense of \$862,000, \$4.3 million and \$120,000 for the years ended December 31, 2004, 2003 and 2002, respectively, related to these shares. These amounts are included in research and development expenses in the accompanying condensed consolidated statement of operations.

At December 31, 2004, the Company's right to repurchase restricted stock from non-employees had not lapsed as to 201,116 shares.

***Restricted Common Stock Issuances to Employees***

During 2002, the Company issued 172,344 shares of restricted common stock to employees for proceeds of \$25,130 and a promissory note of \$39,500 (see Note 8). During 2001, the Company issued 22,666 shares of restricted common stock to employees for proceeds of \$8,500. The restricted stock agreements provide for a repurchase feature, which generally lapses ratably over four years and were deemed to have been purchased by the employees at the then-fair value of the underlying common stock and, accordingly, are not considered to be compensatory.

At December 31, 2004, the Company's right to repurchase had not lapsed as to 75,536 shares.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY  
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Conversion of Preferred Stock into Common Stock***

In connection with the Company's initial public offering of common stock, all of the issued and outstanding redeemable convertible preferred stock converted to common stock at a ratio of one share of common stock for each 3.75 shares of preferred stock then outstanding. Accordingly, on June 2, 2004, 60,410,237 shares of preferred stock converted into 16,109,403 shares of common stock. The par value and additional paid-in capital related to the redeemable convertible preferred stock totaling \$81.8 million was reclassified to common stock in the Company's balance sheet. Under the terms of the preferred stock agreement, accrued dividends totaling \$5.7 million were forfeited in connection with this conversion to common stock.

***Redeemable Convertible Preferred Stock***

On July 6, 2001, the Company issued 10,150,000 shares of Series A Preferred Stock, \$0.001 par value per share, and received proceeds of \$10,150,000. On October 24, 2002, the Company issued 10,150,000 additional shares of Series A Preferred Stock and received proceeds of \$9,860,000 and two promissory notes for \$145,000 each from the chief executive officer in connection with the officer's purchase of Series A Preferred Stock (see Note 8). On October 3, 2003, the Company executed a contractual agreement to sell 40,110,327 shares of Series B Preferred Stock, \$0.001 par value per share. The initial closing was completed on October 31, 2003 for 20,055,167 shares and the Company received proceeds of \$28,077,234. The final closing occurred on March 5, 2004, with the issuance of 20,055,160 shares resulting in gross proceeds of \$28,077,232 to the Company.

**(7) Equity Incentive Plans*****2004 Stock Incentive Plan***

On April 7, 2004, the Company's Board of Directors adopted and on May 6, 2004 the Company's stockholders approved the 2004 Stock Incentive Plan (the "2004 Stock Plan") for the issuance of incentive stock options, nonqualified stock options, and restricted common stock to key employees, directors, consultants, and vendors of the Company and its affiliates.

The 2004 Stock Plan authorizes the issuance of up to 3,680,000 shares of common stock. The exercise price of the stock options will be determined by the compensation committee of the Board of Directors, and may be equal to or greater than the fair market value of the Company's common stock on the date the option is granted. Options generally become exercisable over a period of four years from the date of grant, and expire ten years after the grant date.

***2003 Stock Incentive Plan***

On September 29, 2003, the Company's Board of Directors and Company stockholders adopted the 2003 Stock Incentive Plan (the "2003 Stock Plan") for the issuance of incentive stock options, nonqualified stock options, and restricted common stock to key employees, directors, consultants, and vendors of the Company and its affiliates. On December 9, 2003, the Company's Board of Directors amended the 2003 Stock Plan to increase the total number of shares available to 1,590,666 from 524,000, plus the 284,739 shares available from the 2000 Equity Plan. On June 2, 2004, in connection with the adoption of the 2004 Stock Plan, the Company transferred the 132,561 remaining shares of common stock available for award in the 2003 Stock Plan to the 2004 Stock Plan. Accordingly, there are no shares of common stock available for award under the 2003 Stock Plan at December 31, 2004.

Under the terms of the 2003 Stock Plan, the exercise price of incentive stock options granted shall be established by the Board of Directors. The vesting provisions for stock options and restricted stock are established by the Board of Directors.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**2000 Equity Incentive Plan**

On July 14, 2000, the Company's Board of Directors and Company stockholders adopted the 2000 Equity Incentive Plan (the "2000 Equity Plan") for the issuance of incentive stock options, nonqualified stock options, and restricted common stock to key employees, directors, consultants, and vendors of the Company and its affiliates. On October 24, 2002, the Company's Board of Directors amended the 2000 Equity Plan to increase the total number of shares available to 4,000,000 from 2,000,000. On September 29, 2003, in connection with the adoption of the 2003 Stock Plan, the Company transferred the 284,739 remaining shares of common stock available for award in the 2000 Equity Plan to the 2003 Stock Plan. Accordingly, there are no shares of common stock available for award at December 31, 2004.

