CRITICAL THERAPEUTICS INC
Form 10-K
March 28, 2008

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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, 2007

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 No.)*
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:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value per share	**The NASDAQ Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act:
None.

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, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller Reporting company 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 29, 2007 was approximately $75,463,451, based on a price per share of $2.18, the last reported sale price of the registrant s common stock on the NASDAQ Stock Market on that date.

As of March 19, 2008, the registrant had 42,805,348 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant s proxy statement for the registrant s 2008 annual meeting of stockholders currently expected to be held on May 28, 2008, which is currently expected to be filed pursuant to Regulation 14A within 120 days after the end of the registrant s fiscal year ended December 31, 2007, are incorporated by reference into

Part III of this report.

CRITICAL THERAPEUTICS, INC.

ANNUAL REPORT
ON FORM 10-K

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PART I

Cautionary Statement Regarding Forward-Looking Statements

This annual report on Form 10-K includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. For this purpose, any statements contained herein, other than statements of historical fact, including statements regarding our future sales and marketing efforts for ZYFLO CR™ (zileuton) extended-release tablets, or ZYFLO CR; possible therapeutic benefits and market acceptance of ZYFLO CR; the progress and timing of our drug development programs and related trials; the efficacy of our drug candidates; and our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management, may be forward-looking statements 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 or other words that convey 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: our ability to successfully market and sell ZYFLO CR, including the success of our co-promotion arrangement with Dey, L.P., a wholly-owned subsidiary of Mylan Inc., or DEY; our ability to transition our management team effectively; our current review of our business strategy and future operations, and the implementation of changes in our business strategy and future operations, if any, approved by our board of directors; our ability to develop and maintain the necessary sales, marketing, distribution and manufacturing capabilities to commercialize ZYFLO CR; patient, physician and third-party payor acceptance of ZYFLO CR as a safe and effective therapeutic product; adverse side effects experienced by patients taking ZYFLO CR or ZYFLO® (zileuton tablets) immediate-release formulation of zileuton, or ZYFLO; our heavy dependence on the commercial success of ZYFLO CR; our ability to maintain regulatory approvals to market ZYFLO CR; the success of our co-promotion agreement with DEY for PERFOROMIST™ (formoterol fumarate) Inhalation Solution, or PERFOROMIST; our ability to successfully enter into additional strategic co-promotion, collaboration or licensing transactions on favorable terms, if at all; conducting clinical trials, including difficulties or delays in the completion of patient enrollment, data collection or data analysis; 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; 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., a wholly-owned subsidiary of AstraZeneca PLC; and our ability to obtain, maintain and enforce patent and other intellectual property protection for ZYFLO CR, our discoveries and drug candidates. These and other risks are described in greater detail below under the caption Risk Factors in Part I, Item 1A. 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 on Form 10-K represent our views only as of the date of this annual report on Form 10-K 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. In particular, as discussed elsewhere in this annual report on Form 10-K, we are considering potential changes in our business strategy and future operations. If we determine to pursue an alternative strategy or engage in a strategic transaction, the descriptions of our strategy, future operations and financial position, future revenues, projected costs and prospects and the plans and objectives of management in this annual report on Form 10-K may no longer be applicable. Because of the significant uncertainty regarding our future plans, the

forward-looking statements contained herein do not reflect the potential impact of a potential change in our existing business strategy.

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ITEM 1. *BUSINESS*

Overview

Critical Therapeutics, Inc. is a biopharmaceutical company focused on the development and commercialization of products designed to treat respiratory, inflammatory and critical care diseases linked to the body s inflammatory response. Our marketed product is ZYFLO CR, an extended-release formulation of zileuton, which the U.S. Food and Drug Administration, or FDA, approved in May 2007 for the prevention and chronic treatment of asthma in adults and children 12 years of age or older. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO CR, ZYFLO, an immediate-release tablet formulation of zileuton, and other formulations of zileuton for multiple diseases and conditions. We began selling ZYFLO CR in the United States in September 2007. In addition, we are developing an injectable formulation of zileuton, or zileuton injection.

In preparation for commercialization of ZYFLO CR, we increased our sales force from 18 to 42 representatives. In September 2007, at the time we launched ZYFLO CR, our sales force and the sales force of our co-promotion partner, Dey, L.P., or DEY, began actively promoting ZYFLO CR and ceased actively promoting ZYFLO. However, we expect supplies of ZYFLO to remain in the sales channel into the second quarter of 2008. We have initiated a Phase I clinical trial to examine the pharmacokinetic and pharmacodynamic profile of the R(+) isomer of zileuton to determine if there are potential dosing improvements for patients from this isomer. In addition, we are developing zileuton injection initially for use in emergency room or urgent care centers for patients who suffer acute exacerbations of asthma. In August 2006, we announced results from our Phase I/II clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of zileuton injection in patients with asthma. We initiated a Phase II clinical trial in October 2007 with zileuton injection in asthma patients designed to evaluate the most appropriate dose for later-stage clinical trials.

On March 13, 2007, we entered into an agreement with DEY, under which we and DEY agreed to jointly promote ZYFLO and ZYFLO CR. On June 25, 2007, we entered into a definitive agreement with DEY to jointly promote DEY s product PERFOROMIST for the treatment of chronic obstructive pulmonary disease, or COPD. In October 2007, after expanding our sales force to more than 40 representatives, we announced that we had commercially launched PERFOROMIST with DEY.

We are conducting preclinical work in our alpha-7 program. We believe the successful development of a small molecule product candidate targeting the nicotinic alpha-7 cholinergic receptor, or 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 asthma and rheumatoid arthritis. Based on preclinical studies, we have selected lead and backup molecules for evaluation in good laboratory practices, or GLP, toxicology studies. Provided the data are supportive, we expect to file an investigational new drug application, or IND, in 2009. In addition, we plan to seek collaborations with other pharmaceutical companies for our alpha-7 program to develop and commercialize possible product candidates in multiple development opportunities that may exist within this program prior to the initiation of human clinical trials. We have licensed to Innovative Metabolics, Inc., or IMI, patent rights and know-how relating to the mechanical and electrical stimulation of the vagus nerve. This license agreement specifically excludes from the licensed field pharmacological modulation of the alpha-7 receptor.

We are collaborating with MedImmune, Inc., a subsidiary of AstraZeneca PLC, on the development of monoclonal antibodies directed toward a cytokine called high mobility group box protein 1, or HMGB1, which we believe may be an important target for the development of products to treat diseases mediated by the body s inflammatory response. In addition, we are collaborating with Beckman Coulter, Inc. on the development of a diagnostic directed toward measuring HMGB1 in the bloodstream.

We were incorporated in Delaware on July 14, 2000 as Medicept, Inc. and changed our name to Critical Therapeutics 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 Global Market.

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Review of Strategic Alternatives

We are in the process of reviewing a range of strategic alternatives that could result in potential changes to our current business strategy and future operations. As part of this process, we are considering alternatives to our current business strategy designed to maximize the value of our commercial organization and product development programs. We have engaged an investment bank to advise us in this process. As a result of this process, we could determine to:

engage in one or more potential transactions, such as the sale or divestiture of certain of our assets, the merger or sale of our company or other strategic transactions; or

continue to operate our business in accordance with our existing business strategy.

Pending any decision to change strategic direction, we are continuing our commercial and development activities in accordance with our existing business strategy with an increased focus on managing our cash position. We cannot assure you that our evaluation of strategic alternatives will lead to a change in our current business strategy or future operations, or result in one or more transactions.

Our Product Pipeline

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

* Being developed with MedImmune under an exclusive license and collaboration agreement. Diagnostic assays directed towards HMGB1 are being developed with Beckman Coulter under a license agreement.

