CRITICAL THERAPEUTICS INC
Form 10-K
March 07, 2006

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-K
ANNUAL REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

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

For the fiscal year ended December 31, 2005

OR

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

For the transition period from to

Commission file number: 000-50767

CRITICAL THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**04-3523569**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification Number)*
60 Westview Street, Lexington, Massachusetts	**02421**
(Address of principal executive offices)	*(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 if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No þ

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 þ No o

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o Accelerated filer þ Non-accelerated filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No þ

The aggregate market value of the registrant s common stock held by non-affiliates of the registrant as of June 30, 2005, was approximately $90,619,000, based on $7.02, the price at which the registrant s common stock was last sold on that date.

As of February 28, 2006, the registrant had 34,137,359 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant s proxy statement for the registrant s 2006 annual meeting of stockholders to be held on April 25, 2006, which are expected to be filed pursuant to Regulation 14A within 120 days after the end of the registrant s fiscal year ended December 31, 2005, are incorporated by reference into Part III of this report.

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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 herein regarding possible therapeutic benefits and market acceptance of ZYFLO® (zileuton tablets), the progress and timing of our drug development programs and related trials and the efficacy of our drug candidates, our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management, other than statements of historical facts, are forward-looking statements made under the provisions of The Private Securities Litigation Reform Act of 1995. We may, in some cases, use words such as anticipate, believe, could, estimate, expect, intend, may, plan, project, should, will, would o uncertainty of future events or outcomes to identify these 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: the extent of market acceptance of ZYFLO; our ability to maintain regulatory approval to market and sell ZYFLO; our ability to develop and maintain the necessary sales, marketing, distribution and manufacturing capabilities to commercialize ZYFLO; patient, physician and third-party payor acceptance of ZYFLO as a safe and effective therapeutic product; adverse side effects experienced by patients taking ZYFLO; 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, including the new drug application for the controlled-release formulation of zileuton; our heavy dependence on the commercial success of ZYFLO 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 ZYFLO, our discoveries and drug candidates. These and other risks are described in greater detail below under Item 1A Risk Factors. 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 stimuli such as infection or trauma. Our marketed product is ZYFLO®, 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 have completed the process of validating new manufacturing sites for ZYFLO, and the FDA approved our supplemental new drug application, or sNDA, on September 28, 2005. We began selling ZYFLO in the United States in October 2005. In addition, we believe that zileuton has potential therapeutic benefits in a range of other diseases and conditions, such as acute asthma exacerbations, chronic obstructive pulmonary

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disease, or COPD, and nasal polyposis. We are currently incurring costs to expand our applications of zileuton through development of additional formulations, including controlled-release and intravenous formulations.

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 inhibits the release of protein molecules called cytokines that can amplify harmful immune responses. CTI-01 is currently in Phase II clinical development for prevention of complications that can occur in patients after cardiopulmonary bypass, a procedure commonly performed during heart surgery.

HMGB1. We believe that a protein called HMGB1, or high mobility group box protein 1, may be an important target for the development of products to treat inflammation-mediated diseases. We are currently collaborating with MedImmune, Inc. on the development of monoclonal antibodies directed towards HMGB1. We believe these antibodies could act to neutralize circulating HMGB1 and be used to target diseases such as sepsis or rheumatoid arthritis. In addition, we are currently collaborating with Beckman Coulter, Inc. on development of a diagnostic assay directed towards HMGB1.

Alpha-7. We are developing small molecules designed to inhibit the body s inflammatory response by acting on the nicotinic alpha-7 cholinergic target, 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 were incorporated in Delaware on July 14, 2000. Since our inception, we have incurred significant losses each year. As of December 31, 2005, we had an accumulated deficit of $105.6 million. We expect to incur significant losses for the foreseeable future and we may never achieve profitability. Although the size and timing of our future operating losses are subject to significant uncertainty, we expect our operating losses to continue over the next several years as we fund our development programs, market and sell ZYFLO and prepare for the 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, payments from our collaborators MedImmune and Beckman Coulter, and, beginning in the fourth quarter of 2005, revenues from sales of ZYFLO.

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 marketing and selling ZYFLO in the United States. We launched ZYFLO for commercial sale in October 2005 following FDA approval. In anticipation of this commercial launch, we built a sales force of approximately 80 sales representatives devoted to the promotion of ZYFLO. We plan to continue to focus our sales and marketing infrastructure on the promotion of ZYFLO and, upon regulatory approval from the FDA, 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.

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Expand the potential applications of zileuton. We believe that zileuton has potential therapeutic benefits in a range of diseases and conditions, such as acute asthma exacerbations, COPD and nasal polyposis. We intend to expand the potential applications of zileuton through development of additional formulations, including controlled-release 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 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 exceed 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 our marketing and sales infrastructure 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 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

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an FDA-approved product for the prevention and chronic treatment of asthma that was developed and previously sold by Abbott. The FDA approved our sNDA for ZYFLO on September 28, 2005 and we began selling ZYFLO in the United States in late October 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 the mechanism of action of ZYFLO 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 characterized by the narrowing of the lung airways, making 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, approximately two million hospital emergency room visits in 2002 in the United States involved severe asthma attacks, of which approximately 484,000 resulted in hospitalization. The Centers for Disease Control and Prevention estimate that 20 million people in the United States had asthma in 2002. According to the National Institute of Health, the direct healthcare costs associated with treating asthma in the United States reached an estimated $11.5 billion in 2003.

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 are marketing ZYFLO 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 in adults and children 12 years of age and older. ZYFLO was first launched in the United States in 1997. The FDA approved our sNDA for ZYFLO on September 28, 2005, and we began selling ZYFLO in the United States in October 2005. We recognized $387,000 in revenue from sales of ZYFLO for the year ended December 31, 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

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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 ZYFLO and their rescue bronchodilators as needed to patients taking placebo and rescue bronchodilators as needed. The results of the group taking ZYFLO and their rescue 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 in these patients 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 from the two completed Phase III clinical trials, a three-month efficacy trial and a six-month safety and efficacy trial. The study reports prepared by Abbott for these clinical trials showed:

- In the three-month pivotal efficacy trial, in which 409 patients received either the controlled-release formulation of zileuton or placebo, patients taking the controlled-release formulation of zileuton showed demonstrated statistically significant improvements over placebo, in objective measures of asthma control, such as mean forced expiratory volume. In the trial, patients taking the controlled-

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release formulation of zileuton showed a reduced need for bronchodilatory drugs as a rescue medication to alleviate uncontrolled symptoms. In this trial, 1.94% of the patients taking the controlled-release formulation of zileuton experienced ALT levels greater than or equal to three times the level normally seen in the bloodstream.

The efficacy component of the six-month safety trial included 757 patients and demonstrated statistically significant improvements over a combination of placebo and the patients normal asthma therapies, in mean forced expiratory volume at day 169. In the trial, patients taking the controlled-release formulation of zileuton showed statistically significant mean improvements for morning peak expiratory flow rate, or PEFR, a method for measuring airway obstruction, at all visit assessments and at the majority of visit assessments for evening PEFR. In this trial, 2.6% of the patients taking the controlled-release formulation of zileuton experienced ALT levels greater than or equal to three times the level normally seen in the bloodstream.

We are currently completing the full analysis of the safety and efficacy data generated in the Abbott trials for our NDA submission. We believe that this clinical development package will be sufficient to support the submission in mid-2006 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 two clinical trials in healthy volunteers designed to show that our manufactured tablets behave similarly in the body to the tablets that had been manufactured by Abbott. These studies have been completed in the clinic and we are awaiting completion of the analysis of the blood samples generated in the studies. Once these data are known and we complete six months of stability assessment, we believe we will be able to submit the NDA in mid-2006. In May 2005, we held a pre-NDA meeting with the FDA, during which the FDA informed us that new review guidance issued in April 2005 limits its ability to accept additional data during the NDA review process. Our strategy has been to file the NDA with six months of stability data and provide additional stability data during the NDA review period. We will continue to work with the FDA to explore what options may be available to us regarding a submission based on an initial six months of stability data. If the FDA requires nine or twelve months of stability data in the original NDA, this could delay our NDA submission for the product candidate by three to six months, depending upon the outcome of discussions with the FDA close to the planned time of filing.

Intravenous Formulation of Zileuton

We have developed a new intravenous formulation of zileuton for use in severe acute asthma attacks. In 2002, according to the American Lung Association, approximately two million hospital emergency room visits in the United States involved severe asthma attacks, of which approximately 484,000 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 or her lungs may be impaired by his or her inability to breathe efficiently due to 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 can be achieved after a single oral 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 February 2006, we initiated a Phase I/ II clinical trial of an intravenous formulation of zileuton in patients with asthma. This double-blind, placebo-controlled trial is designed to assess the safety, tolerability and pharmacokinetics of four different doses of zileuton in an intravenous formulation. The trial is also designed to assess the dose response effect of zileuton on lung function in patients with only 40% to 80% of predicted normal lung function. The first patient was dosed on February 7, 2006 and we anticipate completing the trial by the third quarter of 2006.

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Commercialization Strategy

We have built an integrated marketing, managed care and sales infrastructure to support our commercialization of ZYFLO in the United States, which was launched in October 2005. Based on our experience with ZYFLO, we expect this marketing and sales team will develop the positioning and strategies to launch, market and promote the controlled-release formulation of zileuton that we are currently developing for the treatment of asthma. We believe that by targeting respiratory disease specialists, including allergists and pulmonologists, who treat a high proportion of asthma patients, rather than extending our sales reach to primary care physicians, we can successfully promote ZYFLO with an initial sales force of fewer than 100 sales representatives in the United States. We had a sales force of approximately 80 representatives as of February 28, 2006.

We believe that there is a market opportunity for the use of ZYFLO as an add-on therapy option for patients whose asthma symptoms are not adequately controlled with the use of inhaled corticosteroids and other conventional therapies. Our belief is based on information that we have gathered through extensive interactions with specialists and market research, including:

- over 18 months of in-depth interaction between our team of medical science liaisons, or MSLs, and key opinion leaders in the treatment of respiratory diseases, including asthma;
- six months of interaction between our sales force and respiratory specialists who treat asthma; and
- market research that we have conducted since 2004.

In a market research study with 184 allergists and pulmonologists that we conducted in November 2004, 74% of respondents indicated an increased likelihood to prescribe zileuton for moderate to severe asthmatics after reviewing efficacy and safety data that we provided. Following the launch of ZYFLO in October 2005, we conducted additional market research with 95 previously detailed allergists and pulmonologists in December 2005 and January 2006 to assess the early impact of the launch promotional efforts of ZYFLO. This market research study included the following findings:

- 79% of respondents indicated that ZYFLO is an effective add-on therapy for patients who are still symptomatic on moderate to high-dose inhaled steroids;
- 84% of respondents indicated that ZYFLO and Merck s Singulair® work differently; and
- 90% of respondents indicated ZYFLO should be used in patients who are dependent on or non-responsive to oral steroids.

As of February 3, 2006, prescription data indicated that most of the prescribers for ZYFLO appear to be new prescribers who did not prescribe ZYFLO in the 12 months ending September 30, 2003. We believe these data suggest that our sales force could effectively expand the use of ZYFLO to include physicians who did not previously prescribe ZYFLO. Prescription data for the 12 months ending September 30, 2003 revealed that a total of approximately 1,700 physicians had prescribed ZYFLO. Prescription data for the 16 weeks ending February 3, 2006 indicated that a total of approximately 1,000 physicians had prescribed ZYFLO for an aggregate of approximately 2,900 patients.

We are positioning ZYFLO as a treatment for asthma patients who do not gain adequate control of their symptoms with other currently available medications. We are promoting ZYFLO to specialists who treat asthma and managed care decision makers. As part of our marketing strategy, we are attempting to educate key opinion leaders and physicians on the scientific data that differentiates the mechanism of action of ZYFLO from other asthma treatments and emphasize clinical data that show safety and efficacy for ZYFLO in asthma.

We are also attempting to maximize patient and physician access to ZYFLO by addressing the position of ZYFLO on managed care formularies. We believe that in many managed care formularies, as a result of the previous 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.

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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 are exploring the therapeutic benefits of zileuton in treating a range of diseases and conditions, including acute asthma exacerbations, COPD and nasal polyposis. We are aware, for instance, of clinical data available in publications of clinical trials and individual patient case studies that indicate zileuton has shown efficacy in the treatment of nasal polyps and acne. We completed a small Phase II clinical trial in patients with moderate to severe inflammatory acne in 2005. Patients receiving zileuton showed positive responses to treatment and a trend toward significance in certain endpoints. However, the responses did not achieve statistical significance as compared to the responses seen by patients receiving placebo. In the trial, zileuton was found to be safe and well tolerated. The data suggested a positive trend toward significance in the more severe acne patients in the study. Although we may consider conducting a future evaluation of zileuton in more severe acne patients, we have no plans to conduct such a clinical trial in 2006.

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. We also intend to conduct additional trials in specific asthma patient populations, such as smoking asthmatics, 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

- 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. Many previous therapies directed at cytokines, such as tumor necrosis factor alpha, or TNF, in acute diseases have failed in clinical development.

The 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 protein HMGB1; and

- an alpha-7 receptor 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. CTI-01 is currently under development for prevention of complications including organ damage resulting from cardiopulmonary bypass. 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. CTI-01 is currently in development for the prevention of complications, including the damage to vital organs that can occur in patients after cardiopulmonary bypass, a procedure commonly performed during cardiothoracic surgery.

Clinical Trials

In February 2005, we initiated a Phase II clinical trial to determine the safety and preliminary 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. We have enrolled 90 patients as of February 28, 2006, and we expect to complete enrollment by the middle of 2006. We have begun an interim safety analysis, which we expect to complete in the second quarter of 2006.

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 in the bloodstream 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 assay 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.

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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.

Therapeutic Opportunity

We believe that HMGB1 s delayed and prolonged expression offers a new target for the development of products 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, 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.

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. In November 2005, MedImmune agreed that proof of concept had been proven for two preclinical models with human anti-HMGB1 monoclonal antibodies. These antibodies are now undergoing further evaluation with a goal of selecting candidates for use in the clinic. Together with MedImmune, we plan to develop product candidates in parallel for both acute and chronic diseases and conditions.

Alpha-7 Receptor 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. 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 a program to develop a small molecule product that inhibits the inflammatory response by stimulating the alpha-7 receptor on human macrophage cells.

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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 the alpha-7 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 biological therapies, particularly if it avoids the potential immunological response to therapy, which is a known risk with antibody products.

Development Strategy

We are currently seeking to develop novel, small molecules directed towards the alpha-7 receptor. We are currently conducting preclinical evaluation of molecules synthesized by our medicinal chemistry team. In addition to our internal discovery efforts, we licensed from the University of Florida access to a family of molecules known to be active on the alpha-7 receptor in September 2004. We are also investigating the possibility of licensing additional alpha-7 agonists for development in inflammatory conditions.

Collaborations

MedImmune Collaboration

In July 2003, we entered into an exclusive license and collaboration agreement with MedImmune to jointly develop products directed towards HMGB1. This agreement was amended in December 2005. 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 fully human monoclonal antibodies 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 $4.0 million of research and development payments through the end of 2006, of which $3.0 million had been paid by December 31, 2005. 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 The Feinstein Institute for Medical Research (formerly known as The 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 The Feinstein Institute, 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.

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In December 2005, MedImmune agreed that the collaboration demonstrated proof of concept in two preclinical disease models with human anti-HMGB1 monoclonal antibodies. As a result, MedImmune made a $1.25 million milestone payment to us. In December 2005, MedImmune agreed to fund an additional $1.0 million of research work performed by our full-time employees in 2006.

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 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, 2005, we had 43 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, 2003, 2004 and 2005, research and development expenses were $17.5 million, $25.6 million and $30.0 million, respectively.

Sales and Marketing

We have developed a sales and marketing infrastructure to commercialize ZYFLO and the controlled-release formulation of zileuton in the United States. In developing this infrastructure, we have

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hired Frederick Finnegan as our Senior Vice President of Sales and Marketing, a vice president of sales, three regional sales directors and a vice president for managed care to lead the development of this infrastructure, as well as approximately 80 sales representatives and eight regional sales managers. Mr. Finnegan has significant sales and marketing experience from previous roles at biotechnology and large and small pharmaceutical companies.

We are focusing our sales and marketing efforts for zileuton on key opinion leaders and specialists who treat asthma, including allergists, pulmonologists and other respiratory specialists. Because we are targeting our marketing and sales efforts to the patients who do not gain adequate symptomatic control from currently available medications, we believe we can successfully focus our efforts with a relatively small sales force on the approximately 10,000 to 12,000 physicians 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 asthma through their research and publications, and a second tier of practice-based specialists who are responsible for treating the majority of patients who do not gain adequate symptomatic control from currently available medications.

Given the importance of these key opinion leaders, we are directing our scientific message and support to help educate and inform key opinion leaders regarding the scientific rationale and data that support our commercialization strategy. We have entered into consulting arrangements with a number of key opinion leaders who will provide expert advice to the company. We are also expanding our reach to a larger number of key opinion leaders through a group of medical science liaisons who are directed by our vice president of medical affairs.

We initiated contact with the second tier of practice-based specialists when we launched 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 in connection with approval of the controlled-release formulation of zileuton, 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 have positioned 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 physicians. 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 a broader audience of physicians. 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 limited experience in manufacturing our product candidates. We currently outsource the manufacturing of ZYFLO for commercial sale and 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.

We have established the following manufacturing arrangements for zileuton.

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Rhodia

We have contracted with Rhodia Pharma Solutions Ltd. for the commercial production of the zileuton active pharmaceutical ingredient, or API. We had previously contracted with Rhodia to establish and validate a manufacturing process for the API at sites operated by Rhodia, which has been completed. Under our February 2005 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. Under the agreement, we agreed to purchase a minimum amount of API by December 31, 2006. 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.

Rhodia SA, Rhodia s parent company, announced in January 2006 that it had signed a letter of intent to sell its pharmaceutical manufacturing subsidiary to Shasun Chemicals & Drugs, Ltd., which is listed on the Bombay stock exchange. Rhodia SA has announced it expects that this sale will be completed in the first half of 2006. Based on discussions with Rhodia, we expect that the manufacture of zileuton API will not be affected by the sale.