Under the terms of the 2000 Equity Plan, the exercise price of incentive stock options granted must not be less than the fair market value of the common stock on the date of grant, as determined by the Board of Directors. The exercise price of nonqualified stock options and the purchase price of restricted common stock may be less than the fair market value of the common stock on the date of grant, as determined by the Board of Directors, but in no case may the exercise price or purchase price be less than the statutory minimum. The vesting provisions for stock options and restricted stock are established by the Board of Directors.

The following table summarizes stock option activity under all of the plans:

		Number of Shares	Weighted- Average Exercise Price
Outstanding	December 31, 2001	5,418	\$ 0.10
Granted		441,755	0.38
Outstanding	December 31, 2002	447,173	0.37
Granted		1,433,436	1.02
Exercised		(16,980)	0.38
Cancelled		(1,400)	0.38
Outstanding	December 31, 2003	1,862,229	0.87
Granted		2,906,621	6.12
Exercised		(221,902)	0.80
Cancelled		(46,678)	4.39
Outstanding	December 31, 2004	4,500,270	\$ 4.23
Exercisable	December 31, 2002	24,506	\$ 0.30
Exercisable	December 31, 2003	496,744	\$ 0.79
Exercisable	December 31, 2004	717,176	\$ 1.10



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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

The options outstanding and exercisable at December 31, 2004 under the plans are as follows:

Exercise Price	Number of Options Outstanding	Outstanding		Exercisable	
		Weighted- Average Contractual Life	Weighted- Average Exercise Price	Weighted- Average Exercise Price	Weighted- Average Exercise Price
\$0.10	2,724	6.0	\$ 0.10	2,724	\$ 0.10
\$0.38	318,198	7.6	\$ 0.38	165,899	\$ 0.38
\$1.05	1,319,259	9.0	\$ 1.05	519,024	\$ 1.05
\$1.88-\$5.63	565,089	9.5	\$ 5.24	22,001	\$ 5.63
\$5.99	1,434,500	9.7	\$ 5.99		
\$6.00-\$7.75	793,000	9.7	\$ 6.86	8,056	\$ 6.88
\$7.78-\$7.89	55,000	9.9	\$ 7.88		
\$8.10	12,500	9.9	\$ 8.10		
	4,500,270	9.2	\$ 4.23	717,704	\$ 1.10

The weighted-average fair value of stock option grants were \$4.30, \$6.19 and \$0.26, per share in 2004, 2003 and 2002, respectively.

During 2002 and 2001, the Company granted stock options and other equity awards to employees at exercise and purchase prices deemed by the Board of Directors to be equal to the fair value of the common stock at the time of grant except as discussed above. The fair value of the common stock was determined by the Board of Directors of the Company at each stock option measurement date based on a variety of different factors including the Company's financial position and historical financial performance, the status of technological developments within the Company, the composition and ability of the current engineering and management team, an evaluation and benchmark of the Company's competition, the current climate in the marketplace, the illiquid nature of the common stock, arms-length sales of the Company's capital stock (including redeemable convertible preferred stock), the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event, among others.

During 2004 and 2003, the Company issued options to employees to purchase 363,788 and 1,165,027 shares of common stock, respectively, at exercise prices deemed for accounting purposes to be below market value. The Company has recorded the difference between the exercise price and the fair value of \$524,000 in 2004 and \$6.7 million in 2003 as deferred stock-based compensation and is amortizing this deferred compensation as a charge to operations over the vesting periods of the options. The Company recorded compensation expense of \$1.8 million and \$165,000 related to these options for the years ended December 31, 2004 and 2003, respectively. Compensation expense for 2004 related to these options is included in the accompanying consolidated statement of operations as research and development and general and administrative in the amounts of \$198,000 and \$1.6 million, respectively. Compensation expense for 2003 related to these options is included in the accompanying consolidated statement of operations as research and development and general and administrative in the amounts of \$29,000 and \$136,000, respectively. The Company expects to record approximately \$1.8 million, \$1.8 million, \$1.6 million and \$18,000 of stock-based compensation expense related to the amortization of deferred compensation for the years ending

December 31, 2005, 2006, 2007 and 2008, respectively.

During 2004, 2003 and 2002, the Company granted 51,333, 268,409 and 8,666 options, respectively, to nonemployees that are accounted for in accordance with SFAS No. 123 and EITF No. 96-18. The fair value of these awards was estimated using the Black-Scholes option-pricing methodology and was deemed to be de minimus in 2002, \$1.8 million for 2003 and \$278,000 for 2004. The Company recorded

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

compensation expense of approximately \$916,000 and \$572,000 related to these options for the years ended December 31, 2004 and 2003, respectively. Compensation expense in 2004 related to these options is included in the accompanying consolidated statement of operations as research and development and general and administrative in the amounts of \$923,000 and (\$7,000), respectively. Compensation expense in 2003 related to these options is included in the accompanying consolidated statement of operations as research and development and general and administrative in the amounts of \$544,000 and \$28,000, respectively.