Zileuton

In 2003, we acquired from Abbott exclusive worldwide rights to develop and market ZYFLO CR and other formulations of zileuton for multiple diseases and conditions. In 2004, we acquired from Abbott exclusive worldwide rights to develop and market ZYFLO. The FDA approved our supplemental new drug application, or sNDA, for ZYFLO on September 28, 2005 and we began selling ZYFLO in the United States in October 2005. We ceased manufacturing and supplying ZYFLO in February 2008. The FDA approved our NDA for ZYFLO CR on May 30, 2007, and we subsequently launched ZYFLO CR in the United States on September 27, 2007.

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 CR 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

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asthmatic patients. Leukotrienes are also implicated in the disturbance of normal lung airway function in certain other diseases, including chronic obstructive pulmonary disease, or COPD. ZYFLO CR and ZYFLO are the only FDA-approved products that block 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 short of breath as the airways become constricted and inflamed. The National Center for Health Statistics estimates that in 2005 approximately 22.2 million people in the United States had asthma and approximately 12.2 million people in the United States had asthma attacks. Severe asthma attacks can be life threatening. The National Center for Health Statistics estimates that in 2005 approximately 1.8 million hospital emergency room visits in the United States involved asthma attacks and approximately 488,594 hospital discharges were attributable to asthma.

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 long-acting bronchodilator. We believe many prescribing physicians are dissatisfied with the treatment options available for uncontrolled asthmatic patients due to the inability of these treatments to control symptoms reliably. A recent study, titled Real-world Evaluation of Asthma Control and Treatment (REACT): Findings from a National Web-based Survey and published in the American Academy of Allergy, Asthma, and Immunology, stated that nearly 55% of all moderate to severe asthmatics remain uncontrolled despite being treated with asthma medications.

We believe that many patients with asthma may benefit from therapy with ZYFLO CR. ZYFLO CR 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 CR as a treatment for asthma patients who do not gain adequate symptomatic control from other currently available medications.

Zileuton Product Development

ZYFLO: The Tablet Formulation of Zileuton

ZYFLO and ZYFLO CR are the only 5-lipoxygenase inhibitor drugs 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 revenue from sales of ZYFLO of $8.7 million in 2007, $6.6 million in 2006 and $387,000 in 2005. We recognized revenue from sales of ZYFLO CR of $2.3 million in 2007.

The full clinical development program for ZYFLO consisted of 21 safety and efficacy trials in an aggregate of approximately 3,000 patients with asthma. FDA approval was based on pivotal three-month and six-month safety and efficacy clinical trials in 774 asthma patients. The pivotal trials compared patients taking 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 within two hours after the first dose.

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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 the need for steroid rescue medication 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 approximately 50% of the patients who continued therapy and all of the patients 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 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 irreversible liver damage in patients treated with ZYFLO since its approval.

In January 2008, we requested and received from the FDA a waiver from the requirement to provide six-months notice to cease manufacturing ZYFLO, the immediate-release formulation of zileuton. As a result, we no longer manufacture or supply ZYFLO to the market. Through the normal course of our business, we have depleted the remaining inventory available for sale to wholesalers. We anticipate that all of the immediate-release product available from wholesalers to retailers will be depleted in March 2008 and only a limited amount of product will be available at the retail level, such as pharmacies. As a result, we have undertaken a number of initiatives to educate the market about the cessation of manufacturing of ZYFLO to ensure a smooth transition for patients and doctors, including:

- submission of healthcare a professional letter to the FDA s drug shortage group for posting on the FDA website;
- communication to wholesalers, who will provide notification to retail pharmacies, of the discontinuation of ZYFLO and availability of ZYFLO CR;
- delivery by our sales representatives of communications to pharmacists, doctors and other associated healthcare professionals;
- managed care notification and communication to health plans; and
- direct mail notification to identified providers who have prescribed ZYFLO in the last 12 months.

ZYFLO CR: The Extended-Release Formulation of Zileuton

We commercially launched ZYFLO CR in September 2007, following its approval by the FDA in May 2007. We believe ZYFLO CR offers a more convenient regimen for patients because of its twice-daily, two tablets per dose dosing regimen, as compared to ZYFLO s four-times daily dosing regimen, which we believe may increase patient drug compliance. Abbott completed Phase III clinical trials for this formulation in asthma, but did not submit an NDA. We submitted the NDA for ZYFLO CR to the FDA based on safety and efficacy data generated from two completed Phase III clinical trials, a three-month efficacy trial and a six-

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month safety trial, each of which was completed by Abbott. The study reports prepared by Abbott for these clinical trials showed:

In a three-month pivotal efficacy trial, in which 397 patients received either ZYFLO CR or placebo, patients taking ZYFLO CR demonstrated statistically significant improvements over placebo in objective measures of asthma control, such as mean forced expiratory volume in one second, or FEV_1. In the trial, patients taking ZYFLO CR showed a reduced need for bronchodilatory drugs as a rescue medication to alleviate uncontrolled symptoms. In this trial, 2.5% of the patients taking ZYFLO CR experienced ALT levels greater than or equal to three times the level normally seen in the bloodstream, compared to 0.5% of the patients taking placebo.

In a six-month safety trial, in which 706 patients received either a combination of ZYFLO CR and their usual asthma medications or a combination of placebo and their usual asthma medications, 1.78% of the patients taking ZYFLO CR and their usual asthma medications experienced ALT levels greater than or equal to three times the level normally seen in the bloodstream, compared to 0.65% of the patients taking placebo and their usual asthma medications.

To be able to rely on the results of Abbott s pivotal clinical trials, we conducted two comparative bioavailability studies intended to show that the pharmacokinetic profile of ZYFLO CR tablets that we have manufactured was similar to the pharmacokinetic profile of the ZYFLO CR tablets previously manufactured by Abbott and used in Abbott s clinical trials. We conducted both a single-dose and a multiple-dose pharmacokinetic study. The studies assessed the pharmacokinetics of ZYFLO CR in volunteers under both fed and fasting conditions.

We entered into an agreement in March 2007 with DEY under which we and DEY jointly co-promote ZYFLO CR.

Injectable Formulation of Zileuton

We are developing zileuton injection for use as an adjunctive treatment for patients with acute exacerbations of asthma. We believe acute exacerbations of asthma are a significant unmet medical need that occurs in asthma patients who are poorly controlled on their existing medications. According to the American Lung Association, in 2005, approximately 1.8 million hospital emergency room visits in the United States involved asthma attacks and approximately 488,594 hospital discharges were attributable to asthma. We are developing zileuton injection as a new treatment option for acute asthma patients in the emergency department that can be added to existing therapies in order to improve pulmonary function by controlling both bronchospasm and pulmonary inflammation through zileuton s mechanism of action, 5-lipoxygenase inhibition. 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 directly into 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 injectable 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 August 2006, we announced results from a Phase I/II clinical trial with zileuton injection in chronic stable asthmatics. The trial included measurements to detect evidence of improvement in lung function. The double-blind, placebo-controlled trial enrolled 60 patients at 10 clinical sites in the United States. Patients enrolled in the trial had a mean forced expiratory volume in one second, or FEV_1, of 63 percent of predicted normal at baseline and a mean age of 40 years. Patients enrolled in the trial were randomized into four escalating dose groups, 75 mg, 150 mg, 300 mg

and 600 mg, and received one infusion of either zileuton

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injection or placebo. Each of the four dose groups enrolled 15 patients, of whom 12 received zileuton injection and three received placebo. All 60 patients who were randomized completed the trial.

Patients in each of the four zileuton injection cohorts showed a greater mean percentage improvement in FEV_1 than patients in the placebo group when measured at 10, 30 and 60-minute intervals after dosing. The 300 mg dose was predicted to approximate the blood level exposure of the currently approved immediate-release oral dose of ZYFLO. In this trial, the 300 mg dose group showed a mean improvement in FEV_1 from baseline of 13.7 percent at 60 minutes after dosing. In addition, zileuton injection was well tolerated at all doses tested with no serious adverse events reported in the trial.