Patheon

We have contracted with Patheon Pharmaceuticals Inc. for the manufacture of commercial supplies of ZYFLO immediate release tablets. We had previously contracted with Patheon for the manufacture of ZYFLO for clinical trials and regulatory review. Under the commercial manufacturing agreement that we entered into in June 2005, we are responsible for supplying the active pharmaceutical ingredient for ZYFLO to Patheon. Patheon is responsible for manufacturing the ZYFLO immediate release tablets and conducting stability testing, as outlined in our sNDA for ZYFLO. We have agreed to purchase at least 50% of our commercial supplies of ZYFLO immediate release tablets for sale in the United States from Patheon each year for the term of the commercial manufacturing agreement.

The commercial manufacturing agreement has an initial term of three years beginning on September 15, 2005, and will automatically continue for successive one-year periods thereafter, unless we provide Patheon with 12-months prior written notice of termination or Patheon provides us with 18-months prior written notice of termination. In addition, we have the right to terminate the commercial manufacturing agreement upon 30-days prior written notice in the event any governmental agency takes any action, or raises any objection, that prevents us from importing, exporting, purchasing or selling ZYFLO immediate release tablets. If we provide six-months advance notice that we intend to discontinue commercializing ZYFLO, we will not be required to purchase any additional quantities of ZYFLO immediate release tablets, provided that we pay Patheon for a portion of specified fees and expenses associated with orders previously placed by us. Furthermore, each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party. If the commercial manufacturing agreement expires or is terminated for any reason, we have agreed to take delivery of and pay for undelivered quantities of ZYFLO that we previously ordered, purchase at cost Patheon s inventory of ZYFLO maintained in contemplation of filling orders previously placed by us and pay the purchase price for components of the ZYFLO immediate release tablets ordered by Patheon from suppliers in reliance on orders previously placed by us.

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We are also initiating the process of transferring manufacturing technology to Patheon for the controlled-release formulation zileuton tablets. We intend to establish Patheon as an additional supplier for the controlled release tablets, although the FDA approval process for this cannot be completed until after the product manufactured by SkyePharma achieves regulatory approval from the FDA.

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 product candidates for clinical trials in our alpha-7 and CTI-01 programs. We believe that MedImmune will be responsible for manufacturing of any biologic products that result from our HMGB1 program.

Distribution Network

We have limited experience in distributing ZYFLO. We currently rely on third parties to distribute ZYFLO to pharmacies. We have contracted with Integrated Commercialization Services, Inc., or ICS, a third-party logistics company, to warehouse ZYFLO and distribute it to three primary wholesalers, AmerisourceBergen Corporation, Cardinal Health and McKesson Corporation, and a number of smaller wholesalers. The wholesalers in turn distribute it to chain and independent pharmacies. ICS is our exclusive supplier of commerical distribution logistics services. We rely on Phoenix Marketing Group LLC to distribute ZYFLO samples to our sales representatives, who in turn distribute samples to physicians and other prescribers who are authorized under state law to receive and dispense samples. We have contracted with RxHope, Inc. to implement a patient assistance program for ZYFLO. We rely on RxHope to administer our patient assistance program and to distribute ZYFLO to physicians and other prescribers who are authorized under state law to receive and dispense prescription drugs. We believe this patient assistance program will help ensure broader and easier access to ZYFLO for those patients requiring financial assistance. This distribution network requires significant coordination with our supply chain, sales and marketing and finance organizations. We do not have our own warehouse or distribution capabilities. We do not intend to establish these functions in the foreseeable future.

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.

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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. Through December 31, 2005, we have paid milestone and license payments totaling $3.0 million to Abbott under this agreement.

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 paid Abbott an initial fee of $500,000 and a milestone payment of $750,000 upon approval of the sNDA, which we paid in October 2005, and we agreed to pay 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.

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.

The Feinstein Institute

In July 2001, we acquired from The Feinstein Institute for Medical Research (formerly known as The North Shore-Long Island Jewish Research Institute), or The Feinstein Institute, an exclusive worldwide license, under patent rights and know-how controlled by The Feinstein Institute relating to HMGB1, to make, use and sell products covered by the licensed patent rights and know-how. The Feinstein Institute retained the right to make and use the licensed products in its own laboratories solely for non-commercial, scientific purposes and non-commercial research. In consideration for the license, we paid an initial license fee of $100,000. We also agreed to make milestone payments to The Feinstein Institute 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

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product. In addition, we agreed to pay The Feinstein Institute 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 The Feinstein Institute beginning in July 2007 regardless of whether we sell any licensed products. We also agreed to pay The Feinstein Institute fees if we sublicense our rights under the licensed patent rights and know-how. At December 31, 2005, we accrued $250,000 owed to The Feinstein Institute in accordance with this agreement. 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 The Feinstein Institute. In July 2001, we entered into a sponsored research and license agreement with The Feinstein Institute under which, as amended, we agreed to pay The Feinstein Institute $200,000 annually until June 2006 to sponsor research activities at The Feinstein Institute 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 The Feinstein Institute under which we agreed to pay The Feinstein Institute $200,000 annually until January 2006 to sponsor research activities at The Feinstein Institute in the field of cholinergic anti-inflammatory technology. Any future research terms under either of these agreements are subject to agreement between The Feinstein Institute 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. The Feinstein Institute 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 The Feinstein Institute 27,259 shares of our common stock and agreed to make milestone payments to The Feinstein Institute 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 The Feinstein Institute 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 The Feinstein Institute 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 The Feinstein Institute 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 The Feinstein Institute beginning in the first year after termination of research activities regardless of whether we sell any licensed products. We also agreed to pay The Feinstein Institute 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 The Feinstein Institute $2.0 million and issued to The Feinstein Institute 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.

SkyePharma

In December 2003, we entered into an agreement with SkyePharma, through its subsidiary Jagotec AG, 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

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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. Through December 31, 2005, we have made milestone payments totaling $2.0 million to SkyePharma under this agreement. 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. In 2005, SkyePharma agreed to allow us to sublicense our rights to Patheon to permit Patheon to manufacture a portion of our annual requirements for controlled-release formulation of zileuton tablets. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party.

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 Pharmaceuticals, Inc., 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

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breach by the other party. In specified circumstances, we may also terminate the agreement upon either three or twelve-months notice to Xanthus.

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 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.

As of February 28, 2006, we own or exclusively license for one or more indications or formulations a total of 10 issued U.S. patents, 45 issued foreign patents, 40 pending U.S. patent applications and 91 pending foreign patent applications consisting of:

	U.S.		Foreign		
	Issued	Pending	Issued	Pending	Program Total
Zileuton	2	2	33	5	42
HMGB1	3	20	1	42	66
CTI-01	2	7	7	21	37
Alpha-7	3	11	4	23	41
Total	10	40	45	91	186

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 2022.

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 and have received notice that the Critical Therapeutics name and logo have been accepted

for registration in the United States. We have also filed trademark applications to

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register CRTX, 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.

Regulatory Matters

The research, testing, manufacture and marketing of drug and biologic products are extensively regulated in the United States and abroad. In the United States, drugs and biologics 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, sampling and distribution of pharmaceutical and biologic products. 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 file new applications or 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, disease or clinical trials required. 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 marketing or sales 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

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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 human subjects in the United States must be submitted to the FDA as part of the IND. The trial protocol and informed consent information for subjects 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 candidate 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.

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 up to $250,000 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. In addition, the FDA usually conducts audits of the clinical trials for new drug applications and efficacy supplements to ensure that the data submitted reflects the data generated by the clinical sites.

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 trials 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

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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 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 and 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

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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 exclusivity 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 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.

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, consent decrees, 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 development, approval, manufacturing and marketing of drug products. 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 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, such as 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

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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.

Zileuton, including our marketed product, ZYFLO, faces heavy competition in the asthma field. A number of large pharmaceutical and biotechnology companies currently market and sell products to treat asthma that compete with ZYFLO and would compete with the controlled-release formulation of zileuton, if it is approved for sale by the FDA. Many established therapies currently command large market shares in the asthma market, including LTRAs such as Merck & Co., Inc. s Singulair®, inhaled corticosteroid drugs, and combination products such as GlaxoSmithKline plc s Advair®.

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 product, Xolair®, an anti-IgE antibody developed jointly by Novartis, Genentech and Tanox, is approved 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 immunoglobin 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, according to a 2005 article in the Journal of Managed Care Pharmacy, the annual cost for treatment ranges from approximately $7,388 to $44,328, 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, Accolate®, Advair or, in some cases ZYFLO, before Xolair can be considered.

If zileuton is developed as a treatment for COPD, it will also face intense competition. COPD is a disease treated predominantly with asthma drugs, anti-cholinergic 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 Ingleheim and Pfizer, is approved in the United States. Other novel approaches are also in the development process. GlaxoSmithKline is developing a neurokinin-3 receptor antagonist and an -4 integrin

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antagonist. Because both are in early development, their potential impact on the market is difficult to assess.

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 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, 2005, we had 175 full-time employees, 106 of whom were engaged in marketing and sales, 43 of whom were engaged in research, development and regulatory affairs, and 26 of whom were engaged in management, 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. 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.

ITEM 1A. *RISK FACTORS*

Risks Relating to Our Business

If the market is not receptive to ZYFLO or, if approved for sale, the controlled-release formulation of zileuton, we will be unable to generate significant revenues unless we are able to successfully develop and commercialize other product candidates.

The FDA approved our sNDA to manufacture and market ZYFLO for commercial sale on September 28, 2005. In late October 2005, we commercially launched ZYFLO. The commercial success of ZYFLO and, if approved for sale, the controlled-release formulation of zileuton will depend upon their acceptance 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 appropriate for managing their patient s asthma.

Despite being approved by the FDA since 1996, ZYFLO has not achieved broad market acceptance. In the 12-month period ending September 2003, only 1,700 physicians prescribed the product. During the period between our commercial launch in October 2005 through the week ending February 3, 2006, prescription data for ZYFLO indicates that approximately 1,000 physicians prescribed the product. We may have difficulty expanding the prescriber and patient base for ZYFLO if physicians view the product

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as less effective than other products on the market or view its clinical data as outdated. In addition, ZYFLO requires dosing four times per day, 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 the market acceptance of ZYFLO and the controlled-release formulation of zileuton. In the placebo-controlled clinical trials that formed the basis for FDA approval of the NDA for 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 could 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. The absence of ZYFLO from the market prior to our commercial launch in October 2005 may have exacerbated any negative perceptions about ZYFLO if physicians believe the absence of ZYFLO from the market was 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 prior to our commercial launch in October 2005, ZYFLO had been removed from some formularies or relegated to third-tier status, which requires the highest co-pay for patients. In addition, ZYFLO may have been removed from some managed care formularies as a result of the absence of ZYFLO from the market prior to our commercial launch.

If we are unable to expand the use of ZYFLO or if any existing negative perceptions about ZYFLO persist, we will have difficulty achieving market acceptance for our other oral 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.

Our business will depend heavily on the commercial success of ZYFLO and, if approved for sale, the controlled-release formulation of zileuton.

ZYFLO is our only commercial product. Other than 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, ZYFLO and, if approved for sale, the controlled-release formulation of zileuton, 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, initiate manufacturing and, if approved for sale, initiate 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 built in connection with the launch of ZYFLO and the anticipated launch of other product candidates.

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If we do not successfully recruit, train and retain qualified sales and marketing personnel and build and maintain an adequate marketing and sales infrastructure, our ability to independently launch and market our product candidates, including ZYFLO, will be impaired.

We are independently selling and marketing ZYFLO. If approved for sale, we intend to independently launch and market the controlled-release formulation of zileuton and other product candidates. As of February 28, 2006, we had a sales force of approximately 80 sales representatives. The majority of these sales representatives joined us in 2005. For the year ended December 31, 2005, we had incurred sales and marketing costs of approximately $13.7 million, which included costs related to our launch of ZYFLO. We expect to incur additional costs as we further expand our sales and marketing efforts. We may not be able to attract, hire, train and retain qualified sales and marketing personnel to build and maintain a significant or effective sales force. If we are not successful in our efforts to develop and maintain an effective 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 are investing significant amounts of money and management resources to develop internal sales and marketing capabilities. We are using a third party for distribution of ZYFLO. If we are unable to successfully commercialize ZYFLO, we will have incurred significant unrecoverable expenses. Likewise, if we further expand our sales force in anticipation of approval of the controlled-release formulation of zileuton or our other product candidates, we will incur significant costs.

A failure to maintain appropriate inventory levels could harm our reputation and subject us to financial losses.

We purchased quantities of raw materials and supplies of ZYFLO tablets in connection with the commercial launch of ZYFLO. In addition, we could be required to buy excess inventory to meet our minimum purchase obligations under our supply agreements with our third-party manufacturers. If we fail to successfully commercialize ZYFLO, our inventories could be materially impaired and their value diminished, and we will have incurred significant unrecoverable expenses.

We have limited experience managing commercial supplies of ZYFLO since the launch in October 2005. Our current forecasting of inventory levels is based on our estimate of expected customer orders in combination with limited historical information regarding actual sales. In the fourth quarter of 2005, we made an adjustment to inventory of approximately $280,000 related to short dated product in our inventory. Significant differences between our current estimates and judgments and future estimated demand for our product and the useful life of inventory may result in significant charges for excess inventory or unnecessary purchase commitments in the future. These differences could have a material adverse effect on our financial condition and results of operations during the period in which we recognize charges for excess inventory. If we fail to maintain an adequate inventory or if our inventory were to be destroyed or damaged or reached its expiration date, patients might not have access to ZYFLO, our reputation and our brand could be harmed and physicians may be less likely to prescribe ZYFLO in the future. Conversely, if we are unable to sell our inventory in a timely manner, we could experience cash flow difficulties and additional financial losses.

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 benefit 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;

the availability of reimbursement from third-party payors such as state and Federal governments, under programs such as Medicare and Medicaid, and private insurance plans and managed care organizations; and

the extent and success of our sales and marketing efforts.

The failure of our product candidates 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;

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

collaborations with other pharmaceutical or biotechnology companies with complementary clinical development or commercialization capabilities or capital to assist in funding product development and commercialization.

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;

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

we may have inadequate cash resources or may be unable to access public or private financing to obtain rights to suitable products or product candidates from third parties.

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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, ZYFLO and 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 ZYFLO and any other 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 institutions. A number of large pharmaceutical and biotechnology companies currently market and sell products to treat asthma that compete with ZYFLO and, if approved for sale, the controlled-release formulation of zileuton. Many established therapies currently command large market shares in the mild to moderate asthma market, including Merck & Co., Inc. s Singulair®, GlaxoSmithKline plc s Advair® and inhaled corticosteroid products. 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 had U.S. sales of $320.6 million in 2005.

Zileuton will also face intense competition if we are able to develop it as a treatment for COPD. COPD is currently treated predominantly with drugs that are indicated for use in asthma only or asthma and COPD, anti-cholinergic drugs and lung reduction surgery. Spiriva®, a once daily muscarinic antagonist from Boehringer Ingleheim GmbH and Pfizer, has been approved in Europe and the United States. Other novel approaches are also in the development process.

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®, Johnson & Johnson s Remicade®, and Abbott Laboratories Humira®, and diseases such as sepsis, like Eli Lilly and Company s Xigris®.

Our competitors products may be safer, 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.

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If we fail to effectively manage our growth, our business and our operating results could be adversely affected.

We will need to continue to expand our administrative and operational infrastructure to support the growth in our business. As we advance our product candidates through clinical trials, we will need to continue to expand our 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 D. Rubin, M.D., our President and Chief Executive Officer, Frederick Finnegan, our Senior Vice President of Sales and Marketing, 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 and Frank E. Thomas, our Chief Financial Officer, Senior Vice President of Finance and Treasurer. 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 or any of our other scientific and management staff.

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.

We will spend considerable time and money complying with Federal and state laws and regulations, and, if we are unable to fully comply with such laws and regulations, we could face substantial penalties.

We are subject to extensive regulation by Federal and state governments. The laws that directly or indirectly affect our business include, but are not limited to, the following:

Federal Medicare and Medicaid anti-kickback laws, which prohibit persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce either the referral of an individual, or furnishing or arranging for a good or service, for which payment may be made under Federal healthcare programs such as the Medicare and Medicaid programs;

other Medicare laws and regulations that establish the requirements for coverage and payment for our products, including the amount of such payments;

the Federal False Claims Act, which imposes civil and criminal liability on individuals and entities who submit, or cause to be submitted, false or fraudulent claims for payment to the government;

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the Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits executing a scheme to defraud any healthcare benefit program, including private payors and, further, requires us to comply with standards regarding privacy and security of individually identifiable health information and conduct certain electronic transactions using standardized code sets;

the Federal False Statements Statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

the Federal Food, Drug and Cosmetic Act, which regulates development, manufacturing, labeling, marketing, distribution and sale of prescription drugs and medical devices;

the Federal Prescription Drug Marketing Act of 1987, which regulates the distribution of drug samples to physicians and other prescribers who are authorized under state law to receive and dispense drug samples;

state and foreign law equivalents of the foregoing;

state food and drug laws, pharmacy acts and state pharmacy board regulations, which govern sale, distribution, use, administration and prescribing of prescription drugs; and

state laws that prohibit practice of medicine by non-physicians and fee-splitting arrangements between physicians and non-physicians, as well as state law equivalents to the Federal Medicare and Medicaid anti-kickback laws, which may not be limited to government reimbursed items or services.

If our past or present operations are found to be in violation of any of the laws described above or other governmental regulations to which we or our customers are subject, we may be subject to the applicable penalty associated with the violation, including civil and criminal penalties, damages, fines, exclusion from Medicare and Medicaid programs and curtailment or restructuring of our operations. Similarly, if our customers are found non-compliant with applicable laws, they may be subject to sanctions, which could also have a negative impact on us. In addition, if we are required to obtain permits or licenses under these laws that we do not already possess, we may become subject to substantial additional regulation or incur significant expense. Any penalties, damages, fines, curtailment or restructuring of our operations would adversely affect our ability to operate our business and our financial results. Healthcare fraud and abuse regulations are complex, and even minor irregularities can potentially give rise to claims of a violation. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations, and additional legal or regulatory change.