In December 2004, the Company entered into employment agreements with its officers. These agreements provide for, among other things, certain severance benefits and acceleration of vesting for stock options and restricted stock contingent upon future events such as a change-of-control of the Company. Because the terms in the employment agreements modified certain provisions of each officer's existing stock awards, a new measurement date was created for the awards. If a change-of-control occurs, the Company would be required to record the intrinsic value of any options or restricted stock that vest on the date of a change-of-control. The intrinsic value is calculated as the difference between the fair value of common stock on the date of remeasurement and the exercise price of the underlying stock option or the purchase price of restricted stock. As of December 31, 2004, there were 1,389,161 unvested stock options and restricted stock remaining. If a change-of-control were to occur and all of these securities were to vest, the intrinsic value of these securities totaling \$5.9 million would be recorded as stock-based compensation expense.

**(8) Loans to Officers**

In May 2002, the Company issued restricted common stock to an officer of the Company in exchange for a \$39,500 full recourse promissory note. Principal and interest, which accrues at a per year rate of 6%, is due on the first anniversary of the closing of the Company's initial public offering of shares of common stock. The entire unpaid principal and accrued interest are payable upon insolvency of the borrower or other events as defined. The promissory note is recorded as a subscription receivable in the accompanying balance sheet and is reflected as a reduction of stockholders' deficit.

In October 2002, the Company issued 290,000 shares of Series A Preferred Stock to its chief executive officer in exchange for two full recourse promissory notes of \$145,000 each. Each note accrues interest at 6% per annum. In January 2003, one of the notes was repaid. The second note is payable on the earlier of October 24, 2007 or the first anniversary of the closing of the Company's initial public offering of shares of common stock. Both notes to this officer are recorded as subscription receivables in the accompanying balance sheet and are reflected as a reduction of redeemable convertible preferred stock.

In October 2002, the Company provided a \$60,000 interest free loan to an officer of the Company in exchange for a full recourse promissory note. Under the terms of the note, \$10,000 of principal shall be forgiven by the Company on October 7, 2003, October 7, 2004, and October 7, 2005 as long as an event of default has not occurred and the officer continues to be employed by the Company. The remaining balance is payable in annual installments of \$10,000 beginning in 2004 with such payment first to be deducted from any bonus amount payable to the officer by the Company. The entire unpaid principal is payable upon termination of employment, insolvency of the borrower, or other events as defined. The promissory note is recorded in the accompanying balance sheet as a note receivable from officer.

In December 2003, the Board of Directors approved the forgiveness of all outstanding principal and any accrued interest in connection with the loans upon the filing of a registration statement of Form S-1 by the Company with the Securities and Exchange Commission, which occurred in March 2004. In connection with the loan forgiveness, the Board of Directors approved the payment of approximately \$175,000 for state and federal taxes on behalf of the officers. Accordingly, there are no outstanding loans to officers as of December 31, 2004.

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**(9) Employee Benefit Plan**

During 2003, the Company adopted a 401(k) profit sharing plan (the Plan) covering all employees of the Company who meet certain defined requirements. Under the terms of the Plan, the employees may elect to make tax-deferred contributions through payroll deductions within statutory and plan limits and the Company may elect to make matching or voluntary contributions. During 2004, the Company matched 100% of employee contributions up to a maximum of \$1,000 per employee resulting in expense of \$50,000. The Company did not make matching contributions to the Plan during the year ended December 31, 2003.

**(10) Income Taxes**

The Company's deferred tax accounts consisted of the following at December 31 (in thousands):

	2004	2003
Deferred tax assets:		
Start-up expenses	\$ 113	\$ 176
Net operating loss carryforward	13,581	4,620
Deferred revenue	2,990	3,501
Research and experimentation credits	619	566
Depreciation and amortization	151	
Other	122	43
Total	17,576	8,906
Deferred tax liability — depreciation and amortization		(96)
Net deferred tax asset	17,576	8,810
Less valuation allowance	(17,576)	(8,810)
Total	\$	\$

Because of the Company's limited operating history, management has provided a 100% reserve against the Company's net deferred tax assets.

The Company has available federal and state net operating loss carryforwards of approximately \$38.8 million which expire beginning in 2021 and 2006 for federal and state tax purposes, respectively. The Company also has research and experimentation tax credits which expire beginning in 2021. The Company did not pay any income taxes in any of the years presented.