We initiated a Phase II clinical trial with zileuton injection in chronic stable asthmatics in October 2007. This Phase II clinical trial is a placebo-controlled, three-period cross-over study in 36 patients with stable, moderate-to-severe asthma and a FEV_1 of 40-80% of predicted normal. In this trial, patients receive 150 mg or 300 mg doses of zileuton injection or placebo, administered via a peripheral intravenous, or IV, catheter at a standard continuous rate. This trial is designed to help establish the pulmonary function profile, safety, tolerability, and pharmacokinetic profile of zileuton injection and to help identify the optimal dose to be used in future trials.

Commercialization Strategy

Upon receiving approval for ZYFLO CR in May 2007, we began rebuilding our sales and marketing team and infrastructure to commercially launch the product in September 2007. As of February 29, 2008, we have a respiratory sales force of approximately 39 representatives who are focused on promoting ZYFLO CR and PERFOROMIST to prescribing physicians in major markets across the United States. We are seeking to convert prescribing and usage of ZYFLO to ZYFLO CR and to increase utilization of ZYFLO CR by prescribing physicians.

In March 2007, we entered into a co-promotion agreement with DEY, a subsidiary of Mylan Inc., under which we and DEY agreed to jointly promote ZYFLO and, after approval by the FDA, ZYFLO CR. DEY has a respiratory sales force consisting of approximately 200 clinical sales representatives as of February 29, 2008. Under the co-promote agreement, DEY is required to provide a specified number of details per month for ZYFLO CR, in the second position, to office-based physicians and other health care professionals, including a minimum number of details delivered to respiratory specialists, such as allergists and pulmonologists. Under the co-promotion agreement, we have agreed to provide a specified number of details per month for ZYFLO CR in the first position. We anticipate that our sales representatives and DEY s sales representatives will promote ZYFLO CR to a total of approximately 18,000 physicians prescribing high levels of asthma medications. From 2008 through 2010, we and DEY each have agreed to contribute 50 percent of out-of-pocket promotion expenses for ZYFLO CR that are accrued or paid to third-parties and approved by a joint commercial committee. We and DEY each have agreed to contribute a minimum of $3.0 million per year for these promotion expenses. We were responsible for third-party promotion costs during 2007.

We believe that there is a market opportunity for the use of ZYFLO CR 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, including LTRAs and long-acting beta agonists, or LABAs. Our belief is based on information that we have gathered through extensive direct interactions and market research with respiratory specialists, including allergists and pulmonologists and primary care physicians, such as:

- more than 33 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;

- more than two years of interaction between our sales force and respiratory specialists who treat asthma; and

qualitative and quantitative market research that we have conducted since 2004.

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In preparation for the launch of ZYFLO CR, we conducted market research in 2007 with 150 specialists, 75 allergists and 75 pulmonologists, and 153 primary care physicians, or PCPs. This market research study included the following findings:

70% of specialists responded that the release of ZYFLO CR would greatly facilitate the acceptance of the product by the specialist community; and

66% of primary care physicians responded that they would be interested in using ZYFLO CR as part of their treatment regimen, despite the fact that only one in 10 of these physicians had ever prescribed ZYFLO in the past.

We continue to conduct research to refine our messaging, positioning and understanding of prescriber attitudes and perceptions of ZYFLO CR.

We are positioning ZYFLO CR as an alternative treatment for asthma patients who do not gain adequate control of their symptoms with other currently available medications, including inhaled corticosteroids, long-acting beta agonists and LTRAs. We are promoting ZYFLO CR to respiratory specialists, managed care decision makers and some primary care physicians who treat large volumes of asthma patients. As part of our marketing strategy, we attempt to educate key opinion leaders and physicians on the scientific data that differentiates the mechanism of action of ZYFLO CR from other asthma treatments and emphasize clinical data that show safety and efficacy for ZYFLO CR in asthma.

We are also attempting to maximize patient and physician access to ZYFLO CR by addressing the position of ZYFLO CR on managed care formularies. We believe that in many managed care formularies ZYFLO CR has been removed or relegated to third-tier status, which requires the highest co-pay for patients prescribed the product. In some cases, managed care organizations, or MCOs, may require additional evidence that a patient had previously failed another therapy, additional paperwork or prior authorization from the MCO before approving reimbursement for ZYFLO CR.

In June 2007, the National Heart Lung, and Blood Institute, or NHLBI, released an updated version of the Guidelines for the Diagnosis and Management of Asthma. In these guidelines, zileuton is specifically mentioned in steps three and four in the treatment spectrum as an alternative option in the treatment of asthma. This is the first time zileuton has been mentioned in these guidelines, and we believe this may provide additional scientific credibility to ZYFLO CR in the marketplace. In addition to the changes in the recommended treatment protocol for asthma, the updated guidelines continue to support the transition to discussing asthmatic patients in terms of their level of control rather than their severity level.

Since the commercial launch of ZYFLO CR in September 2007, we have experienced growth in overall prescription volume and the number of physicians prescribing ZYFLO CR, and we believe this growth is due to the greater market acceptance of the twice-daily dosing of ZYFLO CR compared to the four-times daily immediate-release formulation of ZYFLO. Prescriptions for ZYFLO CR and ZYFLO increased 38% and the number of active prescribers for the products increased 36% in the fourth quarter of 2007 when compared to the fourth quarter of 2006.

We are exploring the therapeutic benefits of zileuton in treating a range of diseases and conditions, including acute asthma exacerbations and COPD. 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. The NIH sponsored and is funding a clinical trial to evaluate whether using ZYFLO to treat patients admitted to the hospital with acute exacerbations of COPD will shorten their hospital stay. The clinical trial began in September 2007 and is being conducted by the COPD Clinical Research Network. 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.

R(+) Isomer of Zileuton

We have obtained preclinical data that shows a single enantiomer of zileuton possesses higher potency for 5-lipoxygenase inhibition and clinical data after dosing of the racemate that demonstrates this enantiomer

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exhibits a more prolonged plasma pharmacokinetic exposure profile. We believe that these features offer the opportunity for us to develop a product candidate with a reduced tablet size or less frequent dose administration. In 2007, we initiated a Phase I clinical trial in healthy volunteers designed to evaluate this enantiomer to establish its pharmacokinetic and 5-lipoxygenase inhibitory profiles. This trial completed its clinical phase in December 2007, and we are currently evaluating the data. We believe this program could enable us to examine the potential development of a new zileuton tablet product candidate for the treatment of asthma and other indications, such as COPD.

Critical Care: The Inflammatory Response

We are developing product candidates directed towards reducing the potent inflammatory response that we believe is associated with the pathology, morbidity and, in some cases, mortality in many acute and chronic diseases. Our early-stage product development programs center on controlling the production of potent inflammatory mediators that play a key role in regulating the body s immune system. The cascading release of the inflammatory mediators that occurs in many disease settings leads, in large part, to the uncontrolled, pathologic inflammation that can occur in trauma, infection and autoimmune and allergic diseases. We believe that this cascade plays an important role in the severe inflammatory response seen in:

- acute diseases and conditions that lead to admission to the ICU, such as sepsis and septic shock; and
- acute exacerbations of chronic diseases that frequently lead to hospitalization, such as asthma, lupus and rheumatoid arthritis.

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, multiple organ failure and death. Many previous therapies directed at cytokines, such as tumor necrosis factor alpha, or TNF alpha, 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:

- an alpha-7 nicotinic acetylcholine 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 alpha, in response to an inflammatory stimulus; and
- an HMGB1 program directed towards the pro-inflammatory protein HMGB1.

These programs are described in more detail below.