If our promotional activities fail to comply with the FDA s regulations or guidelines, we may be subject to enforcement action by the FDA. For example, we received a warning letter from the FDA on November 8, 2005 relating to certain promotional material that included an illustration of the mechanism of action for ZYFLO. The FDA asserted that the promotional material incorporating the illustration was false or misleading because it presented efficacy claims for ZYFLO, but failed to contain fair balance by not communicating the risks associated with its use and failing to present the approved indication for ZYFLO. In response to the warning letter, and as requested by the FDA, we stopped disseminating the promotional material containing the mechanism of action and we provided a written response to the FDA. As part of our response, we provided a description of our plan to disseminate corrective messages about the promotional material to those who received this material. We revised the promotional material containing the mechanism of action to address the FDA s concerns regarding fair balance. If our promotional activities fail to comply with the FDA s regulations or guidelines, we could be subject to additional regulatory actions by the FDA, including product seizure, injunctions, and other penalties and our reputation and the reputation of ZYFLO in the market could be harmed.

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Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management s attention from operating our business and damage our reputation or our brands. If there is a change in law, regulation or administrative or judicial interpretations, we may have to change or discontinue our business practices or our existing business practices could be challenged as unlawful, which could materially harm our business, financial condition and results of operations.

State pharmaceutical marketing and promotional compliance and reporting requirements may expose us to regulatory and legal action by state governments or other government authorities.

In recent years, several states, including California, Maine, Minnesota, New Mexico, Vermont and West Virginia, and the District of Columbia have enacted legislation requiring pharmaceutical companies to establish marketing and promotional compliance programs and file periodic reports with the state on sales, marketing, pricing, reporting pricing and other activities. For example, California has enacted a statute effective July 1, 2005 requiring pharmaceutical companies to adopt and post on their public web site a comprehensive compliance program that is in accordance with the Pharmaceutical Research and Manufacturers of America *Code on Interactions with Healthcare Professionals* and the Office of Inspector General of the Department of Health and Human Services *Compliance Program Guidance for Pharmaceutical Manufacturers.* In addition, such compliance program must establish a specific annual dollar limit on gifts or other items given to individual healthcare professionals in California.

Maine, Minnesota, New Mexico, Vermont, West Virginia and the District of Columbia have also enacted statutes of varying scope that impose reporting and disclosure requirements upon pharmaceutical companies pertaining to drug pricing and payments and costs associated with pharmaceutical marketing, advertising and promotional activities, as well as restrictions upon the types of gifts that may be provided to healthcare practitioners. Similar legislation is being considered in a number of other states. Many of these requirements are new and uncertain, and available guidance is limited. We are in the process of identifying the universe of state laws applicable to pharmaceutical companies and are taking steps to ensure that we come into compliance with all such laws. Unless and until we are in full compliance with these laws, we could face enforcement action and fines and other penalties, and could receive adverse publicity, all of which could materially harm our business.

Our corporate compliance and corporate governance programs cannot guarantee that we are in compliance with all potentially applicable regulations.

The development, manufacturing, pricing, marketing, sales and reimbursement of ZYFLO and 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 175 employees as of December 31, 2005, the majority of whom joined us in 2005. We rely heavily on third parties to conduct many important functions. 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 or other sanctions. Any action against us for a violation of these regulations, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management s attention and harm our reputation.

As a publicly traded company, we are subject to significant legal and regulatory requirements, including the Sarbanes-Oxley Act of 2002 and related regulations, some of which have either only recently been adopted or are subject to change. For example, we are incurring additional expenses and devoting significant management time and attention to evaluating our internal control systems in order to allow our management to report on, and our independent accounting firm to attest to, our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. If the controls and procedures that we implement do not comply with all of the relevant rules and regulations of the Securities and

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Exchange Commission and the Nasdaq National Market, we may be subject to sanctions or investigation by regulatory authorities, including the Securities and Exchange Commission or the Nasdaq National Market. This type of action could adversely affect our financial results or investors confidence in our company and our ability to access the capital markets. If we fail to develop and maintain adequate controls and procedures, we may be unable to provide the required financial information in a timely and reliable manner, which could cause a decline in our stock price.

Our sales depend on payment and reimbursement from third-party payors, and a reduction in payment rate or reimbursement could result in decreased use or sales of our products.

Our sales of ZYFLO are dependent, in part, on the availability of reimbursement from third-party payors such as state and Federal governments, under programs such as Medicare and Medicaid, and private insurance plans. There have been, there are and we expect there will continue to be, state and Federal legislative and administrative proposals that could limit the amount that state or Federal governments will pay to reimburse the cost of pharmaceutical and biologic products. The Medicare Prescription Drug Improvement and Modernization Act of 2003, or the MMA, was signed into law in December 2003. We cannot predict the full impact of the MMA and its regulatory requirements on our business. However, legislative or administrative acts that reduce reimbursement for our products could adversely impact our business. In addition, we believe that private insurers, such as managed care organizations, or MCOs, may adopt their own reimbursement reductions in response to legislation. Any reduction in reimbursement for our products could materially harm our results of operations. In addition, we believe that the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of our products, which may adversely impact our product sales. Furthermore, when a new drug product is approved, governmental and private reimbursement for that product, and the amount for which that product will be reimbursed, are uncertain. We cannot predict the availability or amount of reimbursement for ZYFLO or our product candidates, including those at a late stage of development, and current reimbursement policies for marketed products may change at any time.

The MMA also establishes a prescription drug benefit beginning in 2006 for all Medicare beneficiaries. We cannot be certain that our products will be included in the Medicare prescription drug benefit. Even if our products are included, the MCOs, health maintenance organizations, or HMOs, preferred provider organizations, or PPOs, and private health plans that administer the Medicare drug benefit have the ability to negotiate price and demand discounts from pharmaceutical and biotechnology companies that may implicitly create price controls on prescription drugs. On the other hand, the drug benefit may increase the volume of pharmaceutical drug purchases, offsetting at least in part these potential price discounts. In addition, MCOs, HMOs, PPOs, healthcare institutions and other government agencies continue to seek price discounts. Because MCOs, HMOs and PPOs and private health plans will administer the Medicare drug benefit, managed care and private health plans will influence prescription decisions for a larger segment of the population. In addition, certain states have proposed and certain other states have adopted various programs to control prices for senior citizen and drug programs for people with low incomes, including price or patient reimbursement constraints, restrictions on access to certain products, and bulk purchasing of drugs.

If we succeed in bringing products in addition to ZYFLO to the market, these products 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 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 rebates from list prices, and third-party payors are increasingly challenging the prices charged for medical products. Because our product candidates other than the controlled-release formulation of zileuton are in the development

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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.

If reimbursement for our marketed products changes adversely or if we fail to obtain adequate reimbursement for our other current or future products, health care providers may limit how much or under what circumstances they will prescribe or administer them, which could reduce use of our products or cause us to reduce the price of our products.

If our Medicaid rebate program practices are investigated or if the Medicaid portion of our ZYFLO sales grows, the costs could be substantial and our operating results could be adversely affected.

On January 1, 2006, we became a participant in the Medicaid rebate program established by the Omnibus Budget Reconciliation Act of 1990, as amended effective in 1993. Under the Medicaid rebate program, we pay a rebate for each unit of our product reimbursed by Medicaid. The amount of the rebate for each product is set by law. We are also required to pay certain statutorily defined rebates on Medicaid purchases for reimbursement on prescription drugs under state Medicaid plans. Both the Federal government and state governments have initiated investigations into the rebate practices of many pharmaceutical companies to ensure compliance with these rebate programs. Any investigation of our rebate practices could be costly, could divert the attention of our management and could damage our reputation.

In addition, because ZYFLO was previously marketed by Abbott prior to our licensing it, the rebate that we are required to pay to Medicaid for prescriptions filled by patients covered under a Medicaid program could be substantial. The calculation of the Medicaid rebate is based on the initial pricing set by Abbott with adjustments for inflation each year. Since the price set by Abbott for ZYFLO is below the price we are currently charging, we are subject to a Medicaid rebate of greater than 75% of our selling price. Based on historical prescribing patterns, we expect Medicaid business to be approximately 8% to 12% of total ZYFLO prescriptions. However, if the Medicaid portion of our ZYFLO sales were to increase such that Medicaid represented a larger than expected percentage of the mix of sales for ZYFLO, the increased level of rebates could have a material adverse effect on our financial condition and results of operations.

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 and sale of drugs. If the use of ZYFLO or one or more of our product candidates harms people, we may be subject to costly and damaging product liability claims. We currently have a $20.0 million annual aggregate limit for insurance covering both product liability claims for ZYFLO and clinical trial liability claims for our product candidates. We may seek additional product liability insurance prior to marketing the controlled-release formulation of zileuton or any of our other product candidates. However, our insurance may not provide adequate coverage against potential liabilities. Furthermore, product liability and clinical trial 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. Any product liability claim against us, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management s attention and harm our reputation.

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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.

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 the controlled-release formation of zileuton or our other product candidates under development, our business may 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. ZYFLO is our only commercial product and can only be marketed in the United States. Before we can submit a NDA to the FDA for the controlled-release formulation of zileuton, we must generate satisfactory comparative bioavailability data from two clinical trials in healthy volunteers designed to show that our manufactured tablets behave similarly in the body to the tablets that had been manufactured by Abbott. These studies have been completed in the clinic and we are awaiting completion of the analysis of the blood samples generated in the studies. Once these data are known and we complete 6 months of stability assessment, we believe we will be able to submit the NDA in mid-2006. In May 2005, we held a pre-NDA meeting with the FDA, during which the FDA informed us that new review guidance issued in April 2005 limits its ability to accept additional data during the NDA review process. Our strategy has been to file the NDA with six months of stability data and provide additional stability data during the NDA review period. We will continue to work with the FDA to explore what options may be available to us regarding a submission based on an initial six months of stability data. If the FDA requires nine or twelve months of stability data in the original NDA, this could delay our NDA submission for the product candidate by three to six months, depending upon the outcome of discussions with the FDA close to the planned time of filing.

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 pivotal clinical trials to support our NDA. If the FDA does not permit us to rely on the prior clinical data or if the data at the clinical sites do not pass FDA audits, we could 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 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 or biologic 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 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.

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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 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.

Our product candidates are still in development and remain subject to clinical testing and regulatory approval or clearance. 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 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 submission and 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 and biologic 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 additional 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 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;

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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 experienced by participants in ongoing or past clinical trials for the same or a different indication;

serious and unexpected drug-related side effects observed during ongoing or past prelinical studies; 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, competing trials with other product 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 requirements and review. If we fail to comply with continuing U.S. and applicable foreign regulations, we could lose permission to manufacture and distribute our products and the sale of our product candidates could be suspended.

Our product candidates are subject to continuing regulatory review after approval, including the review of spontaneous adverse drug experiences and clinical results from any post-market testing 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.

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If we or our third-party manufacturers or service providers fail to comply with applicable 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;

fines;

restrictions on importation of our product candidates;

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 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. We are relying on Beckman Coulter to fund the development and to commercialize diagnostics 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. Our revenues for the year ended December 31, 2005 were derived from fees paid to us by MedImmune and Beckman Coulter under our collaboration agreements with them and revenue from the sale of ZYFLO beginning in the fourth quarter of 2005; however, a significant portion of our revenues for the year ended December 31, 2005 continued 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 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

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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 diagnostic assays for HMGB1 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 detection of HMGB1 likely would be delayed, curtailed or terminated.

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 rely on third parties to manufacture and supply the zileuton API, ZYFLO and our product candidates. We expect to continue to rely on third parties for these purposes and would incur significant costs to independently develop manufacturing facilities.

We have no manufacturing facilities and limited manufacturing experience. In order to continue to develop product candidates, apply for regulatory approvals and commercialize products, we need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities. We currently rely on third parties for production of commercial supplies of the zileuton API and ZYFLO and the production of our product candidates for preclinical and clinical testing purposes. We expect to continue to rely on third parties for these purposes for the foreseeable future.

We have contracted with Rhodia Pharma Solutions Ltd. for commercial production of the zileuton API, subject to specified limitations, through December 31, 2009. Rhodia SA, the parent company of

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Rhodia Pharma Solutions, has experienced significant operating losses since 2001. In 2003, Rhodia SA initiated a corporate reorganization plan to refocus its business portfolio, and has divested a number of its operating units since that time. In addition, Rhodia SA publicly announced that it incurred a 101 million charge in the second quarter of 2005 to fully write off the value of Rhodia Pharma Solutions. On January 5, 2006, Rhodia SA announced that it had signed a letter of intent to sell Rhodia Pharma Solutions to Shasun Chemicals & Drugs Ltd., which is listed on the Bombay stock exchange. Rhodia has announced that this sale will complete in the first half of 2006. Based on discussions with Rhodia, we expect that the manufacture of zileuton API will not be affected by the sale. 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 sites, could result in unintended combustion of the product. The manufacture of the API could be disrupted or delayed if a batch is discontinued or damaged, if the manufacturing sites were damaged, or if local health and safety regulations require a third-party manufacturer to implement additional safety procedures or cease production.

We have contracted with Patheon Pharmaceuticals Inc. for the manufacture of commercial supplies of ZYFLO tablets. We have contracted with Patheon for a technology transfer program to enable Patheon to coat and package the core tablets of the controlled-release formulation of zileuton for clinical trials and regulatory review, and, subject to negotiation of a commercial manufacturing agreement, commercial supplies.

We have 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 supplies. SkyePharma announced that it was the target of an unsolicited acquisition bid in November 2005. SkyePharma subsequently announced that it had retained an investment bank to consider strategic options, including the sale of the company. In February 2006, SkyePharma announced a new senior management team and the conclusion of its strategic review, deciding to concentrate on oral and pulmonary products and divest its injectable business. Sale of SkyePharma as a whole or in parts may impact our ability to produce the controlled-release formulation of zileuton and may affect our schedule for the submission of the NDA for the controlled-release formulation of zileuton.

We have not secured a long-term commercial supply arrangement for any of our product candidates other than the zileuton API. The manufacturing process for our product candidates is an element of the FDA approval process. 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 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. 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.

We are dependent upon Rhodia Pharma Solutions, Patheon and SkyePharma as sole providers, 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. 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 for our product candidates;

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we may be required to cease distribution or issue recalls; and

we may not be able to meet commercial demands.

If we were required to change manufacturers for the zileuton API, ZYFLO or the controlled-release formulation of zileuton, we would be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and all applicable regulations and guidelines, including FDA requirements and approved NDA product specifications. Any delays associated with the verification of a new manufacturer could adversely affect our production schedule or increase our production costs.

We rely on a single source supplier for one of the starting materials for zileuton, and the loss of that supplier could prevent us from selling ZYFLO.

Sumitomo is currently the only qualified supplier of a chemical known as 2-ABT, one of the starting materials for the zileuton API. Rhodia Pharma Solutions, which supplies us with the zileuton API, has an agreement with Sumitomo for the supply of 2-ABT. If Sumitomo stops manufacturing or is unable to manufacture 2-ABT, or if Rhodia is unable to procure 2-ABT from Sumitomo on commercially reasonable terms, we may be unable to continue to sell ZYFLO on commercially viable terms, if at all. In addition, Rhodia s inability to procure 2-ABT could also impact our ability to commercialize the controlled-release formulation of zileuton, if it is approved by the FDA. Furthermore, because Sumitomo is currently the sole supplier of 2-ABT, Sumitomo has unilateral control over the price of 2-ABT. Any increase in the price for 2-ABT may reduce our gross margins.

Any failure to manage and maintain our distribution network could compromise ZYFLO sales and harm our business.

We rely on third parties to distribute ZYFLO to pharmacies. We have contracted with Integrated Commercialization Services, Inc., or ICS, a third-party logistics company, to warehouse ZYFLO and distribute it to three primary wholesalers, AmerisourceBergen Corporation, Cardinal Health and McKesson Corporation, and a number of smaller wholesalers. The wholesalers in turn distribute it to chain and independent pharmacies. ICS is our exclusive supplier of commercial distribution logistics services. We rely on Phoenix Marketing Group LLC to distribute ZYFLO samples to our sales representatives, who in turn distribute samples to physicians and other prescribers who are authorized under state law to receive and dispense samples. We have contracted with RxHope, Inc. to implement a patient assistance program for ZYFLO. We rely on RxHope to administer our patient assistance program and to distribute ZYFLO to physicians and other prescribers who are authorized under state law to receive and dispense samples.

This distribution network requires significant coordination with our supply chain, sales and marketing and finance organizations. Failure to maintain our contracts with our logistics company, the wholesalers, Phoenix and RxHope, or the inability or failure of any of them to adequately perform as agreed under their respective contracts with us, could negatively impact us. We do not have our own warehouse or distribution capabilities, and moreover we lack the resources and experience to establish any of these functions and do not intend to do so in the foreseeable future. We would be unable to replace ICS, AmerisourceBergen, Cardinal, McKesson, Phoenix or RxHope in a timely manner in the event of a natural disaster, failure to meet FDA and other regulatory requirements, business failure, strike or any other difficulty affecting any of them, and the distribution of ZYFLO could be delayed or interrupted, damaging our results of operations and market position. Failure to coordinate financial systems could also negatively impact our ability to accurately report and forecast product sales and fulfill our regulatory obligations. If we are unable to effectively manage and maintain our distribution network, sales of ZYFLO could be severely compromised and our business could be harmed.

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

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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 any of our product candidates 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 assay for HMGB1. 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.

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

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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; or

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

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, one of our product candidates currently in development, 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

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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 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 $47.1 million in the year ended December 31, 2005. As of December 31, 2005, we had an accumulated deficit of approximately $105.6 million. As of December 31, 2005, we recorded $387,000 of revenue from the sale of ZYFLO and have not recorded revenue from any other product. We expect that we will continue to incur substantial losses for the foreseeable future as we spend significant amounts to fund our research, development and commercialization efforts 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

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be substantial. We will need to generate significant revenues to 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, expand our sales and marketing infrastructure, achieve regulatory approvals, commercialize ZYFLO and, subject to regulatory approval, commercially launch the controlled-release formulation of zileuton and any future product candidates. Our funding requirements will depend on numerous factors, including:

the costs of ongoing sales and marketing for ZYFLO;

the timing, receipt and amount of sales from ZYFLO;

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, obtaining and maintaining 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;

our ability to establish and maintain additional collaborative arrangements; and

the ongoing time and costs involved in certain corporate governance requirements, including work related to compliance with the Sarbanes-Oxley Act of 2002.