**(11) Research and License Agreements**

The following is a summary of the Company's significant research and license agreements:

**Abbott**

On December 18, 2003, the Company entered into an agreement to in-license the controlled-release formulation and the intravenous formulation of zileuton from Abbott Laboratories (Abbott). The Company has the right to commercialize this product for all clinical indications except for research, diagnostics, therapeutics and services to humans under age seven and for cardiovascular and vascular devices. The Company is obligated to make milestone payments to Abbott for successful completion of the technology transfer, filing and approval of the product in the United States and commercialization of the product. In addition, the Company will make royalty payments to Abbott based upon sales of the product. The agreement may be terminated by either party for cause. The Company may also terminate the



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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

agreement at any time upon 60 days notice to Abbott and payment of a termination fee. As of December 31, 2004 and 2003, \$0 and \$1.5 million, respectively, was due under the agreement, and was included in accrued expenses.

On March 17, 2004, the Company entered into an agreement to in-license an immediate-release formulation of zileuton from Abbott. The Company agreed to pay a license fee of \$500,000, a milestone payment and royalties to Abbott based upon sales of the product. The agreement may be terminated by either party for cause. The Company may also terminate the agreement at any time upon 60 days notice to Abbott. During 2004, the Company paid the \$500,000 license fee, and did not pay any milestones under this agreement.

***SkyePharma***

On December 3, 2003, the Company entered into an agreement with a subsidiary of SkyePharma PLC ( *SkyePharma* ), to in-license the controlled-release technology relating to zileuton from SkyePharma. The Company is required to make milestone payments to SkyePharma for successful completion of the technology transfer, filing and approval of the product in the U.S. and commercialization of the product. In addition, the Company will make royalty payments to SkyePharma based upon sales of the product. The agreement may be terminated by either party for cause. As of December 31, 2004 and 2003, \$0 and \$750,000, respectively, is due under the agreement and is included in accrued liabilities.

***Xanthus***

On December 15, 2000, the Company entered into a license agreement with Xanthus Life Sciences (formerly Phenome Sciences) ( *Xanthus* ) whereby the Company will utilize certain of Xanthus technology in its research effort in connection with one of its drug candidates, CTI-01. Under the terms of the agreement, the Company, on February 1, 2001, paid and expensed \$103,000 for the license and may be required to pay up to an additional \$2.0 million if certain research milestones are achieved. As of December 31, 2004, none of these milestones had been achieved. In addition, the Company is obligated to pay royalties to Xanthus based on product sales with an annual minimum of \$10,000 beginning in 2006. As of December 31, 2004, no royalties had been paid or accrued by the Company. The Company also agreed to pay all patent maintenance costs as of December 15, 2000 and reimburse Xanthus for all patent costs incurred after December 15, 2000.

***North Shore***

On July 1, 2001, the Company entered into a license agreement with the North Shore Long Island Jewish Research Institute ( *North Shore* ) whereby the Company will utilize certain of North Shore s technology in its research effort in connection with one of its research targets, HMGB1. The Company paid and expensed \$100,000 to North Shore for the license and may be required to pay an additional \$412,500 if certain research milestones are achieved. As of December 31, 2004 none of these milestones had been achieved. In addition, the Company is obligated to pay royalties to North Shore based on product sales. In the event of no product sales, the Company will be required to pay minimum annual royalties of \$15,000 in years 2007 through 2011 and \$75,000 in years 2012 through the expiration of the patent in 2023. The Company also agreed to pay all patent maintenance cost incurred after July 1, 2001 and to reimburse North Shore up to \$50,000 in patent costs incurred prior to July 1, 2001. In December 2003, this agreement was amended to redefine the sublicense fees payable to North Shore. In connection with the amendment, the Company agreed to issue 66,666 shares of common stock having a value of \$485,000 to North Shore (see Note 7). As a result of the collaboration agreement with MedImmune (see Note 3), the Company incurred an obligation to pay a sublicense fee to North Shore in the amount of \$2,025,000. As of December 31, 2003, \$300,000 of the sublicense fee was paid to North Shore and

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

\$1,725,000 was included in accrued liabilities and paid in 2004. The sublicense fee and the value of the common stock issued to North Shore are included in research and development expense in the accompanying consolidated statements of operations for the year ended December 31, 2003. There are no amounts due to North Shore as of December 31, 2004.

Also on July 1, 2001, the Company entered into a sponsored research and license agreement with North Shore whereby the Company committed to \$400,000 of research funding over a period of two years in connection with efforts to identify HMGB1 inhibitors. In July 2003, the Company amended the Agreement to provide for an additional \$600,000 of research funding. During 2004 and 2003, the Company contributed a total of \$200,000 and \$150,000, respectively, in research funding. In connection with obtaining certain licenses from North Shore, the Company issued 102,222 shares of its common stock (see Note 7), subject to repurchase restrictions, and may pay up to an additional \$300,000 if certain research milestones are achieved. As of December 31, 2004, none of these milestones had been achieved. In addition, the Company is obligated to pay royalties to North Shore based on product sales.