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 alpha. Research indicates that acetylcholine exerts anti-inflammatory activity by stimulating the nicotinic alpha-7 cholinergic receptor, or alpha-7 receptor, on cells involved in the inflammatory process.

Historically, a number of companies have focused on the alpha-7 receptor target for 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 candidate that inhibits the inflammatory response by stimulating the alpha-7 receptor on human inflammatory 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 asthma, 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 selectively stimulate the alpha-7 receptor. We believe a drug candidate taken orally could have a strong market position against current injectable anti-TNF alpha biological therapies, particularly if it avoids the potential immunological response to therapy, which is a known risk with antibody products.

Development Strategy

We are currently completing preclinical evaluations of proprietary small molecule product candidates in our alpha-7 program. We have seen positive results with our molecules in animal models of allergic lung inflammation and acute lung injury, including models using alpha-7 knock-out mice. We believe the initial results support the concept that the alpha-7 receptor plays an important role in modulating the severity of inflammation in these models and that our molecules work by stimulating this receptor. We have selected both a lead and a backup molecule, and we believe both have shown promising preclinical pharmacology and non-GLP toxicology results. We moved the lead molecule into GLP toxicology evaluations in 2008 and, provided the data are supportive, expect to file an IND in 2009. We plan to seek a collaborator for our alpha-7 nicotinic receptor agonist program to develop and commercialize possible product candidates in multiple development opportunities that may exist for this program prior to inititation of human clinical trials.

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 alpha, HMGB1 is expressed much later in the inflammatory response and persists at elevated levels in the bloodstream for a longer time period. We believe, therefore, that HMGB1 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 therapeutic products directed towards blocking the pro-inflammatory activity of 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.

As part of the MedImmune collaboration, the research programs are currently aimed at generating antibodies that can neutralize circulating HMGB1 prior to it binding to its receptor. Fully human antibodies directed towards HMGB1, including fully human antibodies identified as part of the MedImmune collaboration, are currently in preclinical development. In December 2005, MedImmune agreed that proof of concept had been achieved for two preclinical models with human anti-HMGB1 monoclonal antibodies. These antibodies are now undergoing further evaluation with the goal of selecting candidates for use in clinical testing.

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 and

lupus.

Sepsis is the body s systemic inflammatory response to infection or trauma. In animal models relating to 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

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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. Human monoclonal antibodies jointly generated by the collaboration with MedImmune have demonstrated promising activity in assays and animal models with relevance to clinical arthritis and lupus.

Clinical Strategy

We have generated a number of fully human 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 sepsis and a reduction in clinical arthritis symptoms in mouse and rat models of arthritis. In some 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.

The research phase of the collaboration has ended and, under the collaboration agreement, MedImmune is responsible for conducting programs necessary to advance potential product candidates into Phase I clinical trials. As of December 31, 2007, no decision to select a clinical candidate had been made.

Collaborations

Zileuton Co-Promotion Agreement with DEY

On March 13, 2007, we entered into an agreement with DEY under which we and DEY agreed to jointly co-promote ZYFLO and, after approval by the FDA, ZYFLO CR. Under the co-promotion and marketing services agreement, we granted DEY an exclusive right and license or sublicense, under patent rights controlled by us, to promote and detail ZYFLO and ZYFLO CR in the United States, together with us and our affiliates, for asthma and, subject to FDA approval, other respiratory conditions.

Both we and DEY have agreed to use diligent efforts to promote the applicable products in the United States during the term of the co-promotion agreement. In addition, DEY has agreed to provide a minimum number of details per month for ZYFLO CR in the second position to office-based physicians and other health care professionals, including a minimum number of details delivered to respiratory specialists, such as allergists and pulmonologists. We have agreed to provide a minimum number of details per month for ZYFLO CR in the first position. From 2008 through 2010, we and DEY each have agreed to contribute 50% of approved out-of-pocket promotional expenses for ZYFLO CR that are accrued or paid to third-parties. We and DEY each have agreed to contribute a minimum of $3.0 million per year for these promotional expenses. We were responsible for third-party promotional costs during 2007.

Under the co-promotion agreement, DEY paid us in 2007 a non-refundable upfront payment of $3.0 million upon signing the co-promotion agreement, non-refundable milestone payments of $4.0 million following approval by the FDA of the NDA for ZYFLO CR and $5.0 million following commercial launch of ZYFLO CR. Under the co-promotion agreement, we record all quarterly net sales of ZYFLO and ZYFLO CR, after third-party royalties, up to $1.95 million. We pay DEY a portion of quarterly net sales of ZYFLO and ZYFLO CR, after third-party royalties, in excess of $1.95 million. From the date DEY began detailing ZYFLO through the commercial launch of ZYFLO CR in September 2007, we agreed to pay DEY 70% of quarterly net sales, after third-party royalties, in excess of $1.95 million. Following the commercial launch of ZYFLO CR in September 2007 through December 31, 2010, we

have agreed to pay DEY 35% of quarterly net sales, after third-party royalties, in excess of $1.95 million. From January 1, 2011 through December 31, 2013, we have agreed to pay DEY 20% of quarterly net sales, after third-party royalties, in excess of $1.95 million.

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The co-promotion agreement has a term expiring on December 31, 2013, which may be extended upon mutual agreement by the parties. Beginning three years after the commercial launch of ZYFLO CR, either party may terminate the co-promotion agreement with six-months advance written notice. In addition, DEY has the right to terminate the co-promotion agreement with two-months prior written notice if ZYFLO CR cumulative net sales for any four consecutive calendar quarters after commercial launch of ZYFLO CR are less than $25 million. Each party has the right to terminate the co-promotion agreement upon the occurrence of a material uncured breach by the other party.

DEY has agreed not to manufacture, detail, sell, market or promote any product containing zileuton as one of the active pharmaceutical ingredients for sale in the United States until the later of one year after expiration or termination of the co-promotion agreement and March 15, 2012. However, if an AB-rated generic product to ZYFLO CR is introduced, DEY would not be subject to these non-competition obligations and DEY will have the exclusive right to market the authorized generic version of ZYFLO CR. DEY also will not be subject to these non-competition obligations if DEY terminates the co-promotion agreement either because ZYFLO CR cumulative net sales for any four consecutive calendar quarters after commercial launch of ZYFLO CR are less than $25 million or upon the occurrence of a material uncured breach by us.

A joint commercial committee with two members from Critical Therapeutics and two members from DEY oversees co-promotion activities under the co-promotion agreement. The co-promotion agreement provides that the joint commercial committee will make decisions by unanimous agreement, with disagreements being referred for resolution by the Chief Executive Officer of each party and further disputes being subject to non-binding mediation.

PERFOROMIST Co-Promotion Agreement with DEY

On June 25, 2007, we entered into a co-promotion agreement with DEY relating to PERFOROMIST, DEY s product for the treatment of COPD. Under the co-promotion agreement, DEY granted us a right and license or sublicense to promote and detail PERFOROMIST in the United States, together with DEY. The co-promotion agreement supersedes a binding letter agreement between DEY and us dated March 13, 2007 relating to the co-promotion of PERFOROMIST.

Both we and DEY have agreed to use diligent efforts to promote PERFOROMIST in the United States during the term of the co-promotion agreement. In addition, we have agreed to provide a minimum number of primary detail equivalents per month for PERFOROMIST to a specified group of office-based physicians and other health care professionals. We are responsible for our own sales force expenses, including the cost of promotional materials used by our sales force. Under this co-promotion agreement, DEY has agreed to pay us a co-promotion fee under a calculation based on retail sales of PERFOROMIST.