Other than payments that we receive from our collaborations with MedImmune and Beckman Coulter, we expect that sales of ZYFLO will represent our only source of operating income until we commercially launch the controlled-release formulation of zileuton if it is approved. In addition to the foregoing factors, we believe that our ability to access external funds will depend upon the market acceptance of ZYFLO, 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 sell ZYFLO and obtain regulatory approval for and successfully commercialize the controlled-release formulation of zileuton. Based on our operating plans, we believe that our available cash and cash equivalents and anticipated cash received from product sales and anticipated payments received under collaboration agreements will be sufficient to fund anticipated levels of operations until the second quarter of 2007.

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For the year ended December 31, 2005, our net cash used for operating activities was $45.0 million and we had capital expenditures of $2.2 million. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we may 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.

If the estimates we make, or the assumptions on which we rely, in preparing our financial statements prove inaccurate, our actual results may vary from these reflected in our projections.

Our financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct. If our estimates are inaccurate, this could adversely affect our stock price.

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 Securities and Exchange Commission, or the SEC. For example, a new accounting rule, which will become effective for us on January 1, 2006, 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. Adoption of the new accounting rule on stock-based compensation expense is expected to increase net losses or reduce net income in future periods. 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.

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.

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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:

- the amount and timing of sales of ZYFLO;
- the timing of operating expenses, including selling and marketing expenses and the costs of maintaining a direct sales force;
- the availability and timely delivery of a sufficient supply of ZYFLO;
- the amount of rebates, discounts and chargebacks to be wholesalers, Medicaid and managed care organizations related to ZYFLO;
- the amount and timing of product returns for ZYFLO;
- 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 development or 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 significant business or product announcements 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 operating results, including the amount and timing of sales of ZYFLO;
- 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, 2006, our directors, executive officers and 5% or greater stockholders, together with their affiliates, to our knowledge, beneficially owned, in the aggregate, approximately 64.7% of our outstanding common stock. As a result, our directors, executive officers and 5% or greater 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 or our board 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 up to 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 1B. ***UNRESOLVED STAFF COMMENTS***

Not applicable.

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, 2005.

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EXECUTIVE OFFICERS OF THE REGISTRANT

Our executive officers, their ages and their positions as of February 28, 2006 are as follows:

Name	Age	Position
Paul D. Rubin, M.D.	52	President and Chief Executive Officer
Frederick Finnegan	46	Senior Vice President of Sales and Marketing
Walter Newman, Ph.D.	60	Chief Scientific Officer and Senior Vice President of Research and Development
Trevor Phillips, Ph.D.	44	Chief Operating Officer and Senior Vice President of Operations
Frank E. Thomas	36	Chief Financial Officer, Senior Vice President of Finance and Treasurer
Scott B. Townsend, J.D.	39	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.

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.

Walter Newman, Ph.D. has served as our Chief Scientific Officer since May 2002, as our Senior Vice President of Research and Development since November 2005, as our Senior Vice President Research and Discovery from December 2004 to November 2005, 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,

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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.

Scott B. Townsend, J.D. 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, North Carolina from July 1999 to July 2000 and an associate with the law firm Goodwin Procter LLP in Boston, Massachusetts 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 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 closing sales prices of our common stock on the Nasdaq National Market.

Year Ended December 31, 2005	High	Low
First Quarter (from January 1 to March 31)	$ 8.05	$ 6.27
Second Quarter (from April 1 to June 30)	$ 7.06	$ 5.00
Third Quarter (from July 1 to September 30)	$ 9.42	$ 5.51
Fourth Quarter (from October 1 to December 31)	$ 9.18	$ 6.11

Year Ended December 31, 2004	High	Low
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, 2006, the closing price per share of our common stock as reported on the NASDAQ National Market was $5.44, and we had approximately 116 stockholders of record. This number does not include beneficial owners for whom shares are held by nominees in street name.

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

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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 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, 2005, we have used:

- approximately $7.4 million of these net proceeds to establish sales and marketing capabilities and manufacturing and distribution arrangements to launch ZYFLO; and

- approximately $6.5 million of these net proceeds to fund preclinical and clinical development of our product candidates.

We have not used any of the net proceeds from the offering to make payments, directly or indirectly, to any of our directors or officers, or any of their associates, to any person owning 10 percent or more of our common stock or to any affiliate of ours. The balance of the net proceeds of the offering is invested in short-term investment grade corporate and U.S. government securities.

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ITEM 6. ***SELECTED 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, 2005, 2004 and 2003 and the balance sheet data as of December 31, 2005 and 2004 from our audited consolidated financial statements, which are included at the end of this report. We derived the statements of operations data for the years ended December 31, 2002 and 2001 and the balance sheet data as of December 31, 2003, 2002 and 2001 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.

	Year Ended December 31,				
	2005	2004	2003	2002	2001
	(In thousands, except share and per share data)				
Statements of Operations Data:					
Net product sales	$ 387	$	$	$	$
Revenue under collaboration agreements	5,837	4,436	1,021		
Total revenues	6,224	4,436	1,021		
Cost of products sold	514				
Research and development expenses	29,959	25,578	17,458	3,284	957
Sales and marketing expenses	13,671	1,199			
General and administrative expenses	11,406	9,679	3,771	1,792	605
Total costs and expenses	55,550	36,456	21,229	5,076	1,562
Loss from operations	(49,326)	(32,020)	(20,208)	(5,076)	(1,562)
Interest income	2,427	1,098	191	149	119
Interest expense	(191)	(172)	(93)	(8)	(5)
Net loss	(47,090)	(31,094)	(20,110)	(4,935)	(1,448)
Accretion of dividends and offering costs on preferred stock		(2,209)	(2,264)	(1,032)	(432)
Net loss available to common stockholders	$ (47,090)	$ (33,303)	$ (22,374)	$ (5,967)	$ (1,880)
Net loss per common share:					

Basic and diluted	$ (1.61)	$ (2.28)	$ (33.99)	$ (23.74)	$ (2.63)
Weighted-average basic and diluted shares outstanding	29,276,243	14,631,371	658,204	251,346	714,820

	As of December 31,				
	2005	**2004**	**2003**	**2002**	**2001**
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 82,811	$ 78,829	$ 40,078	$ 13,539	$ 8,580
Working capital	70,005	64,357	25,218	13,017	8,501
Total assets	91,819	83,114	45,054	14,382	8,638
Long term debt, net of current portion	1,489	1,367	720	202	
Redeemable convertible preferred stock			51,395	21,080	10,270
Accumulated deficit	(105,617)	(58,527)	(27,433)	(7,323)	(1,517)
Total stockholders equity (deficit)	72,247	65,408	(24,851)	(7,554)	(1,750)

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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 in Item 1A Risk Factors appearing elsewhere in this report.

Financial Operations Overview

We are a biopharmaceutical company and have devoted substantially all of our efforts since inception to the commercialization of our recently launched product, ZYFLO, 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. ZYFLO is approved by the FDA for the prevention and chronic treatment of asthma in adults and children 12 years of age and older. We were incorporated in July 2000 as Medicept, Inc. and changed our name to Critical Therapeutics, Inc. in March 2001. We completed an initial public offering of our common stock in June 2004, and our common stock is currently traded on the Nasdaq National Market.

We began selling ZYFLO in the United States in October 2005. In addition, we believe that zileuton has potential therapeutic benefits in a range of other diseases and conditions, such as acute asthma exacerbations, chronic obstructive pulmonary disease, or COPD, and nasal polyposis. We are currently incurring costs to expand the potential applications of zileuton through development of additional formulations, including controlled-release and intravenous formulations. 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.

Since our inception, we have incurred significant losses each year. As of December 31, 2005, we had an accumulated deficit of $105.6 million. We expect to incur significant losses for the foreseeable future and we may never achieve profitability at all. Although the size and timing of our future operating losses are subject to significant uncertainty, we expect our operating losses to continue over the next several years as we fund our development programs, market and sell ZYFLO and prepare for the 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, payments from our collaborators MedImmune and Beckman Coulter, and, beginning in the fourth quarter of 2005, revenues from sales of ZYFLO.

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. Under this collaboration, MedImmune paid us initial fees of $12.5 million in 2003 and an additional $2.75 million in 2005 and $1.5 million in 2004 for milestone payments and to fund certain research expenses incurred by us for the HMGB1 program.

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.

In June 2005, we sold 9,945,261 shares of our common stock, together with warrants to purchase an additional 3,480,842 shares of our common stock, to institutional and other accredited investors. Our net proceeds from the private placement were approximately $51.4 million.

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Revenues. From our inception on July 14, 2000 through the third quarter of 2005, we derived all of our revenues from license fees, research and development payments and milestone payments that we have received from our collaboration agreements with MedImmune and Beckman Coulter. In the fourth quarter of 2005, we began shipping our first commercial product, ZYFLO. We recorded $387,000 in product revenue for the year ended December 31, 2005.

Cost of products sold. Cost of products sold consists of manufacturing, distribution and other costs related to our commercial product, ZYFLO. In addition, it includes royalties to third parties related to ZYFLO. Most of our manufacturing and distribution costs are paid to third party manufacturers. However, there are some internal costs reflected in cost of products sold, including salaries and expenses related to managing our supply chain and for quality assurance and release testing.

Research and Development Expenses. Research and development expenses consist of costs 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 monitoring and analyzing clinical trials, costs related to the development of our new drug application, or NDA, for the controlled-release formulation of zileuton, costs of contract research and manufacturing and the cost of facilities. In addition, research and development expenses include the cost of our medical affairs and medical information functions, which educate physicians on the scientific aspects of our commercial products and the approved indications, labeling and the costs of monitoring adverse events. After FDA approval of a product candidate, manufacturing expenses associated with a product will be recorded as cost of products sold 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 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 the intravenous formulation of zileuton and CTI-01 tend to be higher than earlier stage programs such as our HMGB1 and alpha-7 programs, due to the costs associated with conducting clinical trials and large-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 the controlled-release and intravenous formulations of zileuton, CTI-01 and alpha-7. We also expect manufacturing expenses for some programs included in research and development expenses to increase as we complete registration activities relating to the manufacturing of the controlled-release formulation of zileuton and scale up production of the intravenous formulation of zileuton for late phase clinical trials. We also expect to initiate a post-marketing, Phase IV program for ZYFLO to examine its potential clinical benefits in certain populations of asthma patients, which, if conducted, would be included in research and development expenses.

Sales and Marketing. Sales and marketing expenses consist primarily of salaries and other related costs for personnel in sales and marketing functions as well as costs related to our recent product launch of ZYFLO. Other costs reflected in sales and marketing include the cost of product samples of ZYFLO, promotional materials, market research and sales meetings. We expect to continue to incur significant sales and marketing costs associated with our recent hiring of our sales force and the continued enhancement of the sales and marketing infrastructure to support ZYFLO. If any of our other product candidates are approved for marketing, we expect to incur additional expenses related to enhancing our sales and marketing functions and adding additional sales representatives.

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, information technology and human resource functions. Other costs reflected in general and administrative expenses include certain facility costs as well as professional fees for legal and accounting services. We anticipate that our general and administrative expenses will also increase as we expand our operations,

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facilities and other activities related to operating as a publicly traded company. In addition, we expect to incur increased general and administrative expenses to support our first commercial product, ZYFLO.

Deferred Stock-Based Compensation Expense. As discussed more fully in Note 7 and 8 to our consolidated financial statements included in this report, in lieu of cash payments, we granted options to purchase 161,000 shares of our common stock to non-employees in 2005 and we granted 66,666 shares of our common stock and options to purchase 51,333 shares of our common stock to non-employees in 2004. We recorded these grants at fair value when granted. We periodically remeasure the fair value of the unvested portion of grants to non-employees, 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 $384,000 and $1.8 million during the years ended December 31, 2005 and 2004, respectively, related to grants of common stock, restricted shares and stock options to non-employees.

As discussed more fully in Note 8 to our consolidated financial statements included in this report, we granted options to purchase 1,864,900 and 2,855,288 shares of our common stock to employees during the years ended December 31, 2005 and 2004, respectively. Certain of the employee options granted in the year ended December 31, 2004, prior to our initial public offering, were deemed for accounting purposes to have been granted with exercise prices below their then-current market value. We recorded the intrinsic value of these differences as deferred stock-based compensation expense. 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 in both 2005 and 2004 related to stock options granted to employees at exercise prices below their current market value on the date of grant.

Critical Accounting Policies

The discussion and analysis of our financial condition and results of operations are 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 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 in this report. 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, inventory, accrued expenses, short-term investments, stock-based compensation and income taxes described below fit the definition of critical accounting estimates.

Revenue Recognition. In the fourth quarter of 2005, we launched our first commercial product, ZYFLO. We sell ZYFLO to wholesalers, distributors and pharmacies, which have the right to return purchased product. In accordance with Statement of Financial Accounting Standards No. 48, *Revenue*

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Recognition When Right of Return Exists, or SFAS No. 48, we defer revenue on product shipments until we can reasonably estimate returns relating to these shipments. Because ZYFLO is a new product for us and this is our first commercial product launch, we do not currently have an objective measurement or history to allow us to estimate returns. Accordingly, we are deferring the recognition of revenue on product shipments of ZYFLO to our customers until the product is dispensed through patient prescriptions. Since product dispensed to patients through prescription is not subject to return, there is no remaining contingency that would prohibit revenue recognition. We currently estimate prescription units dispensed based on distribution channel data provided by external sources. We will continue to recognize revenue based upon prescriptions dispensed until we can reasonably estimate product returns based on our product returns experience. When a reasonable estimate can be determined, we will likely record a one-time increase in net product sales related to the recognition of revenue previously deferred, net of an estimate for remaining product returns. In order to match the cost of products shipped to customers with the underlying revenue, we have deferred the recognition of costs related to shipments that have not been recognized as revenue.

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.

Inventory. Inventory is stated at the lower of cost or market with cost determined under the first-in, first-out, or FIFO, method. Our estimate of the net realizable value of our inventories is subject to judgment and estimation. The actual net realizable value of our inventories could vary significantly from our estimates and could have a material effect on our financial condition and results of operations in any reporting period. ZYFLO has a twelve-month shelf life as of December 31, 2005. As of December 31, 2005, inventory consists of zileuton API, which is raw material in powder form, and work-in-process and finished tablets to be used for commercial sale. On a quarterly basis, we analyze our inventory levels and write down inventory that has become obsolete, inventory that has a cost basis in excess of our expected net realizable value and inventory that is in excess of expected requirements to cost of product revenues. During the year ended December 31, 2005, we recorded a reserve to cost of products sold for short-dated ZYFLO commercial product of $280,000 that will expire by September 2006.

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 that 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, rebates to third parties, including government programs such as Medicaid or private insurers, 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 rebates, our estimates are based on our estimated mix of sales to various third-party payors, which either contractually or statutorily are entitled to certain discounts off our listed price of ZYFLO. In the event that our sales mix to certain third-party payors is different from our estimates, we may be required to pay more or less rebates to those parties than our estimates. In connection with service fees, our estimates are most affected by our understanding of the

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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 that we have begun to incur 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 subject to judgment. We make these judgments based upon the facts and circumstances known to us in accordance with generally accepted accounting principles.

Short-term investments. It is our intent to hold our short-term investments until such time as we intend to use them to meet the ongoing liquidity needs to support our operations. However, if the circumstances regarding an investment or our liquidity needs were to change, such as a change in an investment s external credit rating, we would consider a sale of the related security prior to the maturity of the underlying investment to minimize any losses. We review the appropriateness of all investment classifications at each reporting date.

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 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 Issue No. 96-18, or EITF 96-18, Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services. 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.

In December 2004, the Financial Accounting Standards Board, or FASB, issued SFAS No. 123(R), Share-Based Payment. This Statement is a revision of SFAS No. 123, amends SFAS No. 95, Statement of Cash Flows, and supersedes Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees, and its related implementation guidance. SFAS No. 123(R) focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. The Statement requires entities to recognize in their income statement stock compensation expense for awards (with limited exceptions) based on their fair value. In addition, SFAS No. 123(R) 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. SFAS No. 123(R) is effective for us commencing January 1, 2006, at which time we will begin recognizing an expense for unvested share-based compensation that has been issued or will be issued after that date.

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SFAS No. 123(R) permits a prospective or two modified versions of retrospective application under which financial statements for prior periods are adjusted on a basis consistent with the pro forma disclosures required for those periods by the original SFAS No. 123.

Effective January 1, 2006, the Company adopted the provisions of SFAS No. 123(R) using the modified prospective approach using the Black-Scholes option-pricing model. The total compensation expense, including the cost of options that are expected to be granted during 2006, is expected to be up to $6 million. However, uncertainties, including the number of stock option grants, stock price volatility, estimated forfeitures and employee stock option exercise behavior, make it difficult to determine whether the stock-based compensation expense that we will incur for 2006 will be similar to this estimate.

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, 2005, we had federal and state tax net operating loss carryforwards of approximately $85.8 million, which expire beginning in 2021 and 2006, respectively. We also have research and experimentation credit carryforwards of approximately $1.2 million, which expire beginning in 2021. We have recorded a full valuation allowance 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, 2005 and 2004

Revenue from Product Sales. We recognized revenue from product sales of $387,000 in 2005 related to sales of ZYFLO following our product launch in October 2005. This is the first period in which we have recognized revenue from product sales since our inception. Under SFAS No. 48, we cannot recognize revenue from product shipments until the right to return the product has lapsed or until we can reasonably estimate returns relating to the shipments to third parties. In accordance with SFAS No. 48, we are currently deferring recognition of revenue on product shipments of ZYFLO to wholesalers, distributors and pharmacies until the product is dispensed through patient prescriptions. Gross revenue from product sales for prescriptions dispensed was $462,000 in 2005, while product revenue, net of discounts and rebates, was $387,000. Shipments of ZYFLO to third parties that were not recognized as revenue totaled $1.7 million at December 31, 2005 and are included in deferred product revenue on our balance sheet. This deferred revenue will be recognized as revenue as prescriptions are filled in future periods, or will be reversed if the product is returned in future periods. The cost of product shipped to third parties that has not been recognized as revenue in accordance with our revenue recognition policy is deferred until the product is dispensed through patient prescriptions. This deferred cost of product sold totaled $266,000 at December, 31, 2005 and is included in prepaid expenses and other current assets on our balance sheet.