On January 1, 2003, the Company entered into a second sponsored research and license agreement with North Shore whereby the Company committed to \$600,000 of research funding in the field of cholinergic anti-inflammatory technology over a period of three years and paid a \$175,000 license fee during 2003. Research funding under this agreement in 2006 and 2007 will be mutually agreed upon by the parties. During 2004 and 2003, the Company contributed a total of \$150,000 and \$200,000, respectively, in research funding. The Company may be required to pay an additional \$1.5 million in cash and common stock if certain milestones are achieved as well as royalty payments based on product sales. In the event of no product sales, the Company will be required to pay minimum annual royalties of \$100,000 in 2008, which will increase by \$50,000 annually to a maximum of \$400,000 in 2014 through the expiration of the patent in 2023.

***Other Agreements***

During 2004, 2003 and 2002, the Company entered into additional non-exclusive license and sponsored research agreements, none of which are individually material. The Company has paid \$371,000, \$229,000 and \$50,000, during 2004, 2003 and 2002, respectively, under these agreements. The Company has committed to additional payments of approximately \$253,000 and \$47,000 for the years ended December 31, 2005 and 2006, respectively, and the Company is obligated to pay royalties based on product sales with an annual minimum of \$40,000.

**(12) Commitments and Contingencies**

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business. The Company accrues for liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. For all periods presented, the Company is not a party to any pending material litigation or other material legal proceedings.

***Lease Obligations***

The Company leases its facilities, vehicles and certain equipment under operating leases. Rent expense for the years ended December 31, 2004, 2003 and 2002 was \$1.9 million, \$559,000 and \$250,000, respectively. The facility lease contains a rent escalation clause that requires the Company to pay additional rental amounts in the later years of the lease term. Rent expense for this lease is recognized on a straight-line basis over the minimum lease term. Leases expire from April 2007 to March 2009. The

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

minimum aggregate future obligations under noncancelable lease obligations as of December 31, 2004 are as follows (in thousands):

<b>Year Ending</b>	<b>Operating Leases</b>
2005	\$ 1,503
2006	1,310
2007	1,303
2008	1,291
2009	216
Thereafter	
<b>Total</b>	<b>\$ 5,623</b>

**Founders Consulting Agreements**

On January 31, 2001, as amended on January 16, 2003, each of the Company's founders entered into a separate consulting agreement with the Company in which they contracted to provide consulting services to the Company. For the years ended December 31, 2004, 2003 and 2002, amounts paid under these agreements totaled \$305,000, \$299,000 and \$292,000, respectively. Future payments to be made under the agreements are scheduled to be as follows (in thousands):

<b>Year Ending</b>	<b>Payments</b>
2005	\$ 313
2006	321
2007	26
<b>Total</b>	<b>\$ 660</b>

**(13) Relocation of Headquarters**

During 2004, the Company relocated its headquarters to Lexington, Massachusetts and consolidated its research facilities from two to one. Under SFAS No. 146, Costs Associated with an Exit or Disposal Activity, the Company recorded a liability of \$441,000 in the three-month period ended June 30, 2004 related to the remaining obligations under an operating lease that expires in October 2005 at its previous headquarters. During the year ended December 31, 2004, the Company reduced the liability by \$48,000 to adjust for the known effect of rental income expected to be realized under a sublease agreement signed by the Company in September 2004, partially offset by certain other estimated costs associated with the lease termination. The liability is included in accrued expenses in the accompanying consolidated balance sheet as of December 31, 2004.

The following table summarizes the activity related to the remaining lease obligation recorded under SFAS No. 146 (in thousands):

Remaining lease obligation from former headquarter facility	\$ 441
Payments	(208)
Adjustment	(48)



Rental income under sublease agreement 28

Balance December 31, 2004 \$ 213

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**CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**(14) Unaudited Quarterly Financial Data**

The following table summarizes selected unaudited quarterly financial information for 2004 and 2003. The Company believes that all adjustments, consisting of normal recurring adjustments considered necessary for a fair presentation, have been included in the selected quarterly information (in thousands, except per share data).

	<b>Revenue</b>		<b>Net Loss</b>		<b>Basic and Diluted Net Loss Per Common Share</b>
	<b>Under Collaboration Agreement</b>		<b>Net Loss</b>		<b>Available to Common Stockholders</b>
<b>Year Ended December 31, 2003:</b>					
First Quarter	\$		\$ (2,858)	\$ (3,279)	\$ (6.37)
Second Quarter			(3,572)	(3,998)	(6.61)
Third Quarter		401	(3,549)	(3,980)	(5.72)
Fourth Quarter		620	(10,130)	(11,117)	(13.63)
<b>Year Ended December 31, 2004:</b>					
First Quarter	\$	805	\$ (6,385)	\$ (7,546)	\$ (6.85)
Second Quarter		781	(6,946)	(7,994)	(0.81)
Third Quarter		1,886	(6,584)	(6,584)	(0.28)
Fourth Quarter		964	(11,179)	(11,179)	(0.47)

Because of the method used in calculating per share data, the quarterly per share data will not necessarily add to the per share data as computed for the year.