During the term of this co-promotion agreement and for a period of one year after the expiration or termination of the co-promotion agreement, we have agreed not to manufacture, detail, sell, market or promote in the United States any product containing forms or derivatives of formoterol, or FAPI, as one of the active pharmaceutical ingredients for PERFOROMIST s approved indications, other than PERFOROMIST, during the term of the co-promotion agreement. Notwithstanding the foregoing, if we sign a definitive agreement to be acquired by or merged with a third party that markets, manufactures, sells, details or promotes a product containing FAPI for sale in the United States, then, in lieu of the foregoing non-competition provision, we have agreed to specified restrictions on the activities of our sales representatives for a specified 180-day period.

The co-promotion agreement has a term expiring on December 31, 2013, which may be extended upon mutual agreement by the parties. We have the right to terminate the co-promotion agreement after June 30, 2008 with 90-days advance written notice to DEY. In addition, each party has the right to terminate the co-promotion agreement with

90-days advance written notice in the event that the zileuton co-promotion agreement between us and DEY dated March 13, 2007 is terminated. If we sign a definitive agreement to be acquired by or merged with a third party that markets, manufactures, sells, details or promotes a product containing FAPI for sale in the United States, each party will have the right to terminate the co-promotion

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agreement with three business days advance written notice. Each party has the right to terminate the co-promotion agreement upon the occurrence of a material uncured breach by the other party.

In October 2007, after expanding our sales force to over 40 representatives, we announced that we had commercially launched PERFOROMIST with DEY.

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 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 research and development payments from MedImmune, including a minimum of $4.0 million of research and development payments through the end of 2006, all of which had been paid by December 31, 2007. 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 10 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.

In December 2005, MedImmune agreed that the collaboration demonstrated proof of concept in two preclinical disease models with human 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. In March 2007, MedImmune agreed to fund an additional $125,000 of research work performed by our full-time employees in 2007.

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

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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. Beckman Coulter exercised its development option under the license agreement in December 2006 and paid us $400,000 in January 2007. Under the agreement, we may also receive additional aggregate license fees of up to $450,000 upon 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.

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

As of December 31, 2007, we had 10 employees engaged in research, development, regulatory and medical 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 utilize sponsored research arrangements with academic and research institutions to help advance our research programs.

During the fiscal years ended December 31, 2007, 2006 and 2005, research and development expenses were $21.7 million, $26.9 million and $30.0 million, respectively.

Sales and Marketing

We have a respiratory sales force of approximately 39 representatives as of February 29, 2008 who are focused on promoting ZYFLO CR and PERFOROMIST to prescribing physicians within major markets across the United States. Under our co-promotion agreement with DEY for ZYFLO CR, DEY has agreed to provide a minimum number of details per month for ZYFLO CR in the second position to office-based physicians and other health care professionals, including a minimum number of details delivered to respiratory specialists, such as allergists and pulmonologists. We have agreed to provide a minimum number of details per month for ZYFLO CR in the first position. In addition, under our co-promotion agreement with DEY for PERFOROMIST, we have agreed to provide a minimum number of primary detail equivalents per month for PERFOROMIST to a specified group of office-based physicians and other health care professionals.

We are focusing our sales and marketing efforts for ZYFLO CR on respiratory specialists who treat asthma, including allergists and pulmonologists, and primary care physicians who treat large numbers of asthma patients. We believe that we can successfully market ZYFLO CR to this target group through the combined efforts of our sales representatives and DEY s sales representatives. We believe that within this targeted group there are approximately

100 to 200 national and regional scientific and clinical key opinion leaders who serve to influence the direction of the diagnosis and treatment of asthma through their publications and presentations at scientific and clinical medical conferences. We also expect to focus our medical outreach efforts on local, clinically-based key opinion leaders.

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Given the importance of the scientific and clinical key opinion leaders, we are directing our scientific message and support to help educate and inform key opinion leaders regarding the scientific rationale and clinical data that support our commercialization strategy. We have entered into consulting arrangements with a number of key opinion leaders who provide expert advice to our 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 senior vice president of regulatory.

In June 2007, the NHLBI released an updated version of the Guidelines for the Diagnosis and Management of Asthma. In these guidelines, zileuton is specifically mentioned in steps three and four in the treatment spectrum as an alternative option in the treatment of asthma. This is the first time zileuton has been mentioned in these guidelines, and we believe this may provide additional scientific credibility to ZYFLO CR in the marketplace. In addition to the changes in the recommended treatment protocol for asthma, the updated guidelines continue to support the transition to the discussion of asthmatic patients in terms of their level of control rather then there severity level.

Part of our overall strategy for ZYFLO CR also includes repositioning the product within the managed care market. We have positioned ZYFLO CR 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 ZYFLO CR will reach potential prescribing physicians through managed care pharmacies communicating the product s modified formulary status.

Manufacturing

We have limited experience in manufacturing our product candidates. We currently outsource the manufacturing of ZYFLO CR 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.

Shasun Pharma Solutions

We originally contracted with Rhodia Pharma Solutions Ltd. for the commercial production of the zileuton active pharmaceutical ingredient, or API. On March 31, 2006, Rhodia SA, the parent company of Rhodia Pharma Solutions, sold the European assets of its pharmaceutical custom synthesis business to Shasun Chemicals and Drugs Ltd. As part of this transaction, Rhodia SA assigned our contract with Rhodia Pharma Solutions Ltd. to Shasun Pharma Solutions. Under our agreement with Shasun, as amended, Shasun has agreed to manufacture our commercial supplies of API, subject to specified limitations, through the earlier of the date on which we have purchased a specified amount of the API for zileuton and December 31, 2010. The agreement will automatically extend for successive one-year periods after December 31, 2010, unless Shasun provides us with 18-months prior written notice of cancellation. We have the right to terminate the agreement upon 12-months prior written notice for any reason, provided that we may not cancel prior to the earlier of December 31, 2010 or the date on which we have purchased a specified amount 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. In addition, we have the right to terminate the agreement upon 30-days prior written notice if any governmental agency takes any action, or raises any objection, that prevents us from importing, exporting, or selling our zileuton products or the API. If we exercise our right to terminate the agreement prior to its scheduled expiration, we are obligated to reimburse Shasun 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 Shasun for all API manufactured by Shasun 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.

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SkyePharma

We have contracted with SkyePharma PLC, through its subsidiary Jagotec AG, for the manufacture and supply of bulk, uncoated tablets of ZYFLO CR for us for commercial sale. We have agreed to purchase minimum quantities of ZYFLO CR during each 12-month period for the first five years following marketing approval of ZYFLO CR by the FDA. For the term of the contract, we have agreed to purchase specified amounts of our requirements for ZYFLO CR from Jagotec. The commercial manufacturing agreement has an initial term of five years beginning on May 22, 2007, and will automatically continue thereafter, unless we provide Jagotec with 24-months prior written notice of termination or Jagotec provides us with 36-months prior written notice of termination. In addition, we have the right to terminate the 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 or selling ZYFLO CR. We also may terminate the agreement upon six-months advance notice in the event that an AB-rated generic pharmaceutical product containing zileuton is introduced in the United States and we determine to permanently cease commercialization of ZYFLO CR. Likewise, we may terminate the agreement upon 12-months advance notice if we intend to discontinue commercializing ZYFLO CR tablets. Furthermore, each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party. In the event either party terminates the agreement, we have agreed to purchase quantities of ZYFLO CR tablets that are subject to binding forecasts.