Revenue under Collaboration Agreements. We recognized collaboration revenues of $5.8 million in 2005 compared to $4.4 million in 2004. These revenues were primarily due to the portion of the $12.5 million of initial fees MedImmune paid us that we recognized in each period, and the $2.75 million and $1.5 million billed to MedImmune for milestone payments and development support in 2005 and 2004, respectively. Since we entered into the agreement with MedImmune in 2003, we have billed a total of $16.75 million to MedImmune, consisting of the $12.5 million up-front payment, a $1.25 million milestone payment and $3.0 million of development support. We have recognized $11.2 million of these amounts as collaboration revenue to date. We have reported the balance of the payments, totaling $5.6 million, as deferred collaboration revenue and will recognize such amount over the remaining

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estimated 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. We currently estimate that the balance in deferred revenue will be recognized during 2006 and 2007. In December 2005, we revised our estimate of remaining total costs and increased the period over which those costs would be allocated under the collaboration agreement with MedImmune. The change in estimate resulted in a decrease in revenue recognized of approximately $237,000 for the three months ended December 31, 2005. As of December 31, 2005, we had a total of $5.7 million in deferred collaboration revenue remaining to be recognized under our collaboration agreements with MedImmune and Beckman Coulter.

Cost of products sold. Cost of products sold in 2005 were $514,000. Cost of products sold consisted primarily of the expenses associated with manufacturing and distributing ZYFLO, a royalty payment to Abbott from the license agreement for ZYFLO and a charge of $280,000 to write-down excess finished goods inventory that we do not currently expect to be sold in the future. The write-down resulted from excess inventory on-hand at December 31, 2005 with an expiration date in 2006.

Research and Development Expenses. Research and development expenses in 2005 were $30.0 million compared to $25.6 million in 2004, an increase of approximately $4.4 million. This increase was primarily due to higher expenses associated with the technology transfer and manufacturing activities associated with ZYFLO and the controlled-release formulation of zileuton, as well as 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 in 2005 as compared to 2004. With the commercial launch of ZYFLO in October 2005, the costs of manufacturing ZYFLO are now included in cost of products sold.

The following table summarizes the primary components of our direct research and development expenses for the years ended December 31, 2005 and 2004:

	Year Ended December 31,	
	2005	2004
	(In thousands)	
Zileuton	$ 14,326	$ 12,369
CTI-01	3,045	3,329
Alpha-7	2,434	1,533
HMGB1	2,030	1,702
General research and development expenses	7,260	4,637
Stock-based compensation expense	864	2,008
Total research and development expenses	$ 29,959	$ 25,578

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 2005, we incurred $14.3 million in expenses related to our zileuton program as compared to $12.4 million during 2004, a 16% increase. This increase was primarily due to the following:

- manufacturing costs related to the product registration of ZYFLO;
- our completed Phase II clinical trial of ZYFLO for moderate to severe inflammatory acne;

the initiation of the ZYFLO open-label study in patients with asthma or mastocytosis;

the development and manufacturing costs related to our intravenous and controlled-release formulations; and

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the payment of several milestones related to our license agreements with Abbott and Skypharma.

CTI-01. During 2005, we incurred $3.0 million in expenses related to our CTI-01 program as compared to $3.3 million during 2004, a 9% decrease. This decrease was primarily due to lower preclinical costs in 2005, partially offset by higher clinical and manufacturing costs. We expect to incur additional costs for this program in 2006 as we continue enrollment of a Phase II clinical trial of CTI-01 in patients undergoing major cardiac surgery including the use of a cardiopulmonary bypass machine.

Alpha-7. During 2005, we incurred $2.4 million of expenses in connection with our alpha-7 program as compared to $1.5 million during 2004, a 59% increase. The increase was primarily due to an increase in the number of employees working on the alpha-7 program and higher contract research costs associated with our efforts to discover and develop small molecule product candidates.

HMGB1. During 2005, we incurred $2.0 million of expenses for our HMGB1 program as compared to $1.7 million during 2004, a 19% increase. This increase was primarily due to higher license fees, sponsored research and lab supplies for our continued testing under our collaboration agreement with MedImmune offset in part by lower personnel costs devoted to this program. In 2005, we paid a $250,000 milestone payment to the licensor of HMGB1 for establishing preclinical proof-of-concept. The collaboration revenue recognized by us in 2005 for this program totaled $5.8 million. We currently anticipate that certain research and development costs relating to HMGB1 in 2006 will be covered by funding and potential milestone payments from MedImmune under our collaboration agreement.

Our general research and development expenses, which are not allocated to any specific program, increased by $2.6 million, or 57%, in 2005 compared to 2004. This increase was primarily due to a $1.2 million increase in personnel costs and a $1.6 million increase in facility and related costs, partially offset by a $624,000 decrease in leasehold amortization expense. These costs, which are incurred in support of all of our research and development programs, are not easily allocable to any individual program, and therefore, have been included in general research and development expenses. In addition, since the launch of ZYFLO, we have incurred expenses associated with medical affairs, medical education and medical information, which are part of our general research and development expenses.

Stock-based compensation expense that is related to research and development decreased by $1.1 million from $2.0 million in 2004 compared to $864,000 in 2005. This includes expenses for certain employee grants as well as grants made to non-employees who are primarily working on research and development activities. The adjustment to stock-based compensation expense for non-employees is calculated based on the change in fair value of our common stock during the period. The fair value of our common stock declined approximately 10% during 2005 resulting in lower overall stock-based compensation expense.

Sales and Marketing Expenses. Sales and marketing expenses for 2005 were $13.7 million compared to $1.2 million for 2004. The $12.5 million increase in 2005 was primarily attributable to the following:

hiring and training our 80-person specialty sales force, the majority of whom we hired in August 2005;

hiring our sales and customer management team;

market research conducted in anticipation of the approval and launch of ZYFLO; and

marketing, product samples, promotional materials and other costs associated with our recent launch of ZYFLO.

The number of employees performing sales and marketing functions increased from 6 employees at December 31, 2004 to 106 employees at December 31, 2005.

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General and Administrative Expenses. General and administrative expenses for 2005 were $11.4 million compared to $9.7 for 2004. The $1.7 million, or 18%, increase in 2005 was primarily attributable to the following:

Personnel costs increased $476,000 as a result of an increase in the number of employees performing general and administrative functions.

Directors and officers insurance and general business insurance costs increased $291,000 due to an increase in premiums.

Audit fees related to our Sarbanes-Oxley compliance and consulting increased $724,000 as we prepared for the audit of our internal controls systems as of December 31, 2005.

Other Income. Interest income in 2005 was $2.4 million compared to $1.1 million in 2004. The increase was primarily attributable to higher interest income earned on our investments due to higher interest rates and higher cash and investment balances from our financings completed in 2004 and 2005. Interest expense amounted to $191,000 and $172,000 in 2005 and 2004, respectively. The interest expense relates to borrowings under our loan with Silicon Valley Bank for capital expenditures.

Years Ended December 31, 2004 and 2003

Revenue Under Collaboration Agreement. We recognized revenues of $4.4 million in 2004 compared to $1.0 million in 2003. These revenues represent the portion of the $12.5 million of initial fees MedImmune paid us that we recognized in each 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 estimated 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 the third quarter of 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 in 2004 were $25.6 million compared to $17.5 million in 2003, an increase of $8.1 million. This increase was primarily due 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 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.

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

	Year Ended December 31,	
	2004	2003
	(In thousands)	
Zileuton	$ 12,369	$ 3,269
CTI-01	3,329	1,579
HMGB1	1,702	3,483
Alpha-7	1,533	630
General research and development expenses	4,637	3,589
Stock-based compensation expense	2,008	4,908
Total research and development expenses	$ 25,578	$ 17,458

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 2004, we incurred $12.4 million in expenses related to our zileuton program as compared to $3.3 million during 2003. This increase was primarily due to 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. The aggregate technology transfer and validation costs associated with the change of manufacturing sites for ZYFLO and the controlled-release formulation of zileuton were $7.2 million in 2004. In addition, we initiated a Phase II clinical trial in moderate to severe inflammatory acne patients during 2004.

CTI-01. Expenses for CTI-01 increased by $1.8 million in 2004 as compared to 2003. This increase is 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.

HMGB1. Expenses for HMGB1 decreased by $1.8 million in 2004 as compared to 2003. The increase in expenses is 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.

Alpha-7. During 2004, we incurred $1.5 million of expenses in connection with our alpha-7 program as compared to $630,000 during 2003. The increase is primarily due to costs associated with our efforts to develop small molecules.

Our general research and development expenses, which are not allocated to any specific program, increased by $1.0 million in 2004 compared to 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.

Stock-based compensation expense decreased by $2.9 million from $4.9 million in 2004 compared to $2.0 million in 2003. The adjustment to stock-based compensation expense for non-employees is calculated based on the change in fair value of our common stock during the period.

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Sales and Marketing Expenses. Sales and marketing expenses in 2004 were $1.2 million. The $1.2 million consisted of personnel costs related to the hiring of our head of sales and marketing as well as certain market research conducted in anticipation of our launch of ZYFLO. We did not incur any sales and marketing expenses prior to 2004. These costs were included in general and administrative expense in our 2004 annual report on Form 10-K for the year ended December 31, 2004, but have been reclassified to conform with the 2005 presentation.

General and Administrative Expenses. General and administrative expenses in 2004 were $9.7 million compared to $3.8 million in 2003. The $7.1 million increase in 2004 was primarily attributable to the following:

Personnel costs increased approximately $2.0 million 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.

Professional services fees increased $349,000 associated with our licensing and other corporate development activities.

Directors and officers insurance and general business insurance costs increased $415,000 as a result of an increase in premiums following our initial public offering.

Facility and equipment costs increased by $1.7 million as a result of our move in April 2004 to a larger facility.

Cancellation of employee loans increased $419,000 plus the costs associated with gross-up payments for state and federal taxes.

Stock-based compensation expense increased $1.4 million primarily as a result of additional amortization on the issuance of certain employee stock options granted during 2003 and the first half of 2004 with an exercise price deemed to be 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.

Other Income. Interest income in 2004 was $1.1 million compared to $191,000 in 2003. The increase 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. Interest expense amounted to $172,000 and $93,000 in 2004 and 2003, respectively. 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.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception on July 14, 2000, we have financed our operations through the sale of common and preferred stock, debt financings, the receipt of interest income, payments from our collaborators MedImmune and Beckman Coulter and, beginning in the fourth quarter of 2005, revenue generated from sales of ZYFLO. As of December 31, 2005, we had $82.8 million in cash, cash equivalents and short-term investments. We have invested the net proceeds from our financings and collaborations in highly liquid,

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interest-bearing, investment grade securities in accordance with our established corporate investment policy.

In October 2005, we launched our first commercial product, ZYFLO, and began recognizing revenue from product sales. Customer orders totaled $2.1 million in 2005, net of discounts and rebates. Cash flows from customers are dependent upon demand for the product by physicians or patients.

In June 2005, we sold 9,945,261 shares of our common stock at a price of $5.48 per share, together with warrants to purchase an additional 3,480,842 shares of our common stock, in a private placement to certain institutional and other accredited investors. Our gross proceeds from the private placement were approximately $54.5 million, before deducting fees paid to placement agents and other transaction expenses paid by us.

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 $4.25 million through December 31, 2005 for milestone payments and to fund certain research expenses incurred by us for the HMGB1 program.

Under our collaboration 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 The Feinstein Institute on milestone payments we receive from MedImmune. We anticipate that by the end of 2006, in addition to payments already received, we will receive $1.0 million in aggregate milestone payments from MedImmune, after taking into account payments we are obligated to make to The Feinstein Institute.

In December 2005, we entered into an amendment to our agreement with MedImmune. Pursuant to the amendment, MedImmune has agreed to increase its funding of development support to us by $1.0 million through the end of 2006.

Credit Agreement with Silicon Valley Bank. 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 January 6, 2006. We have 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. As of December 31, 2005, we had $2.6 million in debt outstanding under this credit agreement related to equipment advances.

The equipment advances made prior to the modification of our credit agreement on June 30, 2004 accrue interest at a weighted-average effective interest rate of approximately 8.7% 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. Upon the maturity of any advance made prior to June 30, 2004, we are required to make a final payment in addition to the repayment of principal and interest. The final payment will be in an amount equal to a specified percentage of the original advance amount up to 8.5% of the original principal. As of December 31, 2005, we had $371,000 in outstanding equipment advances made prior to June 30, 2004.

Advances made under the modified credit agreement accrue interest at a rate equal to the prime rate plus 2% per year. As of December 31, 2005, outstanding equipment advances under the modified credit agreement had a weighted-average effective interest rate of approximately 8.8% per year. Advances made under the modified credit agreement are required to be repaid in equal monthly installments of principal plus interest accrued through the repayment term, which range from 36 to 42 months. Repayment begins the first day of the month following the advance. During 2005, $1.3 million in advances were made under the modified credit agreement and we had no borrowing capacity under the modified credit agreement available at December 31, 2005.

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On January 6, 2006, we entered into a fourth loan modification agreement that amends our credit agreement with Silicon Valley Bank. As a result of this latest loan modification, we had total unused borrowing capacity under the credit agreement of approximately $576,000 as of January 6, 2006. We are currently considering financing alternatives to fund capital expenditures after this borrowing capacity is used.

Cash Flows

Operating Activities. Net cash used in operating activities was $45.1 million in 2005 compared to $25.1 million in 2004. Net cash used in operations for 2005 consisted of a net loss of $47.1 million, offset by non-cash depreciation and amortization expense and the amortization of premiums on short-term investments of $1.7 million, stock-based compensation expense of $2.1 million plus cash used to fund working capital of $2.0 million.

Investing Activities. Investing activities provided $38.5 million of cash in 2005 compared to $70.0 million of cash used in investing activities in 2004. In 2005, we made capital expenditures of $2.2 million primarily for laboratory equipment associated with our increased research and development activities and upgrades to our financial and accounting software and we sold $72.9 million of our short-term investments which was offset by purchases of $32.3 million of short-term investments. As interest rates have gradually increased and our cash needs have increased from the launch of ZYFLO, we have maintained more of our proceeds from recent financings as cash equivalents rather than short-term investments.

Financing Activities. Financing activities provided $51.9 million of cash in 2005 compared to $67.0 million in 2004. Net cash provided by financing activities for the year ended December 31, 2005 related primarily to our private placement of common stock and warrants in June 2005 to certain institutional and other accredited investors. We sold 9,945,261 shares of our common stock in the private placement at a price of $5.48 per share, together with warrants to purchase an additional 3,480,842 shares of our common stock, resulting in gross proceeds of $54.5 million. In connection with the private placement, we paid approximately $3.1 million in offering expenses and placement agent fees.

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, 2005. 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 to continue our research and development efforts, including preclinical testing and clinical trials, expand our sales and marketing infrastructure, achieve regulatory approvals, commercialize ZYFLO and, subject to regulatory approval, commercially launch the controlled-release formulation of zileuton and any future product candidates. We also expect to spend approximately $2.0 million in capital expenditures in 2006 for the purchase of software, computer equipment, manufacturing equipment and equipment for our laboratories which will be purchased, in part, with funds available under our credit agreement with Silicon Valley Bank. Our funding requirements will depend on numerous factors, including:

the costs of ongoing sales and marketing for ZYFLO;

the timing, receipt and amount of sales from ZYFLO;

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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, obtaining and maintaining 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;

our ability to establish and maintain additional collaborative arrangements; and

the ongoing time and costs involved in certain corporate governance requirements, including work related to compliance with the Sarbanes-Oxley Act of 2002.

Other than payments that we receive from our collaborations with MedImmune and Beckman Coulter, we expect that sales of ZYFLO will represent our only source of operating income until we commercially launch the controlled-release formulation of zileuton if it is approved. In addition to the foregoing factors, we believe that our ability to access external funds will depend upon the market acceptance of ZYFLO, 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 sell ZYFLO and obtain regulatory approval for and successfully commercialize the controlled-release formulation of zileuton. Based on our operating plans, we believe that our available cash and cash equivalents and anticipated cash received from product sales and anticipated payments received under collaboration agreements will be sufficient to fund anticipated levels of operations until the second quarter of 2007.

For the year ended December 31, 2005, our net cash used for operating activities was $45.0 million and we had capital expenditures of $2.2 million. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we may 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.

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Contractual Obligations

We have summarized in the table below our fixed contractual obligations as of December 31, 2005.

		Payments Due by Period			
Contractual Obligations	**Total**	**Less Than One Year**	**One to Three Years**	**Three to Five Years**	**After Five Years**
		(In thousands)			
Short- and long-term debt	$ 2,837	$ 1,310	$ 1,527	$	$
Research and license agreements	7,389	263	201	384	6,541
Consulting agreements	404	377	27		
Manufacturing and clinical trial agreements	13,097	11,966	1,131		
Lease obligations	6,367	2,186	4,181		
Total contractual cash obligations	$ 30,094	$ 16,102	$ 7,067	$ 384	$ 6,541

The amounts listed for short- and long-term debt represent the principal and interest 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.

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. Through December 31, 2005, we have paid aggregate milestones of $4.25 million to Abbott under our license agreements related to the immediate and controlled-release formulations of zileuton.

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. Through December 31, 2005 we have paid aggregate milestones of $2.0 million to SkyePharma under our agreement.

The amounts shown in the table 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 MedImmune. Our license agreements are described more fully in Note 12 to our consolidated financial statements.

The amounts listed for consulting agreements are for fixed payments due to our scientific and business consultants.

The amounts listed for manufacturing and clinical trial agreements represent amounts due to third parties for manufacturing, clinical trials and preclinical studies. As discussed in Note 12 to our consolidated financial statements included in this report, we entered into a manufacturing and supply agreement with Rhodia Pharma Solutions Ltd., or Rhodia, for commercial production of the API of ZYFLO, subject to specified limitations, through December 31, 2009. Under this agreement, we committed to purchase a minimum amount of API by December 31, 2006. The API

purchased from

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Rhodia currently has a retest period of 24 months. We evaluate the need to provide reserves for contractually committed future purchases of inventory that may be in excess of forecasted future demand. In making these assessments, we are required to make judgments as to the future demand for current or committed inventory levels and as to the expiration dates of its product. While our purchase commitment for API from Rhodia exceeds our current forecasted demand in 2006, we expect that any excess API purchased in 2006 under our agreement with Rhodia will be used in commercial production batches in 2007 and 2008 and sold before it requires retesting. Therefore no reserve for this purchase commitment has been recorded as of December 31, 2005.