**(15) Subsequent Event**

In January 2005, the Company entered into a license agreement with Beckman Coulter, Inc. relating to the development of diagnostic products for measuring HMGB1. Under the terms of the agreement, the Company granted to Beckman Coulter and its affiliates an exclusive worldwide license to evaluate, develop, make, use and sell a kit or assemblage of reagents for measuring HMGB1. In consideration for the license, Beckman Coulter paid the Company \$250,000 and agreed to pay potential additional aggregate license fees of up to \$850,000. Beckman Coulter also agreed to pay the Company royalties based on net sales of licensed products.

In February 2005, the Company entered into a commercial supply agreement with Rhodia Pharma Solutions Ltd. for the commercial production of the active pharmaceutical ingredient of zileuton. Under the commercial supply agreement, Rhodia has agreed to manufacture the Company's commercial supplies, subject to specified limitations, through December 31, 2009.

**Table of Contents****ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

There have been no disagreements with our independent auditors on accounting and financial disclosure matters.

**ITEM 9A. CONTROLS AND PROCEDURES**

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2004. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by the company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2004, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended December 31, 2004 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION****2004 Executive Compensation**

On November 30, 2004, our independent directors approved discretionary cash bonuses for our executive officers in respect of our 2004 fiscal year in the following amounts, which were to be pro rated for any executive officer employed for less than the full year:

27% of annual 2004 salary for Paul D. Rubin, M.D., our President and Chief Executive Officer; and

18% of annual 2004 salary for each of our other executive officers.

Accordingly, on January 10, 2005, we paid cash bonuses to our executive officers in the following amounts, which were included in accrued expenses as of December 31, 2004:

Executive Officer	Cash Bonus
Paul D. Rubin, M.D.	\$ 90,000
Trevor Phillips, Ph.D.	\$ 41,400
Walter Newman, Ph.D.	\$ 44,400
Frederick Finnegan	\$ 40,200
Frank E. Thomas	\$ 29,000
Scott B. Townsend	\$ 15,000

In addition, on November 30, 2004, our independent directors approved a one-time payment to the following executive officers in the amounts listed below to gross-up, for federal income taxes, state income taxes and Medicare withholding, the amount of outstanding principal and accrued interest that was

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forgiven by us prior to the completion of our initial public offering in respect of loans we previously made to the executive officers:

Executive Officer	Payment
Paul D. Rubin, M.D.	\$ 110,205
Trevor Phillips, Ph.D.	\$ 35,211
Walter Newman, Ph.D.	\$ 29,110

**2005 Company Goals**

Under the employment agreements that we have entered into with our executive officers, each of our executive officers is eligible for an annual cash bonus and an annual equity award in amounts determined by the Compensation Committee of our board of directors. On March 15, 2005, our board of directors approved, based on the recommendation of the Compensation Committee, company goals for 2005 for the purpose of bonus calculations at the end of the year. The company goals for 2005 include:

enhancing the commercial value of zileuton by making specified regulatory filings, launching ZYFLO and achieving specified business development goals;

advancing our research and development pipeline by achieving specified pre-clinical and clinical development milestones and business development goals for our other product candidates;

maintaining our financial position by managing our cash balance; and

recruiting and retaining key employees to create an effective organization.

**PART III****ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT****Directors and Executive Officers**

Information regarding our directors may be found under the caption *Election of Directors* in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Information regarding our executive officers may be found under the caption *Executive Officers of the Registrant* in Part I of this annual report. Such information is incorporated herein by reference.

**Audit Committee**

We have a separately designated standing Audit Committee established in accordance with Section 3(a)(58)(A) of the Exchange Act. Additional information regarding the Audit Committee may be found under the captions *Corporate Governance Board Committees Audit Committee* and *Corporate Governance Report of the Audit Committee* in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

**Audit Committee Financial Expert**

The Board of Directors has designated Richard W. Dugan as the *Audit Committee Financial Expert* as defined by Item 401(h) of Regulation S-K of the Exchange Act and determined that he is independent within the meaning of Item 7(d)(3)(iv) of Schedule 14A of the Exchange Act.

**Director Nominees**

Information regarding procedures for recommending nominees to the Board of Directors may be found under the caption *Corporate Governance Director Candidates* in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

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**Section 16(a) Beneficial Ownership Reporting Compliance**

Information regarding Section 16(a) Beneficial Ownership Reporting Compliance may be found under the caption Stock Ownership Information Section 16(a) Beneficial Ownership Reporting Compliance in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

**Code of Ethics**

We have adopted a code of business conduct and ethics that applies to our directors, officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions) as well as our employees. A copy of our code of business conduct and ethics is available on our website at [www.crtx.com](http://www.crtx.com) under Investors Corporate Governance . We intend to post on our website all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or Nasdaq listing standards concerning any amendment to, or waiver from, our code of business conduct and ethics.