Patheon Pharmaceuticals

We have contracted with Patheon Pharmaceuticals Inc., or Patheon, to coat, conduct quality control and quality assurance and stability testing and package commercial supplies of ZYFLO CR. Under this agreement, we are responsible for supplying uncoated ZYFLO CR tablets to Patheon. We have agreed to purchase at least 50% of our requirements for such manufacturing services for ZYFLO CR for sale in the United States from Patheon each year during the term of this agreement. This agreement has an initial term of three years beginning May 9, 2007, 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 this agreement upon 30-days prior written notice in the event that any governmental agency takes any action, or raises any objection, that prevents us from importing, exporting, purchasing or selling ZYFLO CR. We also have the right to terminate this agreement upon 90-days prior written notice if an AB-rated generic product to ZYFLO CR is introduced in the United States. If we provide six-months advance notice that we intend to discontinue commercializing ZYFLO CR, we will not be required to purchase any additional quantities of ZYFLO CR finished tablets from Patheon, provided that we pay Patheon for a portion of specified fees and expenses associated with orders we previously placed. Patheon has the right to terminate this agreement if we assign any of our rights under the agreement to an assignee other than a purchaser or merger partner that, in Patheon s reasonable opinion, is not a credit worthy substitute for us, is a competitor of Patheon or is an entity with whom Patheon has had prior unsatisfactory business relations. Furthermore, each party has the right to terminate this agreement upon the occurrence of a material uncured breach by the other party. If this agreement expires or is terminated for any reason, we have agreed to take delivery of and pay for undelivered quantities of ZYFLO CR that we previously ordered, purchase, at cost, Patheon s inventory of ZYFLO CR maintained in contemplation of filling orders previously placed by us and pay the purchase price for components ordered by Patheon from suppliers in reliance on orders we previously placed.

CyDex

We have entered into a license and supply agreement with CyDex, Inc., or CyDex, relating to our clinical development and planned commercialization of zileuton injection. Under this agreement, CyDex granted to us a worldwide, exclusive license, under patent rights controlled by CyDex relating to CyDex s CAPTISOL® drug enablement technology, for use with zileuton, under which we can develop, make, use and sell zileuton combined with

or formulated using CAPTISOL in an injectable dosage form for ultimate use in humans. In addition, CyDex granted us a worldwide, non-exclusive license to utilize CyDex s toxicology and safety and other relevant scientific data, relating to CAPTISOL, to develop, make, use and sell in combination with

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zileuton. Under this agreement, we agreed that we and our affiliates and sublicensees will purchase CAPTISOL exclusively from CyDex, and CyDex has agreed to supply 100% of our and our affiliates and sublicensees requirements for CAPTISOL up to a specified amount per year during the term of the agreement.

In consideration for the licenses granted to us under the agreement, we paid CyDex an initial license fee of $50,000 and agreed to make aggregate milestone payments of up to $2.9 million upon the achievement of specified development, regulatory and commercialization milestones for the combined product. In addition, we agreed to pay royalties to CyDex based on net sales of the combined product by us and our affiliates and licensees. Our obligation to pay royalties expires, with respect to each country in which the combined product is commercialized, upon the later of the expiration of the last relevant patent that claims CAPTISOL in such country or ten years from the first commercial sale of the combined product in such country.

The term of the agreement expires upon the expiration of our obligation to pay royalties. CyDex has the right to terminate the agreement upon the occurrence of an uncured breach by us. We have the right to terminate the agreement at any time upon 75-days prior written notice.

Other

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 program. Under our collaboration agreement with MedImmune, MedImmune would be responsible for manufacturing any biologic products that result from our HMGB1 program.

Distribution Network

We currently rely on third parties to distribute ZYFLO CR to pharmacies. We have contracted with Integrated Commercialization Services, Inc., or ICS, a third-party logistics company, to warehouse ZYFLO CR 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 samples of ZYFLO CR 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 CR. We rely on RxHope to administer our patient assistance program and to distribute ZYFLO CR 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 CR 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 on our own 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 or under which we have licensed intellectual property and other rights to third parties, including the license agreements summarized below.

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 injectable 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-

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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. Abbott waived its right of first negotiation with respect to our co-promotion arrangement with DEY for ZYFLO CR. 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, 2007, we have paid milestone and license payments totaling $6.5 million to Abbott under this agreement. In addition, after the FDA approved the NDA for ZYFLO CR in May 2007, we accrued $2.8 million in milestone payments we owe to Abbott on the first and second anniversary of the approval of the ZYFLO CR NDA.

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 injectable formulation of zileuton. In the event that we choose to pursue the commercialization of a specified injectable formulation developed by Baxter that is based on the formulation technology of a third party, Baxter granted us an exclusive, worldwide, non-revocable license to the formulation intellectual property in return for our agreement to pay Baxter royalties based on net sales of that formulation. However, we would need to finalize the license agreement to document such license based on the agreed financial terms, which we may not be able to negotiate on favorable terms, if at all. It is also possible that we may instead determine to pursue the commercialization of an injectable formulation developed by Baxter based on its own proprietary formulation technology. If we determine to do so, we would need to license from Baxter rights to that injectable formulation. In that case, we may not be able to negotiate a license agreement on favorable terms, if at all. Furthermore, although Baxter has filed two U.S. patent applications, one for the specified injectable formulation developed by Baxter based on the formulation technology of a third party and another for an injectable formulation developed by Baxter based on its own proprietary formulation technology, neither of these patent applications may result in issued patents.

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

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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 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 paid The Feinstein Institute $15,000 for minimum royalties in 2007. 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, 2007, we accrued $13,000 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 paid 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, as amended, we agreed to pay The Feinstein Institute to sponsor research activities at The Feinstein Institute in the field of cholinergic anti-inflammatory technology. We paid the Feinstein Institute $200,000 annually until January 2006 and $150,000 in 2006 and $120,000 in 2007 for this sponsored research. 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. Each party has the right to terminate each agreement upon the occurrence of a material uncured breach of that agreement by the other party.

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. At December 31, 2007, we owed $30,000 to The Feinstein Institute in accordance with the January 2003

agreement.

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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 sublicenses to MedImmune and Beckman Coulter of our rights with respect to HMGB1, we have paid The Feinstein Institute $2.5 million and issued to The Feinstein Institute 66,666 shares of our common stock. In connection with our January 2007 sublicense to IMI of our rights with respect to vagus nerve stimulation, we have paid The Feinstein Institute $100,000 and arranged for the issuance by IMI to The Feinstein Institute 100,000 shares of junior preferred stock of IMI.

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 ZYFLO CR covered by SkyePharma s patent rights and know-how. Under the terms of the agreement, SkyePharma also agreed to manufacture ZYFLO CR for clinical trials, regulatory review and, upon FDA approval and subject to negotiating a 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, 2007, we have made milestone payments totaling $3.0 million to SkyePharma under this agreement. In addition, after the FDA approved the NDA for ZYFLO CR in May 2007, we accrued an additional $699,000 in milestone payments we owe to SkyePharma on the first and second anniversary of the approval of the NDA for ZYFLO CR. 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 ZYFLO CR tablets. Each party has the right to terminate the agreement upon the occurrence of a material uncured breach by the other party.

Innovative Metabolics

In January 2007, we entered into an exclusive license agreement with Innovative Metabolics, Inc., or IMI, under which we granted to IMI an exclusive worldwide license under patent rights and know-how controlled by us relating to the stimulation of the vagus nerve to make, use and sell products and methods covered by the licensed patent rights and know-how in the licensed field. The licensed field includes mechanical and electrical stimulation of the vagus nerve and excludes pharmacological modulation of a cholinergic receptor, including the alpha-7 receptor. In consideration for the license, IMI paid us an initial license fee of $400,000 in cash after taking into account payments that we are obligated to make to The Feinstein Institute. In addition, in connection with IMI s first financing, IMI issued us a number of shares of junior preferred stock of IMI equal to the number of shares of preferred stock that could be purchased for $400,000 in such financing after taking into account payments that we are obligated to make to The Feinstein Institute. The junior preferred stock issued to us has a liquidation preference subordinate to the preferred stock issued in such financing. In March 2008, we sold these 400,000 shares of junior preferred stock to two investors, which had participated in IMI s first financing, for an aggregate purchase price of $400,000. The purchase price is subject to adjustment if these investors sell or receive consideration for these shares of junior preferred stock pursuant to an acquisition of IMI prior to February 1, 2009 at a price per share greater than they paid us.