Significant differences between our current estimates and judgments and future estimated demand for our product and the useful life of inventory may result in significant charges for excess inventory or unnecessary purchase commitments in the future. These differences could have a material adverse effect on our financial condition and results of operations during the period in which we recognize charges for excess inventory. For example, we recorded a charge of $280,000 in the fourth quarter of 2005 to reserve for excess inventory that had an expiration date such that the product was unlikely to be sold. The charge was included in cost of products sold in the accompanying statement of operations.

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 lease obligations represent the amount we owe under our office, computer, vehicle and laboratory space lease agreements under both operating and capital leases.

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 SFAS No. 123(R), Share-Based Payment. This Statement is a revision of SFAS No. 123, Accounting for Stock-Based Compensation, amends SFAS No. 95, Statement of Cash Flows, and supersedes Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees, and its related implementation guidance. SFAS No. 123(R) focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. The Statement requires entities to recognize in their income statement stock compensation expense for awards (with limited exceptions) based on their fair value. In addition, SFAS No. 123(R) 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. SFAS No. 123(R) is effective for us commencing January 1, 2006, at which time we will begin recognizing an expense for unvested share-based compensation that has been issued or will be issued after that date. SFAS No. 123(R) permits a prospective or two modified versions of retrospective application under which financial statements for prior periods are adjusted on a basis consistent with the pro forma disclosures required for those periods by the original SFAS No. 123.

Effective January 1, 2006, we adopted the provisions of SFAS No. 123(R) using the modified prospective approach using the Black-Scholes option-pricing model. The total compensation expense,

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including the cost of options that are expected to be granted during 2006, is expected to be up to $6 million. However, uncertainties, including the number of stock option grants, stock price volatility, estimated forfeitures and employee stock option exercise behavior, make it difficult to determine whether the stock-based compensation expense that we will incur in future periods will be similar to this estimate. If SFAS No. 123(R) had been adopted in a prior period, the impact on our net loss and net loss per share would approximate the impact of SFAS No. 123 as described in the disclosure of pro forma net loss and loss per share included in this quarterly report.

In May 2005, the FASB issued SFAS No. 154, Accounting Changes and Error Corrections. SFAS No. 154 is a replacement of APB No. 20 and FASB Statement No. 3. SFAS No. 154 provides guidance on the accounting for and reporting of accounting changes and error corrections. It establishes retrospective application as the required method for reporting a change in accounting principle. SFAS No. 154 provides guidance for determining whether retrospective application of a change in accounting principle is impracticable and for reporting a change when retrospective application is impracticable. The reporting of a correction of an error by restating previously issued financial statements is also addressed by SFAS No. 154. SFAS No. 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. We do not expect the adoption of SFAS No. 154 will have a material impact on our financial position or results of 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 of U.S. government treasury and agency notes, corporate debt obligations, municipal debt obligations, auction rate securities and money market funds, 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, 2005, we estimate that the fair value of our investment portfolio would decline by approximately $40,000. 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 and Stockholders of Critical Therapeutics, Inc.:
Lexington, MA

We have audited the accompanying consolidated balance sheets of Critical Therapeutics, Inc. and subsidiary (the Company) as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders equity (deficit) and comprehensive loss, and cash flows for each of the three years in the period ended December 31, 2005. 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes 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 subsidiaries as of December 31, 2005 and 2004, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2005, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of the Company s internal control over financial reporting as of December 31, 2005, based on the criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 1, 2006 expressed an unqualified opinion on management s assessment of the effectiveness of the Company s internal control over financial reporting and an unqualified opinion on the effectiveness of the Company s internal control over financial reporting.

/s/ DELOITTE & TOUCHE LLP
Boston, MA
March 1, 2006

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONSOLIDATED BALANCE SHEETS

	December 31, 2005	December 31, 2004
	(In thousands except share and per share data)	
ASSETS:		
Current assets:		
Cash and cash equivalents	$ 57,257	$ 11,980
Accounts receivable, net	1,024	
Amount due under collaboration agreements	205	16
Short-term investments	25,554	66,849
Inventory, net	1,869	
Prepaid expenses and other	2,179	1,851
Total current assets	88,088	80,696
Fixed assets, net	3,563	2,205
Other assets	168	213
Total assets	$ 91,819	$ 83,114
LIABILITIES AND STOCKHOLDERS EQUITY:		
Current liabilities:		
Current portion of long-term debt and capital lease obligations	$ 1,179	$ 837
Accounts payable	4,615	4,218
Accrued compensation	1,836	1,034
Accrued expenses	3,040	1,707
Revenue deferred under collaboration agreements	5,706	8,543
Deferred product revenue	1,707	
Total current liabilities	18,083	16,339
Long-term debt and capital lease obligations, less current portion	1,489	1,367
Commitments and contingencies (Note 13)		
Stockholders equity:		
Preferred stock, par value $0.001; authorized 5,000,000 shares; no shares issued and outstanding		
Common stock, par value $0.001; authorized 90,000,000 shares; issued and outstanding 34,126,977 and 24,085,481 shares at December 31, 2005 and 2004, respectively	34	24
Additional paid-in capital	181,718	130,374
Deferred stock-based compensation	(3,794)	(6,101)
Accumulated deficit	(105,617)	(58,527)

Accumulated other comprehensive loss	(94)	(362)
Total stockholders equity	72,247	65,408
Total liabilities and stockholders equity	$ 91,819	$ 83,114

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

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2005	2004	2003
	(In thousands except share and per share data)		
Revenues:			
Net product sales	$ 387	$	$
Revenue under collaboration agreements	5,837	4,436	1,021
Total revenues	6,224	4,436	1,021
Costs and expenses:			
Cost of products sold	514		
Research and development	29,959	25,578	17,458
Sales and marketing	13,671	1,199	
General and administrative	11,406	9,679	3,771
Total costs and expenses	55,550	36,456	21,229
Operating loss	(49,326)	(32,020)	(20,208)
Other income (expense):			
Interest income	2,427	1,098	191
Interest expense	(191)	(172)	(93)
Total other income	2,236	926	98
Net loss	(47,090)	(31,094)	(20,110)
Accretion of dividends and offering costs on preferred stock		(2,209)	(2,264)
Net loss available to common stockholders	$ (47,090)	$ (33,303)	$ (22,374)
Net loss per share available to common stockholders	$ (1.61)	$ (2.28)	$ (33.99)
Basic and diluted weighted-average common shares outstanding	29,276,243	14,631,371	658,204

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

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF
STOCKHOLDERS EQUITY (DEFICIT) AND COMPREHENSIVE LOSS
YEARS ENDED DECEMBER 31, 2005, 2004 AND 2003

	Redeemable Convertible Preferred Stock	Common Stock	Additional Paid-In Capital	Deferred Stock-Based Compensation	Due from Stockholders	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders Equity	Comprehensive Loss
				(In thousands except share data)					
BALANCE January 1, 2003	$ 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 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 non-employees			6,745	(6,745)					
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)	$ (20,110)

Comprehensive loss								$ (20,110)
BALANCE December 31, 2003	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 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 stock-based compensation				3,562			3,562	
Reversal of deferred stock based compensation			(21)	21				
Forgiveness of officer notes	145				40		40	
Issuance of 6,110,000 shares of common stock in initial public offering, including underwriters over-allotment, net		6	37,811				37,817	

of $2.0 million in offering costs							
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 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)
BALANCE December 31, 2004		24	130,374	(6,101)	(58,527)	(362)	65,408	
Issuance of 96,235 shares of common stock, upon exercise of options under stock plan			158			158	
Deferred stock-based compensation to non-employees			(458)	458			
Amortization of deferred stock-based compensation				2,141		2,141	
Reversal of deferred stock based compensation			(221)	221			
Issuance of 9,945,261 shares of common stock and warrants to purchase 3,480,842 shares of common stock in		10	51,352			51,362	

private placement, net of $3.1 million in placement fees								
Grant of stock options to non-employees		513	(513)					
Net loss				(47,090)		(47,090)	$ (47,090)	
Unrealized loss on investments					268	268	268	
Comprehensive loss							$ (46,822)	
BALANCE December 31, 2005	$	$ 34	$ 181,718	$ (3,794)	$ $ (105,617)	$ (94)	$ 72,247	

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

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2005	2004	2003
	(In thousands)		
Cash flows from operating activities:			
Net loss	$ (47,090)	$ (31,094)	$ (20,110)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization expense	800	1,092	482
Amortization of premiums on short-term investments and other	903	755	
Loss on disposal of fixed assets	149	278	
Loss on conversion of warrants		46	
Stock-based compensation expense	2,141	3,562	5,072
Forgiveness of notes receivable		185	
Changes in assets and liabilities:			
Accounts receivable	(1,024)		
Amount due under collaboration agreement	(189)	2,484	(2,500)
Inventory	(1,869)		
Prepaid expenses and other	(328)	(1,421)	(622)
Other assets	45	277	
Accounts payable	397	3,895	(94)
Accrued expenses	2,135	(2,211)	5,267
Revenue deferred under collaboration agreements	(2,837)	(2,935)	11,479
Deferred product revenue	1,707		
Net cash used in operating activities	(45,060)	(25,087)	(1,026)
Cash flows from investing activities:			
Purchases of fixed assets	(2,182)	(2,019)	(1,492)
Proceeds from sales and maturities of short-term investments	72,915	52,900	
Purchases of short-term investments	(32,255)	(120,866)	
Net cash provided by (used in) investing activities	38,478	(69,985)	(1,492)
Cash flows from financing activities:			
Net proceeds from private placement of common stock	51,362		
Proceeds from exercise of stock options and other	158	175	5
Net proceeds from the initial public offering of common stock		37,817	
Net proceeds from issuance of convertible preferred stock		28,050	27,906
Proceeds from long-term debt and other	1,300	1,623	1,533
Repayments of long-term debt and capital lease obligation	(961)	(691)	(387)

Net cash provided by financing activities	51,859	66,974	29,057
Net increase (decrease) in cash and cash equivalents	45,277	(28,098)	26,539
Cash and cash equivalents at beginning of period	11,980	40,078	13,539
Cash and cash equivalents at end of period	$ 57,257	$ 11,980	$ 40,078
Supplemental disclosures of cash flow information:			
Cash paid during the period for:			
Interest	$ 172	$ 126	$ 94
Non-cash investing and financing activities:			
Fixed assets acquired under capital lease obligation	$ 125	$	$
Adjustment to deferred stock-based compensation for services to be performed	$ (285)	$ 1,127	$ 13,417
Unrealized gain (loss) on investments	$ 268	$ 362	$
Conversion of redeemable convertible preferred stock into common stock	$	$ 81,799	$
Dividends forfeited on preferred stock conversion into common stock	$	$ 5,713	$
Accretion of dividends and offering costs on preferred stock	$	$ 2,209	$ 2,264
Settlement of accrued licensing fee with common stock	$	$ 485	$

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.

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. As of December 31, 2005, the Company s investment portfolio, including its cash, cash equivalents and short-term investments had a weighted average time to maturity of approximately 26 days. The unrealized gain (loss) during the period is recorded as an adjustment to stockholders equity unless it is determined to be other-than-temporary. During the years ended December 31, 2005 and 2004, the Company recorded an unrealized loss on cash equivalents and short-term investments of $93,000 and $362,000, respectively. The original cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. The amortization or accretion is included in interest income (expense) in the corresponding period. The Company has determined the unrealized gain (loss) on its investments is temporary; therefore no impairment losses were recorded for the years ended December 31, 2005, 2004 and 2003.

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

The unrealized losses as of December 31, 2005 and 2004 were primarily caused by interest rate increases. The following table shows, for the years ended December 31, 2005 and 2004, the gross unrealized gains and losses and the fair value of the Company s investments with unrealized gains and losses that are not deemed to be other-than-temporarily impaired, aggregated by investment category:

	As of December 31, 2005			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(In thousands)			
Cash and cash equivalents:				
Cash	$ 490	$	$	$ 490
Commercial Paper	51,181	3	(43)	51,141
Money market mutual funds	3,231			3,231
U.S. government and agency securities	2,395			2,395
Cash and cash equivalents	57,297	3	(43)	57,257
Short-term investments:				
U.S. government and agency securities	2,689		(1)	2,688
Corporate bonds	16,668		(52)	16,616
Auction rate securities	6,250			6,250
Short-term investments	25,607		(53)	25,554
Cash and cash equivalents and short-term investments	$ 82,904	$ 3	$ (96)	$ 82,811

	As of December 31, 2004			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(In thousands)			
Cash and cash equivalents:				
Cash	$ 4,319	$	$	$ 4,319
Commercial Paper	2,019			2,019
Money market mutual funds	5,642			5,642
Cash and cash equivalents	11,980			11,980
Short-term investments:				
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
Short-term investments	67,211		(362)	66,849
Cash and cash equivalents and short-term investments	$ 79,191	$	$ (362)	$ 78,829

Inventory

Inventory is stated at the lower of cost or market with cost determined under the first-in, first-out (FIFO) method. The Company analyzes its inventory levels quarterly and writes-down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory

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

in excess of expected requirements. Expired inventory is disposed of and the related costs are expensed in the period.

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 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. In 2005, the Company recorded an impairment charge of approximately $69,000 primarily related to computer equipment.

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. In addition, research and development expenses include the cost of the Company s medical affairs and medical information functions, which educate physicians on the scientific aspects of the Company s commercial products and the approved indications, labeling and the costs of monitoring adverse events. After FDA approval of a product candidate, manufacturing expenses associated with a product will be recorded as cost of products sold rather than research and development expenses. The Company expenses research and development costs and patent related costs as incurred. Because of the Company s ability to utilize resources across several projects, many of our research and development costs are not tied to any particular project and are allocated among multiple projects. The Company records direct costs on a project-by-project basis. The Company records indirect costs in the aggregate in support of all research and development.

Revenue Recognition and Deferred Revenue

The Company recognizes revenue in accordance with the Securities and Exchange Commission s 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. The Company s revenue is currently derived from product sales of its only commercial product, ZYFLO, and its collaboration agreements. These agreements provide for various payments, including research and development funding, license fees, milestone payments and royalties.

The Company sells ZYFLO, a tablet formulation of zileuton, to wholesalers, distributors and pharmacies, which have the right to return purchased product. In accordance with Statement of Financial Accounting Standards (SFAS) No. 48, Revenue Recognition When Right of Return Exists , the

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

Company cannot recognize revenue on product shipments until it can reasonably estimate returns relating to these shipments. Under SFAS No. 48, the Company defers recognition of revenue on product shipments of ZYFLO to its customers until the product is dispensed through patient prescriptions. The Company estimates prescription units dispensed based on distribution channel data provided by external, independent sources. ZYFLO received by patients through prescription is not subject to return. Gross revenue for prescriptions dispensed was $462,000 for the year ended December 31, 2005, while product revenue net of discounts and rebates was $387,000. Product shipments not recognized as revenue was $1.7 million at December 31, 2005 and is included in deferred product revenue on the accompanying consolidated balance sheet. The cost of product shipped to customers that has not been recognized as revenue in accordance with the Company s policy is deferred until the product is dispensed through patient prescriptions. The Company will continue to recognize revenue upon prescription units dispensed until it can reasonably estimate product returns based on its product returns experience. At this time, the Company will record a one-time increase in net product sales related to the recognition of revenue previously deferred. In addition, the Company product sales are subject to various rebates, discounts and incentives that are customary in the pharmaceutical industry.

Under the Company s collaboration agreements with MedImmune and Beckman Coulter, the Company is 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 the Company s statement of operations when earned. The Company must make significant estimates in determining the performance period and periodically review these estimates, based on joint management committees and other information shared by the Company s collaborators. The Company recognizes 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 the Company s 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, the Company does not recognize revenues in excess of cumulative cash collections. It is difficult to estimate the impact of the adjustments on the results of the Company s operations because, in each case, the amount of cash received would be a limiting factor in determining the adjustment.

At December 31, 2005, the Company s account receivable balance was net of allowances of $21,000.

Fair Value of Financial Instruments

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

Concentrations of Credit Risk and Limited Suppliers

SFAS No. 105, Disclosure of Information about Financial Instruments with Off-Balance-Sheet Risk and Financial Instruments with Concentrations of Credit Risk, requires disclosure of any significant off-balance-sheet and credit risk concentrations. The Company has no off-balance-sheet or concentrations of credit risk such as foreign exchange contracts, options contracts or other foreign hedging arrangements.

The financial instruments that potentially subject the Company to concentrations of credit risk are cash, cash equivalents, short-term investments and accounts receivable. 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.

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

The Company relies on certain materials used in its development and manufacturing processes, some of which are procured from a single source. The Company purchases the active pharmaceutical ingredient pursuant to a long-term supply agreement with one supplier. 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. In addition, a disruption in the commercial supply of ZYFLO or a significant increase in the cost of the active pharmaceutical ingredient from these sources could have a material adverse effect on the Company s business, financial position and results of operations.

As is customary in the pharmaceutical industry, the Company sells primarily to large national wholesalers, which in turn, may resell the product to smaller or regional wholesalers, retail pharmacies or chain drug stores. The following tables summarize the number of customers that individually comprise greater than 10% of total billings, some of which have been recognized as revenue in 2005, and their aggregate percentage of the Company s total billings for the year ended December 31, 2005 and comprise more than 10% of total account receivable and their aggregate percentage of the Company s total account receivable at December 31, 2005:

	Year Ended December 31, 2005 Billings
Company A	30%
Company B	29%
Company C	26%
Total	85%

	December 31, 2005 Accounts Receivable
Company B	61%
Company D	11%
Total	72%

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 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

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

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 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):

	Year Ended December 31,		
	2005	2004	2003
Net loss available to common stockholders as reported	$ (47,090)	$ (33,303)	$ (22,374)
Add: Employee stock-based compensation expense included in reported net loss	1,757	1,784	165
Deduct: Employee stock-based compensation expense determined under fair value method	(3,398)	(1,162)	(201)
Net loss available to common stockholders pro forma	$ (48,731)	$ (32,681)	$ (22,410)
Net loss per share (basic and diluted):			
As reported	$ (1.61)	$ (2.28)	$ (33.99)
Pro forma	$ (1.67)	$ (2.23)	$ (34.05)

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

	December 31,		
	2005	2004	2003
Weighted average risk free interest rate	4.1%	3.3%	2.4%
Expected dividend yield	0%	0%	0%
Expected lives	4 years	4 years	4 years
Expected volatility	59%	100%	100%
Weighted-average fair value of options granted equal to fair value	$ 3.26	$ 4.38	$ 0.26
	N/A	$ 3.73	$ 6.26

Weighted-average fair value of options granted below fair value

In December 2004, the Financial Accounting Standards Board, or FASB, issued SFAS No. 123(R), Share-Based Payment. This Statement is a revision of SFAS No. 123, Accounting for Stock-Based Compensation, amends SFAS No. 95, Statement of Cash Flows, and supersedes Accounting Principles

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Board Opinion No. 25, Accounting for Stock Issued to Employees, and its related implementation guidance. SFAS No. 123(R) focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. SFAS No. 123(R) requires entities to recognize in their income statement stock compensation expense for awards (with limited exceptions) based on their fair value. In addition, SFAS No. 123(R) 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. SFAS No. 123(R) is effective for the Company commencing January 1, 2006, at which time the Company will begin recognizing an expense for unvested share-based compensation that has been issued or will be issued after that date. SFAS No. 123(R) permits a prospective or two modified versions of retrospective application under which financial statements for prior periods are adjusted on a basis consistent with the pro forma disclosures required for those periods by the original SFAS No. 123.