**ITEM 11. EXECUTIVE COMPENSATION**

Information with respect to this item may be found under the captions Corporate Governance Compensation of Directors and Information About Executive Compensation in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

**ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

Information with respect to this item may be found under the captions Stock Ownership Information and Securities Authorized for Issuance Under Equity Compensation Plans in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

Information with respect to this item may be found under the caption Corporate Governance Certain Relationships and Related Transactions in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

**ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

Information with respect to this item may be found under the caption Corporate Governance Independent Auditors Fees in the Proxy Statement for our 2005 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

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**PART IV**

**ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

(a)(1) *Financial Statements.*

For a list of the financial information included herein, see Index to Financial Statements on page 63.

(a)(2) *Financial Statement Schedules.*

All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or Notes thereto.

(a)(3) *List of Exhibits.*

The list of Exhibits filed as a part of this annual report on Form 10-K are set forth on the Exhibit Index immediately preceding such Exhibits, and is incorporated herein by this reference.

Critical Therapeutics®, Critical Therapeutics logo and ZYFLO® are trademarks or service marks of Critical Therapeutics, Inc. Other trademarks or service marks appearing in this report are the property of their respective holders.

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

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

CRITICAL THERAPEUTICS, INC.

By: /s/ Paul D. Rubin

Paul D. Rubin, M.D.

President and Chief Executive Officer

Date: March 16, 2005

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

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Paul D. Rubin Paul D. Rubin, M.D.	President and Chief Executive Officer (Principal Executive Officer)	March 16, 2005
/s/ Frank E. Thomas Frank E. Thomas	Senior Vice President of Finance, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 16, 2005
/s/ Richard W. Dugan Richard W. Dugan	Director	March 16, 2005
/s/ Nicholas Galakatos Nicholas Galakatos, Ph.D.	Director	March 16, 2005
/s/ Jean George Jean George	Director	March 16, 2005
/s/ Christopher Mirabelli Christopher Mirabelli, Ph.D.	Director	March 16, 2005
/s/ Christopher Walsh Christopher Walsh, Ph.D.	Director	March 16, 2005
/s/ H. Shaw Warren H. Shaw Warren, M.D.	Director	March 16, 2005

/s/ Robert H. Zeiger

Director

March 16,  
2005

Robert H. Zeiger



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**EXHIBIT INDEX**

<b>Exhibit No.</b>	<b>Description</b>
3.1	Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767))
3.2	Amended and Restated Bylaws of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767))
10.1*	2000 Equity Incentive Plan, as amended (Incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.2*	2003 Stock Incentive Plan, as amended (Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.3*	2004 Stock Incentive Plan (Incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.4	Amended and Restated Investor Rights Agreement by and between the Registrant and the investors named therein dated as of October 3, 2003 (Incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.5+	License Agreement between the Registrant and North Shore-Long Island Jewish Research Institute dated July 1, 2001, as amended by the First Amendment Agreement dated May 15, 2003 (Incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.6+	Sponsored Research and License Agreement between the Registrant and North Shore-Long Island Jewish Research Institute dated July 1, 2001, as amended by the First Amendment Agreement dated July 1, 2003 (Incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.7+	Sponsored Research and License Agreement between the Registrant and North Shore-Long Island Jewish Research Institute dated January 1, 2003 (Incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.8+	Exclusive License and Collaboration Agreement between the Registrant and MedImmune, Inc. dated July 30, 2003 (Incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.9+	Exclusive License Agreement between the Registrant and Xanthus Life Sciences, Inc. (formerly Phenome Sciences, Inc.) dated December 15, 2000 (Incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.10+	