Under this license agreement, IMI also agreed to:

- make a one-time milestone payment to us of $1.0 million upon the achievement of all regulatory approvals from the FDA or any foreign counterpart agency required for the marketing and sale in the applicable country of any product or method covered by the licensed patent rights;

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pay us royalties based on net sales of licensed products and methods by IMI and its affiliates until the expiration of the patent rights covering the licensed product or method in the country of actual or intended use; and

pay us a percentage of any royalties, fees and payments actually received from third parties, with limited exceptions, in connection with sublicenses by IMI of its rights under the licensed patent rights and know-how.

The patent rights and know-how licensed by us to IMI include patent rights and know-how arising from research conducted by The Feinstein Institute under the sponsored research and license agreement, as amended, that we entered into with The Feinstein Institute in January 2003.

Under this license agreement, IMI agreed to be responsible for specified obligations we owe to The Feinstein Institute pursuant to our sponsored research and license agreement. IMI agreed to financially support sponsored research under the sponsored research and license agreement to the extent that the sponsored research is in the licensed field under the IMI license agreement. IMI also agreed to reimburse us for a portion of:

amounts payable to The Feinstein Institute 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; and

minimum annual royalties payable to The Feinstein Institute beginning in the first year after termination of research activities under the sponsored research agreement.

Each party has the right to terminate the license agreement upon the occurrence of a material uncured default by the other party. IMI has the right to terminate the IMI license agreement at any time on 90-days prior written notice to us.

Two of our co-founders, Kevin J. Tracey, M.D. and H. Shaw Warren, M.D., are founders of IMI. Dr. Warren served as a member of our Board of Directors until October 2006. Dr. Tracey is a member of the medical staff at The Feinstein Institute. In addition, we are a party to a consulting agreement with Dr. Tracey that terminates on December 31, 2009. In addition, we were previously a party to a consulting agreement with Dr. Warren that terminated on January 1, 2008. Under our consulting agreement with Dr. Tracey, we agreed to pay certain royalties to Dr. Tracey in connection with selling or sublicensing certain licensed alpha-7 products as defined in the agreement.

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 29, 2008, we own or exclusively license for one or more indications or formulations a total of 16 issued U.S. patents, 45 issued foreign patents, 23 pending U.S. patent applications and 67 pending foreign patent applications consisting of:

	U.S.	**Foreign**	**Program**

	Issued	Pending	Issued	Pending	Total
Zileuton	2	1	18	2	23
HMGB1	10	13	20	39	82
Alpha-7	4	9	7	26	46
Total	16	23	45	67	151

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The U.S. patent covering the composition of matter of zileuton that we licensed from Abbott expires in December 2010. The patent for ZYFLO CR will expire in June 2012 and relates only to the controlled-release technology used to control the release of zileuton. The U.S. issued patents that we own or exclusively license covering our product candidates other than zileuton expire on various dates between 2019 and 2021.

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

Trademarks, Trade Secrets and Other Proprietary Information

We have registered the Critical Therapeutics name and logo in both the United States and the European Community. We have registered CT2 in the United States. We have also filed trademark applications to register CRTX and ZYFLO CR in the United States. In March 2004, we acquired the U.S. trademark for 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

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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 during the IND stage of development and as part of the NDA.

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 may need to be resolved to the satisfaction of the FDA prior to commencement of clinical trials. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The IND process can result in substantial delay and expense.

Clinical trials involve the administration of the investigational new drug or biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and requirements, under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the safety and effectiveness criteria to be evaluated. Each protocol for an unapproved drug 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, safety, including side effects associated with increasing doses, and, at times, pharmacological actions. 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 all clinical and preclinical safety testing and a compilation of the 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 $1,100,000, the fee for submission of supplemental applications exceeds $580,000 and the manufacturer and/or sponsor under an approved NDA

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are also subject to annual product and establishment user fees, currently exceeding $65,000 per product and up to $392,000 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 and restricted distribution, which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Supplemental applications must be filed for many post-approval changes, including changes in manufacturing facilities.

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

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

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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 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,

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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 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 previous research and development processes involved 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.

A number of large pharmaceutical and biotechnology companies currently market and sell products to treat asthma that compete with ZYFLO CR. Many established therapies currently command large market shares in the asthma

market, including Merck & Co., Inc. s Singulair®, GlaxoSmithKline plc s Advair® and inhaled corticosteroid products. In addition, we may face competition from pharmaceutical companies seeking to develop new drugs for the asthma market. For example, in June 2007, AstraZeneca commercially launched

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in the United States Symbicort®, a twice-daily asthma therapy combining budesonide, an inhaled corticosteroid, and formoterol, a long-acting beta2-agonist.

In the COPD market, PERFOROMIST and zileuton, if we are able to develop it as a treatment for COPD, will face intense competition. COPD patients are currently treated primarily with a number of medications that are indicated for COPD, asthma, or both COPD and asthma. The primary products used to treat COPD are anticholinergics, long-acting beta-agonists and combination long-acting beta-agonists and inhaled corticosteroids. These medications are delivered in various device formulations, including metered dose inhalers, dry powder inhalers and by nebulization. Lung reduction surgery is also an option for COPD patients.

Many therapies for COPD are already well established in the respiratory marketplace, including GlaxoSmithKline s Advair® and Serevent® and Spiriva®, a once-daily muscarinic antagonist from Boehringer Ingleheim GmbH and Pfizer. In April 2007, Sepracor began marketing a direct competitor to PERFOROMIST called Brovana®. Brovana is an isomer of formoterol that is delivered in a nebulized formulation. DEY has sued Sepracor for infringement of DEY s patents, and Sepracor has counterclaimed. Other novel approaches are also in development.

We are also developing zileuton injection for use in the hospital emergency department for the treatment of acute asthma attacks. We may face intense competition from companies seeking to develop new drugs for use in severe acute asthma attacks. For example, Merck & Co., Inc. is conducting clinical trials of an intravenous formulation of its product Singulair®.

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

Our competitors products may be safer, more effective, more convenient 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

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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.

Employees

As of December 31, 2007, we had 80 full-time employees, 52 of whom were engaged in marketing and sales, 13 of whom were engaged in research, development and regulatory affairs, and 15 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*

You should carefully consider the following risk factors, in addition to other information included in this annual report on Form 10-K and the other reports that we file with the Securities and Exchange Commission, in evaluating Critical Therapeutics and our business. If any of the following risks occur, our business, financial condition and operating results could be materially adversely affected.

Risks Relating to Our Business

Our business depends heavily on the commercial success of ZYFLO CR.

ZYFLO CR is currently our only commercially marketed product. We commercially launched ZYFLO CR on September 27, 2007. In February 2008, we discontinued the production and marketing of ZYFLO, the immediate-release formulation of zileuton, which we had commercially launched in October 2005. ZYFLO did not achieve broad market acceptance. If we are able to successfully commercialize ZYFLO CR, we expect it will account for a significant portion of our revenues for the foreseeable future. However, we cannot assure you that ZYFLO CR will not suffer the same lack of broad market acceptance that has affected ZYFLO.

Our product candidates are in early clinical and preclinical stages of development and are a number of years away from commercialization. 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 CR is 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 development or commercialization programs.

If ZYFLO CR does not achieve market acceptance, we may not be able to generate significant revenues unless we are able to successfully develop and commercialize other product candidates.

The commercial success of ZYFLO CR will depend upon its acceptance by the medical community, third-party payors and patients. Physicians will prescribe ZYFLO CR only if they determine, based on experience, clinical data, side effect profiles or other factors, that this product either alone or in combination with other products is appropriate for managing their patient s asthma. We believe that the primary advantage

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of ZYFLO CR over ZYFLO is ZYFLO CR s more convenient dosing schedule, but this advantage may not result in broad market acceptance of ZYFLO CR, and we may experience the same lack of market acceptance with ZYFLO CR that we have experienced with ZYFLO.