Effective January 1, 2006, the Company adopted the provisions of SFAS No. 123(R) using the modified prospective approach with the Black-Scholes option-pricing model. The total compensation expense, including the cost of options that are expected to be granted during 2006, is expected to be up to $6 million. However, uncertainties, including the number of stock option grants, stock price volatility, estimated forfeitures and employee stock option exercise behavior, make it difficult to determine whether the stock-based compensation expense that we will incur for 2006 will be similar to this estimate.

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 9,809,751, 4,776,922 and 42,928,818 as of December 31, 2005, 2004 and 2003, respectively. These anti-dilutive securities consist of outstanding stock options, warrants and unvested restricted common stock as of December 31, 2005, 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.

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:

	Year Ended December 31,		
	2005	**2004**	**2003**
Weighted-average common shares outstanding	29,405,045	15,077,169	1,553,309
Less: weighted-average restricted common shares Outstanding	128,802	445,798	895,105
Basic and diluted weighted-average common shares Outstanding	29,276,243	14,631,371	658,204

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 which as of June 2, 2004 totaled $5.7 million.

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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 years ended December 31, 2005 and 2004, respectively, and comprehensive loss is the unrealized gain (loss) on short-term investments for the period. There were no items affecting comprehensive loss for the year ended December 31, 2003. Total comprehensive loss was $46.8 million and $31.5 million for the years ended December 31, 2005 and 2004, respectively. The unrealized loss on investments is the only component of accumulated other comprehensive loss in the accompanying consolidated balance sheet as of December 31, 2005 and 2004.

Disclosure about Segments of an Enterprise

The Company follows the provisions of SFAS No. 131, Disclosures about Segments of an Enterprise and Related Information. SFAS No. 131 establishes standards for reporting information regarding operating segments in annual financial statements and requires selected information for those segments to be presented in interim financial reports issued to stockholders. SFAS No. 131 also establishes standards for related disclosures about products and services and geographic areas. 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 as to how to allocate resources and assess performance. The Company s chief decision makers, as defined under SFAS No. 131, are the chief executive officer and chief financial officer. The Company believes it operates in one segment which includes its product sales. The financial information disclosed in this report represents all of the material financial information related to the Company s one operating segment. All of the Company s revenues are generated in the United States and all assets are located in the United States.

(3) Collaboration Agreements

MedImmune

In July 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. The original term of the research plan was expected to be approximately 41 months which began on July 30, 2003. In 2005, the Company changed its estimate of the term covered by the research plan to 47 months. During the term of the research plan, the Company has received 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. In 2005, the Company revised its estimate of remaining total costs in addition to increasing the period over which those costs would be incurred under the collaboration agreement with MedImmune. The change in estimate resulted in a decrease in revenue recognized of approximately $237,000 in 2005.

In connection with this agreement, the Company received $12.5 million in up front license fees and research funding which was paid in two components in 2003 and 2004. In 2005 the Company reached a specified milestone and received $1.25 million from MedImmune. In the event that specified research and development and commercialization milestones are achieved, MedImmune will be obligated to make further payments to the Company. In addition, the Company received approximately $1.5 million in research funding from MedImmune in each of the years ended December 31, 2005 and 2004.

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In December 2005, the Company entered into an amendment to the exclusive license and collaboration agreement with MedImmune. Pursuant to the amendment, MedImmune has agreed to increase research funding to the Company by $1.0 million through the end of 2006. MedImmune had previously agreed to make a total of $3.0 million of development support payments to the Company through the end of 2006, all of which had been billed to MedImmune through December 31, 2005.

Revenue under this arrangement is being recognized under a proportional performance model. During 2005, 2004 and 2003, the Company recognized revenue of approximately $5.7 million, $4.4 million and $1.0 million, respectively, under this agreement. As of December 31, 2005 and 2004, the Company had deferred revenue of approximately $5.6 million and $8.5 million, respectively, related to this agreement. The deferred revenue consists of a portion of the up-front payments, milestone and research funding received in advance of revenue recognized under the agreement.

Beckman Coulter

In January 2005, the Company entered into a license agreement with Beckman Coulter, Inc., or Beckman Coulter, under which the Company granted to Beckman Coulter and its affiliates an exclusive worldwide license to patent rights and know-how controlled by the Company relating to the use of High Mobility Group Box Protein 1, or 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 or on behalf of the Company.

In consideration for the license, Beckman Coulter paid the Company a product evaluation license fee of $250,000 in February 2005. Beckman Coulter also agreed to pay the Company additional aggregate license fees of up to $850,000 upon the occurrence of the following: 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 the Company 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 the Company s written consent, which the Company has agreed not to unreasonably withhold. Beckman Coulter agreed to pay the Company a percentage of any license fees, milestone payments or royalties actually received by Beckman Coulter from its sublicensees.

(4) Inventory

As of December 31, 2005 the Company held $1.9 million in inventory to be used for commercial sales of ZYFLO, net of reserves. In 2005, the Company reserved for inventory of approximately $280,000 related to finished goods with an expiration date that would make it unlikely to be sold. Inventory consisted of the following at December 31 (in thousands):

	2005
Raw material	$ 1,425
Work in process	332
Finished goods	392
Total	2,149
Less: reserve	(280)
Inventory, net	$ 1,869

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

(5) Fixed Assets

Fixed assets consisted of the following at December 31 (in thousands):

	2005	2004
Laboratory equipment	$ 2,087	$ 1,591
Computer and office equipment	747	473
Equipment in process	599	
Furniture and fixtures	550	471
Software	443	107
Leasehold improvements	280	203
Assets held under capital lease	125	
Total	4,831	2,845
Less accumulated depreciation and amortization	(1,268)	(640)
Fixed assets net	$ 3,563	$ 2,205

In 2005, the Company entered into a capital lease arrangement primarily for computers for its sales force totaling $125,000. Assets acquired under capital lease agreements are recorded at the present value of the future minimum rental payments using interest rates appropriate at the inception of the lease. Property and equipment subject to capital lease agreements are amortized over the shorter of the life of the lease or the estimated useful life of the asset unless the lease transfers ownership or contains a bargain purchase option. Depreciation and amortization expense on fixed assets for the years ended December 31, 2005, 2004 and 2003 was approximately $800,000, $1.1 million, and $482,000, respectively.

(6) Long Term Debt

In June 2002, the Company entered into a loan and security agreement (the Agreement) with a lender that allows the Company to borrow up to $2.25 million 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 warrants to purchase 90,000 shares of Series A Redeemable Convertible Preferred Stock. 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. In 2005, the Company had 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 terms 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 years ended December 31, 2005 and 2004, the Company borrowed $1.3 million and $1.6 million, respectively, under the modified credit agreement.

As of December 31, 2005, there was $2,561,000 million in debt outstanding under the Agreement. The outstanding borrowings bear interest at a weighted average interest rate of approximately 8.8% with rates ranging from 8.6% to 9.0%.

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
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The repayments of principal and interest are scheduled to be made as follows (in thousands):

	Principal	Interest	Total
2006	$ 1,131	$ 179	$ 1,310
2007	1,010	83	1,093
2008	420	14	434
	$ 2,561	$ 276	$ 2,837

On January 6, 2006, the Company entered into another loan modification agreement with the same lender. The modification allows the Company to 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 the Agreement. This loan modification allows the Company to borrow up to an additional $500,000 under the Agreement through March 31, 2006. As a result of the modification, the Company has total unused borrowing capacity under the Agreement of approximately $576,000 on January 6, 2006. Future advances under the Agreement will accrue interest at a rate equal to the prime rate plus 2% per year and are required to be repaid in 36 equal monthly installments of principal plus accrued interest. Repayment begins the first day of the month following the advance.

(7) Stockholders Equity (Deficit)

Private Placement

In June 2005, the Company sold an aggregate of 9,945,261 shares of its common stock at a price of $5.48 per share, together with warrants to purchase an additional 3,480,842 shares of common stock, for a total purchase price of approximately $54.5 million. The sales were made to institutional and other accredited investors. The net proceeds from the private placement were approximately $51.4 million, after deducting placement agents fees and other offering costs of approximately $3.1 million.

In connection with this private placement, the Company issued and sold an aggregate of 5,200,732 shares of common stock and warrants to purchase 1,820,257 shares of common stock to existing stockholders and affiliated entities associated with four members of the Company s Board of Directors. These holders paid an aggregate consideration of $28.5 million and participated on the same terms as the other purchasers in the private placement.

The warrants issued in connection with the private placement have an exercise price per share of $6.58, with a five-year life and are fully vested and exercisable from June 20, 2005. The warrants may also be exercised on a cashless basis at the option of the warrant holder. The warrants have been included in permanent equity at their fair value of $9.2 million. The fair value of the warrants was determined using the Black-Scholes model with the following assumptions: dividend yield of 0%; estimated volatility of 58%; risk-free interest rate of 3.65% and a contractual life of five years. As of December 31, 2005, none of these warrants had been exercised.

Initial Public Offering of Common Stock

In June 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. 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 affected 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

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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, 2005, 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.

Restricted Common Stock Issuances to Non-Employees

The Company has made several grants of restricted common stock to non-employees since its inception. Many of these restrictions have lapsed, and therefore, no longer require periodic remeasurement in our financial statements.

During 2002, the Company issued 43,998 shares of common stock to its founders, who are non-employees, subject to restriction for total 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. As of December 31, 2005, 9,165 shares remain unvested from these grants.

During 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 the Feinstein Institute (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. As of December 31, 2005, 13,630 shares remain unvested from these grants.

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 did not issue restricted stock in either 2005 or 2004. The Company recorded deferred compensation of $4.9 million in 2003. The Company reduced by approximately $137,000 its previously recorded deferred stock-based compensation for year ended December 31, 2005 and recorded stock-based compensation expense of $862,000 and $4.3 million for the years ended December 31, 2004 and 2003, respectively, related to these shares. These amounts are included in operating expenses in the accompanying consolidated statement of operations.

At December 31, 2005, the Company s right to repurchase restricted stock from non-employees had not lapsed as to 22,795 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. 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, 2005, the Company s right to repurchase restricted stock from employees had not lapsed as to 31,638 shares.

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
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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.

(8) 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 up to 3,680,000 shares of common stock to be granted through incentive stock options, nonqualified stock options, and restricted common stock to key employees, directors, consultants, and vendors of the Company and its affiliates.

On March 15, 2005, the Company s Board of Directors adopted and on June 17, 2005 the Company s stockholders approved an amendment the 2004 Stock Plan to increase the total number of shares available by 860,000.

As of December 31, 2005, the 2004 Stock Plan authorizes the issuance of up to 4,540,000 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.

Effective January 1, 2006, the Company s Board of Directors amended the 2004 Stock Plan to increase the total number of shares authorized for issuance by an additional 1,333,333, bringing the total authorized under the 2004 Stock Plan to 5,873,333 shares.

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

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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, subject to future adjustment based upon further cancellations in the 2003 Stock Plan or the 2000 Equity Plan. Accordingly, there are no shares of common stock available for award under the 2003 Stock Plan at December 31, 2005.

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.

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, 2005.

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.

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

		Number of Shares	Weighted-Average Exercise Price
Outstanding	January 1, 2003	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
Granted		2,025,900	6.70
Exercised		(96,235)	7.54
Cancelled		(229,829)	5.54
Outstanding	December 31, 2005	6,200,106	$ 5.03
Exercisable	December 31, 2003	496,744	$ 0.79
Exercisable	December 31, 2004	717,176	$ 1.10
Exercisable	December 31, 2005	1,809,920	$ 3.42

The options outstanding and exercisable at December 31, 2005 under the plans are as follows:

	Outstanding			Exercisable	
Exercise Price	Number of Options Outstanding	Weighted-Average Contractual Life Outstanding (In Years)	Weighted-Average Exercise Price	Options Exercisable	Weighted-Average Exercise Price
$0.01	2,724	5.0	$ 0.01	2,724	$ 0.10
$0.38	305,950	6.8	$ 0.38	246,217	$ 0.38
$1.05	1,199,430	8.0	$ 1.05	695,288	$ 1.05
$1.88-$5.98	864,039	8.8	$ 5.39	231,293	$ 5.31

$5.99	1,431,688	8.7	$ 5.99	341,111	$ 5.99
$6.00-$6.45	494,500	9.5	$ 6.29	21,266	$ 6.21
$6.50	333,825	8.6	$ 6.50	95,636	$ 6.50
$6.51-$6.77	281,000	9.7	$ 6.65		
$6.80-$6.85	440,000	10.0	$ 6.83	5,000	$ 6.80
$6.89-$7.52	359,000	9.2	$ 7.06	45,500	$ 7.01
$7.75	308,000	9.0	$ 7.75	85,750	$ 7.75
$7.78-$8.10	76,000	8.9	$ 7.91	40,135	$ 7.90
$8.55-$9.05	103,950	9.8	$ 8.67		
	6,200,106	8.7	$ 5.03	1,809,920	$ 3.42

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The weighted-average fair value of stock option grants using the Black-Scholes option pricing model were $3.26, $4.30 and $6.19 per share in 2005, 2004 and 2003, respectively.

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. During 2005, all options issued to employees were granted at exercise prices equal to market value. The Company has recorded the difference between the exercise price and the fair value of $523,000 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, $1.8 million and $165,000 related to these options for the years ended December 31, 2005, 2004 and 2003, respectively. Compensation expense for 2005 related to these options is included in the accompanying consolidated statement of operations as research and development, sales and marketing and general and administrative expense in the amounts of $489,000, $119,000 and $1.2 million, 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 expense 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 expense in the amounts of $29,000 and $136,000, respectively.

During 2005, 2004 and 2003, the Company granted 161,000, 51,333 and 268,409 options, respectively, to non-employees 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 $513,000 for 2005, $278,000 for 2004 and $1.8 million for 2003. The Company recorded compensation expense of approximately $520,000, $916,000 and $572,000 related to these options for the years ended December 31, 2005, 2004 and 2003, respectively. Compensation expense in 2005 related to these options is included in the accompanying consolidated statement of operations as research and development and general and administrative expense in the amounts of $512,000 and $8,000, 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, 2005, there were 946,490 unvested stock options and restricted stock subject to the modification. If a change-of-control were to occur and all of these securities were to vest, the intrinsic value of these securities totaling $3.8 million would be recorded as stock-based compensation expense.

In November 2005, the Company s Board of Directors approved that any unvested shares underlying outstanding options held by employees under the 2000 Equity Plan and 2003 Stock Plan would vest upon the same terms as such employee s unvested options under the 2004 Stock Plan upon a change of control event. As a result, if the Company terminates the employee s employment other than for cause or if the

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

employee terminates his or her employment for good reason on or prior to one year after the occurrence of a change of control, then the vesting of all options issued under the 2000 Equity Plan and the 2003 Stock Plan then held by such employee shall automatically be accelerated by two years so that such options shall immediately become vested and exercisable with respect to the number of shares of common stock covered by such options that would otherwise have been vested as of the second anniversary of the employees termination date as if the employee continue to be employed by the Company for such period. As of December 31, 2005, there were unvested options to purchase 64,500 shares of common stock remaining to employees subject to the modification. If a change-of-control were to occur and all of these options were to vest, the intrinsic value of these options totaling approximately $182,000 would be recorded as stock-based compensation expense.

(9) Loans to Officers

In December 2003, the Board of Directors approved the forgiveness of all outstanding principal and any accrued interest in connection with loans to certain officers of the Company 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. The total principal and interest forgiven resulted in a charge to operations in 2004 of $251,000. In connection with the forgiven loans, 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 since the Company s initial public offering in June 2004.

(10) 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 eligibility 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 2005 and 2004, the Company matched 100% of employee contributions up to a maximum of $1,000 per employee resulting in expense of $122,000 and $50,000, respectively. No employer contributions were made in 2003. In November 2005, the Company s Board of Directors amended, effective January 1, 2006, the Company s plan to provide a matching contribution to each participant of fifty percent of the participant s elective deferrals for a plan year up to six percent of the participant s salary, as defined.

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

(11) Income Taxes

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

	2005	2004
Deferred tax assets:		
Net operating loss carryforward	$ 30,033	$ 13,581
Deferred revenue	2,483	2,990
Research and experimentation credits	1,245	619
Start-up expenses	98	113
Depreciation and amortization	135	151
Other	(90)	122
Total	33,904	17,576
Deferred tax liability depreciation and amortization		
Net deferred tax asset	33,904	17,576
Less valuation allowance	(33,904)	(17,576)
Total	$	$

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

As of December 31, 2005, the Company had federal and state tax net operating loss carryforwards of approximately $85.8 million, which expire beginning in 2021 and 2006, respectively. The Company also has research and experimentation credit carryforwards of approximately $1.2 million which begin to expire in 2021. The Company has recorded a full valuation allowance 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 the Company determines in the future that it 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.

(12) Research and License Agreements

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

Abbott

In December 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 agreement at any time upon 60 days notice to Abbott and payment of a termination fee. Milestone and license payments totaling $3.0 million have been paid to Abbott under this agreement through December 31, 2005.