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- License Agreement between the Registrant and Abbott Laboratories dated December 18, 2003 (Incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
- 10.11+ License Agreement between the Registrant and Abbott Laboratories dated March 17, 2004 (Incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
- 10.12+ License Agreement between the Registrant and the University of Pittsburgh of the Commonwealth System of Higher Education dated November 15, 2002 (Incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
- 10.13+ Agreement between the Registrant and Jagotec AG dated December 3, 2003 (Incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
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<b>Exhibit No.</b>	<b>Description</b>
10.14+	Proposal by and between the Registrant and Rhodia Pharma Solutions for qualification of Zileuton dated August 14, 2003 (Incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.15	Consulting Agreement by and between the Registrant and H. Shaw Warren, Jr., M.D. dated January 31, 2001, as amended on February 6, 2003 (Incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.16	Consulting Agreement by and between the Registrant and Mitchell Fink, M.D. dated January 31, 2001, as amended on January 22, 2003 (Incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.17	Consulting Agreement by and between the Registrant and Kevin J. Tracey, M.D. dated January 31, 2001, as amended on January 16, 2003 (Incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.18	Assignment, Assumption and Amendment of Lease made as of April 10, 2002 among Central Plaza/ Wells Avenue LLC, TolerRx, Inc. and the Registrant for Lease dated October 25, 2000 (Incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.19	Lease Agreement between ARE 60 Westview Street, LLC and the Registrant dated as of November 18, 2003 (Incorporated by reference to Exhibit 10.21 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.20+	Development and Scale-Up Agreement between the Registrant and Jagotec AG dated May 6, 2004 (Incorporated by reference to Exhibit 10.25 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-113727))
10.21	Loan and Security Agreement by and between the Registrant and Silicon Valley Bank dated June 28, 2002, as modified by the Loan Modification Agreement dated as of December 11, 2002, the Second Loan Modification Agreement dated as of April 10, 2003 and the Third Loan Modification Agreement dated as of June 30, 2004 (Incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767))
10.22	Sublease Termination Agreement dated as of May 21, 2004, by and between the Registrant and Elixir Pharmaceuticals, Inc. (successor-in-interest to Centagenetix, Inc. by merger), and related Warranty Bill of Sale (Incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767))

- 10.23++ Standard Exclusive License Agreement with Sublicense Terms between Registrant and the University of Florida Research Foundation, Inc. effective September 2, 2004 (Incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
  - 10.24++ Proposal Between Registrant and Patheon Pharmaceuticals, Inc. dated August 12, 2004 (Incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
  - 10.25++ Feasibility Study Agreement between Baxter Healthcare Corporation and the Registrant effective June 9, 2004
  - 10.26 Form of Incentive Stock Option Agreement granted under 2004 Stock Incentive Plan
  - 10.27 Form of Nonstatutory Stock Option Agreement granted under 2004 Stock Incentive Plan
  - 10.28 Form of Restricted Stock Agreement granted under 2004 Stock Incentive Plan
  - 10.29 Form of Nonstatutory Stock Option Agreement for a Non-Employee Director granted under the 2004 Stock Incentive Plan
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<b>Exhibit No.</b>	<b>Description</b>
10.30*	Incentive Stock Option Agreement between Registrant and Paul Rubin dated September 8, 2004 (Incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
10.31*	Incentive Stock Option Agreement between Registrant and Trevor Phillips dated September 8, 2004 (Incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
10.32*	Incentive Stock Option Agreement between Registrant and Walter Newman dated September 8, 2004 (Incorporated by reference to Exhibit 10.6 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
10.33*	Incentive Stock Option Agreement between Registrant and Frederick Finnegan dated September 8, 2004 (Incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
10.34*	Incentive Stock Option Agreement between Registrant and Frank Thomas dated September 8, 2004 (Incorporated by reference to Exhibit 10.8 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 (SEC File No. 000-50767))
10.35*	Employment Agreement dated December 21, 2004 by and between the Registrant and Paul D. Rubin, M.D. (Incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K dated December 21, 2004 (SEC File No. 000-50767))
10.36*	Employment Agreement dated December 21, 2004 by and between the Registrant and Walter Newman, Ph.D. (Incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K dated December 21, 2004 (SEC File No. 000-50767))
10.37*	Employment Agreement dated December 21, 2004 by and between the Registrant and Trevor Phillips, Ph.D. (Incorporated by reference to Exhibit 99.3 to the Registrant's Current Report on Form 8-K dated December 21, 2004 (SEC File No. 000-50767))
10.38*	Employment Agreement dated December 21, 2004 by and between the Registrant and Frederick Finnegan (Incorporated by reference to Exhibit 99.4 to the Registrant's Current Report on Form 8-K dated December 21, 2004 (SEC File No. 000-50767))
10.39*	Employment Agreement dated December 21, 2004 by and between the Registrant and Frank E. Thomas (Incorporated by reference to Exhibit 99.5 to the Registrant's Current Report on Form 8-K dated December 21, 2004 (SEC File No. 000-50767))
10.40*	Employment Agreement dated December 21, 2004 by and between the Registrant and Scott B. Townsend (Incorporated by reference to Exhibit 99.6 to the Registrant's Current Report on Form 8-K dated December 21, 2004 (SEC File No. 000-50767))

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10.41++	Agreement for Manufacturing and Supply of ZILEUTON by and between Rhodia Pharma Solutions Ltd. and the Registrant dated February 8, 2005
10.42*	Critical Therapeutics, Inc. 2005 Company Goals
21.1	Subsidiaries of the Registrant
23.1	Consent of Deloitte & Touche LLP
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

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<b>Exhibit No.</b>	<b>Description</b>
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

\* Management contract or compensation plan or arrangement required to be filed as an exhibit pursuant to Item 15(c) of Form 10-K.

+ Confidential treatment granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission

++ Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.