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

In March 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. During 2005, the Company paid milestone payments of $750,000 to Abbott under this agreement.

SkyePharma

In December 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. During 2005, the Company paid $1.3 million to SkyePharma under this agreement. Milestone payments totaling $2.0 million have been paid to Skyepharma under this agreement through December 31, 2005.

Xanthus

In December 2000, the Company entered into a license agreement with Xanthus Pharmaceuticals, Inc. (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, 2005, 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, 2005, no royalties had been paid or accrued by the Company.

The Feinstein Institute

In July 2001, the Company entered into a license agreement with The Feinstein Institute for Medical Research (formerly known as The North Shore-Long Island Jewish Research Institute), or The Feinstein Institute, whereby the Company will utilize certain of The Feinstein Institute s technology in its research effort in connection with one of its research targets, HMGB1. The Company paid and expensed $100,000 to The Feinstein Institute for the license and may be required to pay an additional $412,500 if certain research milestones are achieved. As of December 31, 2005 none of these milestones had been achieved. In addition, the Company is obligated to pay royalties to The Feinstein Institute 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 The Feinstein Institute 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 The Feinstein Institute. In connection with the amendment, the Company agreed to issue 66,666 shares of common stock having a value of $485,000 to The Feinstein Institute (see Note 8). As a result of the collaboration agreement with MedImmune (see Note 3), the Company incurred an obligation to pay a sublicense fee to The Feinstein Institute in the amount of approximately $2.0 million. As of December 31, 2003, $300,000 of the sublicense fee was paid to The Feinstein Institute and $1.7 million was included in accrued liabilities and paid in 2004. The sublicense fee and the value of the common stock issued to The

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

Feinstein Institute are included in research and development expense in the accompanying consolidated statements of operations for the year ended December 31, 2003.

Also in July 2001, the Company entered into a sponsored research and license agreement with The Feinstein Institute 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 2005, 2004 and 2003, the Company contributed a total of $200,000, $200,000 and $150,000, respectively, in research funding. In connection with obtaining certain licenses from The Feinstein Institute, the Company issued 27,259 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, 2005, none of these milestones had been achieved. In addition, the Company is obligated to pay royalties to The Feinstein Institute based on product sales.

In January 2003, the Company entered into a second sponsored research and license agreement with The Feinstein Institute whereby the Company committed to $600,000 of research funding in the field of alpha-7 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 2005, 2004 and 2003, the Company contributed a total of $250,000, $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. As of December 31, 2005 none of these milestones had been achieved.

Patheon Pharmaceuticals Inc.

In June 2005, the Company entered into a commerical manufacturing agreement with Patheon Pharmaceuticals Inc., or Patheon, for the manufacture of commercial supplies of ZYFLO immediate release tablets. The Company had previously contracted with Patheon for the manufacture of ZYFLO for clinical trials and regulatory review. Under the agreement, the Company is responsible for supplying the active pharmaceutical ingredient for ZYFLO to Patheon and Patheon is responsible for manufacturing the ZYFLO immediate release tablets and conducting stability testing. The Company has agreed to purchase at least 50% of its commercial supplies of ZYFLO immediate release tablets for sale in the United States from Patheon each year for the term of the agreement.

The commercial manufacturing agreement has an initial term of three years beginning on the date commercial manufacturing of the ZYFLO immediate release tablets commences and will automatically continue for successive one-year periods thereafter, unless the Company provides Patheon 12-months prior written notice of termination or Patheon provides the Company 18-months prior written notice of termination. If the Company provides six months advance notice that it intends to discontinue commercializing ZYFLO, the Company will not be required to purchase any additional quantities of ZYFLO immediate release tablets, provided that the Company pays Patheon for a portion of specified fees and expenses associated with orders previously placed by the Company.

Rhodia Pharma Solutions Ltd.

In February 2005, the Company entered into an agreement with Rhodia Pharma Solutions Ltd or Rhodia, for the manufacture of commercial supplies of the zileuton active pharmaceutical ingredient, or API. The Company had previously contracted with Rhodia to establish and validate a manufacturing process for the zileuton API and to manufacture supplies of the zileuton API sufficient for the Company s

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

clinical trials. Under the new commercial supply agreement, Rhodia has agreed to complete its validation process at sites operated by Rhodia and to manufacture the Company s required commercial supplies of the zileuton API, subject to specified limitations, through December 31, 2009.

The Rhodia agreement will automatically extend for successive one-year periods after December 31, 2009, unless Rhodia provides the Company with 18-months prior written notice of cancellation. The Company has the right to terminate the agreement upon 12-months prior written notice for any reason, provided that the Company may not cancel prior to January 1, 2008 for the purpose of retaining any other company to act as its exclusive supplier of the API.

In addition, under this agreement, the Company committed to purchase a minimum amount of API by December 31, 2006. The API purchased from Rhodia currently has a retest schedule of every 24 months. The Company evaluates the need to provide reserves for contractually committed future purchases of inventory that may be in excess of forecasted future demand. In making these assessments, the Company is required to make judgments as to the future demand for current or committed inventory levels and as to the expiration dates of its product.

Unless otherwise noted all milestone and other payments are included in research and development.

(13) 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 computer equipment under operating leases. Rent expense under these operating leases for the years ended December 31, 2005, 2004 and 2003 was $1.6 million, $1.9 million and $559,000, 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. As such, the Company has recorded a liability for rent expense in excess of payments made-to-date. As of December 31, 2005, this liability totaled $209,000. Operating leases expire from July 2007 to March 2009. In addition, in 2005, the Company entered into a capital lease arrangement primarily for computers for its sales force totaling $125,000.

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

The minimum aggregate future obligations under non-cancelable lease obligations as of December 31, 2005 are as follows (in thousands):

Year Ending	Operating Leases	Capital Leases
2006	$ 2,127	$ 59
2007	2,111	59
2008	1,790	5
2009	216	
Total minimum lease payments	$ 6,244	$ 123
Less Amount representing interest		(16)
Present value of future minimum lease payments		107
Less current portion		(48)
Long-term portion		$ 59

Founders Consulting Agreements

In January 2001, as amended in January 2003, each of the Company s three founders, one of whom is a member of the Company s Board of Directors, 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, 2005, 2004 and 2003, amounts paid under these agreements totaled $313,000, $305,000 and $299,000, respectively. Future payments to be made under the agreements are scheduled to be as follows (in thousands):

Year Ending	Payments
2006	$ 321
2007	26
Total	$ 347

The Company has entered into various agreements with third parties and certain related parties in connection with the research and development activities of its existing product candidates as well as discovery efforts on potential new product candidates. These agreements include costs for research and development and license agreements that represent the Company s fixed obligations payable to sponsor research and minimum royalty payments for licensed patents. These agreements include costs related to manufacturing, clinical trials and preclinical studies performed by third parties. The estimated amount that may be incurred in the future under these agreements totals approximately $20.9 million as of December 31, 2005. The amount and timing of these commitments may change, as they are largely dependent on the rate of enrollment in and timing of the development of the Company s product candidates. Some of these agreements have been described in more detail in Note 12.

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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 condensed quarterly financial information for 2005 and 2004. 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).

	Quarter Ended December 31,	Quarter Ended September 30,	Quarter Ended June 30,	Quarter Ended March 31,
	(Unaudited) (In thousands except share and per share data)			
2005				
Revenues:				
Net product sales	$ 387	$	$	$
Revenue under collaboration agreements	1,712	1,335	1,431	$ 1,359
Total revenues	2,099	1,335	1,431	1,359
Total costs and expenses	(17,544)	(16,025)	(11,148)	(10,833)
Operating loss	(15,445)	(14,690)	(9,717)	(9,474)
Other income, net	758	733	390	355
Net loss	$ (14,687)	$ (13,957)	$ (9,327)	$ (9,119)
Net loss per share	$ (0.43)	$ (0.41)	$ (0.37)	$ (0.38)
2004				
Revenues:				
Net product sales	$	$	$	$
Revenue under collaboration agreements	964	1,886	781	$ 805
Total revenues	964	1,886	781	805
Total costs and expenses	(12,463)	(8,768)	(7,951)	(7,274)
Operating loss	(11,499)	(6,882)	(7,170)	(6,469)
Other income, net	320	298	225	83
Net loss	(11,179)	(6,584)	(6,945)	(6,386)
Accretion of dividends and offering costs on preferred stock			(1,049)	(1,160)
	$ (11,179)	$ (6,584)	$ (7,994)	$ (7,546)

Net loss available to common stockholders				
Net loss per share available to common stockholders	$ (0.47)	$ (0.28)	$ (0.81)	$ (6.85)

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.

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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***

Conclusion Regarding the Effectiveness of Disclosure 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, 2005. 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, 2005, 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.

Management s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2005. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework.

Based on this assessment, our management believes that, as of December 31, 2005, our internal control over financial reporting is effective based on those criteria.

Our independent auditors have issued an audit report on our management s assessment of our internal control over financial reporting. This report appears below.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Critical Therapeutics, Inc.:
Lexington, MA

We have audited management s assessment, included in the accompanying Management Report on Internal Control over Financial Reporting, that Critical Therapeutics, Inc. and subsidiary (the Company) maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. The Company s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management s assessment and an opinion on the effectiveness of the Company s internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management s assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

A company s internal control over financial reporting is a process designed by, or under the supervision of, the company s principal executive and principal financial officers, or persons performing similar functions, and effected by the company s board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

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Because of the inherent limitations of internal control over financial reporting, including the possibility of collusion or improper management override of controls, material misstatements due to error or fraud may not be prevented or detected on a timely basis. Also, projections of any evaluation of the effectiveness of the internal control over financial reporting to future periods are subject to the risk that the controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management s assessment that the Company maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on the criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements as of and for the year ended December 31, 2005 of the Company and our report dated March 1, 2006, expressed an unqualified opinion on those financial statements.

/s/ DELOITTE & TOUCHE LLP

Boston, MA

March 1, 2006

Changes in Internal Control Over Financial Reporting

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, 2005 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. ***OTHER INFORMATION***

On March 7, 2006, we entered into an approval agreement with each of H. Shaw Warren, M.D., a member of our Board of Directors and one of our co-founders, and Kevin J. Tracey, M.D., one of our co-founders, in connection with their existing consulting agreements. The approval agreements permit Drs. Warren and Tracey to render advice and services to a new entity that they are forming that will seek to develop products in the field, as defined in the consulting agreements. The field is defined in the consulting agreements as the discovery and development of therapeutic products for application in critical care and inflammation, and diagnostic products intended to be sold in conjunction with such therapeutic products. The approval agreements permit Drs. Warren and Tracy to render advice and services in the field to the new entity solely with respect to our technology related to physical and electrical stimulation of the vagus nerve. Our approval is conditioned upon:

Drs. Warren and Tracey continuing to maintain an ownership interest in the new entity;

the completion within one year of a financing transaction by the new entity; and

the negotiation and execution within one year by us and the new entity of a license agreement for our technology related to physical and electrical stimulation of the vagus nerve on terms agreeable to us and the new entity.

Our approval would terminate if one of these conditions is no longer satisfied or is not capable of being satisfied.

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We are not currently utilizing the technology that may be licensed to the new entity. We will only enter into a license agreement if it is approved by our Audit Committee and our Board of Directors. Dr. Warren will not participate in any of the deliberations or voting regarding this matter.

Copies of the consulting agreements and the approval agreements are filed as Exhibits 10.16, 10.18, 10.19 and 10.20 to this Annual Report on Form 10-K.

We make the foregoing disclosure in this report in lieu of making a filing pursuant to Item 1.01 of Form 8-K.

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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 2006 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 2006 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 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

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 2006 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 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 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

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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 2006 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 2006 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 Registered Public Accounting Firm s Fees in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

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 Consolidated Financial Statements on page 70 of this report.

(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.

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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 7, 2006

We, the undersigned officers and directors of Critical Therapeutics, Inc., hereby severally constitute and appoint Paul D. Rubin, M.D. and Frank E. Thomas, and each of them singly, our true and lawful attorneys, with full power to them and each of them singly, to sign for us in our names in the capacities indicated below, all amendments to this report, and generally to do all things in our names and on our behalf in such capacities to enable Critical Therapeutics, Inc. to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all requirements of the Securities and Exchange Commission.

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.

Signature	Title	Date
/s/ PAUL D. RUBIN Paul D. Rubin, M.D.	President and Chief Executive Officer (Principal Executive Officer)	March 7, 2006
/s/ FRANK E. THOMAS Frank E. Thomas	Chief Financial Officer, Senior Vice President of Finance and Treasurer (Principal Financial and Accounting Officer)	March 7, 2006
/s/ RICHARD W. DUGAN Richard W. Dugan	Director	March 7, 2006
/s/ NICHOLAS GALAKATOS Nicholas Galakatos, Ph.D.	Director	March 7, 2006
/s/ JEAN GEORGE Jean George	Director	March 7, 2006
/s/ CHRISTOPHER MIRABELLI Christopher Mirabelli, Ph.D.	Director	March 7, 2006
/s/ JAMES B. TANANBAUM	Director	March 7, 2006

James B. Tananbaum, M.D.

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Signature	Title	Date
/s/ CHRISTOPHER WALSH Christopher Walsh, Ph.D.	Director	March 7, 2006
/s/ H. SHAW WARREN H. Shaw Warren, M.D.	Director	March 7, 2006
/s/ ROBERT H. ZEIGER Robert H. Zeiger	Director	March 7, 2006

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Exhibit Index

Exhibit No.	Description
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*	Amendment No. 1 to the 2004 Stock Incentive Plan of the Registrant.
10.5	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)).
10.6+	License Agreement between the Registrant and The Feinstein Institute for Medical Research (formerly known as The 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)).
10.7+	Sponsored Research and License Agreement between the Registrant and The Feinstein Institute for Medical Research (formerly known as The 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)).
10.8+	Sponsored Research and License Agreement between the Registrant and The Feinstein Institute for Medical Research (formerly known as The 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)).
10.9+	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)).

10.10+	Exclusive License Agreement between the Registrant and Xanthus Life Sciences, Inc. (formerly known as 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)).
10.11+	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)).
10.12+	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)).
10.13+	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)).
10.14+	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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Exhibit No.	Description
10.15+	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)).
10.16	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)).
10.17	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)).
10.18	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)).
10.19	Approval Agreement dated March 7, 2006 by and between the Registrant and H. Shaw Warren, Jr., M.D.
10.20	Approval Agreement dated March 7, 2006 by and between the Registrant and Kevin J. Tracey, M.D.
10.21	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)).
10.22+	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)).
10.23	Loan and Security Agreement 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)).
10.24	The Fourth Loan Modification Agreement dated as of January 6, 2006 to the Loan and Security Agreement by and between the Registrant and Silicon Valley Bank dated June 28, 2002 (as previously amended).
10.25+	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)).
10.26+	Feasibility Study Agreement between Baxter Healthcare Corporation and the Registrant effective June 9, 2004 (Incorporated by Reference to Exhibit 10.25 to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2004 ((SEC File No. 000-50767)).
10.27	Form of Incentive Stock Option Agreement granted under 2004 Stock Incentive Plan (Incorporated by Reference to Exhibit 10.25 to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2004 ((SEC File No. 000-50767)).
10.28	Form of Nonstatutory Stock Option Agreement granted under 2004 Stock Incentive Plan (Incorporated by Reference to Exhibit 10.25 to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2004 ((SEC File No. 000-50767)).
10.29	Form of Restricted Stock Agreement granted under 2004 Stock Incentive Plan (Incorporated by Reference to Exhibit 10.25 to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2004 ((SEC File No. 000-50767)).
10.30	Form of Nonstatutory Stock Option Agreement for a Non-Employee Director granted under the 2004 Stock Incentive Plan (Incorporated by Reference to Exhibit 10.25 to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2004 ((SEC File No. 000-50767)).

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Exhibit No.	Description
10.31*	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)).
10.32*	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)).
10.33*	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)).
10.34*	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)).
10.35*	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)).
10.36*	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)).
10.37*	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)).
10.38*	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)).
10.39*	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)).
10.40*	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)).
10.41*	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)).
10.42+	Agreement for Manufacturing and Supply of ZILEUTON by and between Rhodia Pharma Solutions Ltd. and the Registrant dated February 8, 2005 (Incorporated by Reference to

	Exhibit 10.25 to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2004 ((SEC File No. 000-50767)).
10.43+	License Agreement between the Registrant and Beckman Coulter, Inc. dated January 10, 2005 (Incorporated by Reference to Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q for the quarter ended March 31, 2004 ((SEC File No. 000-50767)).
10.44	Warrant Agreement between the Registrant and Mellon Investor Services LLC as Warrant Agent, dated June 20, 2005 (Incorporated by reference to Exhibit 99.1 to the Registrant s Current Report on Form 8-K filed on June 23, 2005 (SEC File No. 000-50767)).
10.45	Form of Warrant (Included in Exhibit 10.42).
10.46	Form of Securities Purchase Agreement between the Registrant and certain Purchasers, dated June 6, 2005 (Incorporated by reference to Exhibit 99.1 to the Registrant s Current Report on Form 8-K filed on June 7, 2005 (SEC File No. 000-50767)).
10.47	Management Rights Letter Agreement between the Registrant and Prospect Venture Partners III, L.P., dated June 20, 2005 (Incorporated by reference to Exhibit 99.2 to the Registrant s Current Report on Form 8-K filed on June 23, 2005 (SEC File No. 000-50767)).
10.48++	Manufacturing Services Agreement between Patheon Pharmaceuticals Inc. and the Registrant, dated June 28, 2005 (Incorporated by Reference to Exhibit 10.3 to the Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2005 ((SEC File No. 000-50767)).

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Exhibit No.	Description
10.49	Critical Therapeutics, Inc. Non-Employee Director Compensation and Reimbursement Policy.
10.50	Amendment No. 1, dated December 7, 2005, to the Registrant s Exclusive License and Collaboration Agreement with MedImmune, Inc. dated July 30, 2003.
10.51*	Critical Therapeutics, Inc. 2006 Company Goals.
10.52*	Critical Therapeutics, Inc. 2005 Cash Bonuses for Executive Officers.
10.53*	Critical Therapeutics, Inc. 2006 Salaries for Executive Officers.
10.54*	Critical Therapeutics, Inc. Maximum Annual Cash Bonuses for Executive Officers.
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.
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.

\+ 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.