Despite being approved by the FDA since 1996, ZYFLO did not achieve broad market acceptance. During the period between our commercial launch of ZYFLO in October 2005 through December 2007, prescription data for ZYFLO indicates that approximately 5,409 physicians prescribed the product. We recorded revenue from the sale of ZYFLO of $8.7 million for the year ended December 31, 2007 and $6.6 million for the year ended December 31, 2006. We recorded revenue from the sale of ZYFLO CR of $2.3 million for the year ended December 31, 2007. We experienced difficulty expanding the prescriber and patient base for ZYFLO, in part, we believe, because some physicians view ZYFLO as less effective than other products on the market or view its clinical data as outdated and because it requires dosing of one pill four times per day, which some physicians and patients may find inconvenient or difficult to comply with compared to other available asthma therapies that require dosing only once or twice daily. In addition, if physicians do not prescribe ZYFLO CR for the recommended dosing regimen of two pills twice daily, or if patients do not comply with the dosing schedule and take less than the prescribed number of tablets, our sales of ZYFLO CR will be limited and our revenues will be adversely affected.

Market perceptions about the safety of ZYFLO may limit the market acceptance of ZYFLO CR. In the clinical trials that were reviewed by the FDA prior to its approval of ZYFLO, 3.2% of the approximately 5,000 patients who received ZYFLO experienced increased levels of a liver enzyme called alanine transaminase, or ALT, of over three times the levels normally seen in the bloodstream. In these trials, one patient developed symptomatic hepatitis with jaundice, which resolved upon discontinuation of therapy, and three patients developed mild elevations in bilirubin. In clinical trials for ZYFLO CR, 1.94% of the patients taking ZYFLO CR in a three-month efficacy trial and 2.6% of the patients taking ZYFLO CR in a six-month safety trial experienced ALT levels greater than or equal to three times the level normally seen in the bloodstream. Because ZYFLO CR can elevate liver enzyme levels, periodic liver function tests are recommended for patients taking ZYFLO CR, based upon its product label, which was approved by the FDA in May 2007. 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 CR and any other zileuton product candidates that we successfully develop and commercialize. As a result, many physicians may have negative perceptions about the safety of ZYFLO CR 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. These negative perceptions could carry over to ZYFLO CR.

The position of ZYFLO CR in managed care formularies, which are lists of approved products developed by managed care organizations, or MCOs, may make it more difficult to expand the current market share for this product. In many instances, ZYFLO CR had been relegated to a third-tier status, which typically requires the highest co-pay for patients. In some cases, MCOs may require additional evidence that a patient had previously failed another therapy, additional paperwork or prior authorization from the MCO before approving reimbursement for ZYFLO CR.

If any existing negative perceptions about ZYFLO persist, we will have difficulty achieving market acceptance for ZYFLO CR. If we are unable to achieve market acceptance of ZYFLO CR, we will not generate significant revenues unless we are able to successfully develop and commercialize other product candidates.

We are considering alternatives to our current business strategy that could significantly impact our future operations and financial position.

In November 2007, we announced that we are in the process of reviewing a range of strategic alternatives that could result in potential changes to our current business strategy and future operations. As part of this process, we are

considering alternatives to our current business strategy designed to maximize the value of our

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commercial organization and product development programs. We have engaged an investment bank to advise us in this process. As a result of this process, we could determine to engage in one or more potential transactions, such as the sale or divestiture of certain of our assets, the sale or merger of our company or other strategic transactions, or to continue to operate our business in accordance with our existing business strategy. Pending any decision to change strategic direction, we are continuing our commercial and development activities in accordance with our existing business strategy with an increased focus on managing our cash position. We cannot assure you that our evaluation of strategic alternatives will lead to a change in our current business strategy, or result in one or more transactions. If we determine to pursue an alternative strategy or engage in a strategic transaction, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management. Because of the significant uncertainty regarding our future plans, we are not able to accurately predict the impact of a potential change in our existing business strategy.

If our marketing and sales infrastructure and presence are not adequate or our collaborative marketing arrangements are not successful, our ability to market and sell our products will be impaired.

After reducing the size of our sales force as part of cost reduction programs that we announced in 2006, we then increased the size of our sales force in connection with the commercial launch of ZYFLO CR. As of February 29, 2008, our sales force consists of approximately 39 sales representatives. Rebuilding our sales force involved significant time and expense. If we are not successful in our efforts to retain an adequate sales force, our ability to market and sell ZYFLO CR will be impaired.

In March 2007, we entered into a co-promotion agreement with Dey, L.P., a wholly-owned subsidiary of Mylan Inc., or DEY, for the co-promotion of ZYFLO CR and ZYFLO. We cannot predict whether the co-promotion arrangement will lead to increased sales for ZYFLO CR. DEY initiated promotional detailing activities for ZYFLO CR on September 27, 2007 and for ZYFLO on April 30, 2007. Given the recent initiation of DEY s efforts, the potential success of the co-promotion arrangement is uncertain. Under the co-promotion agreement, we agreed to provide a minimum number of promotional details per month by our sales representatives to a specified group of office-based physicians and other health care professionals for ZYFLO CR. If we are not successful in our efforts to provide the required level of promotional detailing, DEY s co-promotion fee may be increased and DEY may have a right to terminate the co-promotion agreement for ZYFLO CR. For example, if we experience greater than expected turnover of sales representatives, we may have difficulty satisfying our minimum detailing obligations. In February 2008, Mylan Inc., which acquired DEY in October 2007 as part of its acquisition of Merck KGaA s generic business, of which DEY was a part, announced that it is pursing strategic alternatives for DEY, including the potential sale of the business. Any decision by DEY or Mylan not to devote sufficient resources to the co-promotion arrangement or any future reductions in efforts under the co-promotion arrangement, including as a result of the sale or potential sale of DEY by Mylan, would limit our ability to generate significant revenues from product sales.

On June 25, 2007, as contemplated by the terms of the zileuton co-promotion agreement, we and DEY entered into a separate definitive co-promotion agreement providing for us to co-promote DEY s product PERFOROMIST™ (formoterol fumarate) Inhalation Solution for the long-term, twice-daily maintenance treatment of bronchoconstriction for emphysema and chronic bronchitis, which is also known as chronic obstructive pulmonary disease, or COPD. Under the PERFOROMIST co-promotion agreement, DEY agreed to pay us a co-promotion fee based on retail sales of PERFOROMIST and we agreed to provide a minimum number of promotional details per month by our sales representatives to a specified group of office-based physicians and other health care professionals. If we are not successful in our efforts to provide the required level of promotional detailing for PERFOROMIST, our co-promotion fee may be reduced and DEY may have a right to terminate the PERFOROMIST co-promotion agreement. Promoting both ZYFLO CR and PERFOROMIST may be challenging for our sales representatives and may reduce their efficiency, which could negatively impact our revenues.

The amount of any co-promotion fee that DEY pays to us under the PERFOROMIST co-promotion agreement will be limited if PERFOROMIST does not achieve market acceptance. For example, safety concerns relating to PERFOROMIST may harm potential sales. PERFOROMIST belongs to a class of

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medications known as long-acting beta2-adrenergic agonists, or LABAs, which may increase the risk of asthma-related death. Data from a large placebo-controlled study in the United States comparing the safety of the LABA salmeterol or placebo plus usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding also may apply to formoterol, the active ingredient in PERFOROMIST. For the year ended December 31, 2007, we did not receive any co-promotion fees from DEY in connection with the PERFOROMIST co-promotion agreement because the level of quarterly retail sales for PERFOROMIST did not exceed a specified level. In addition, Mylan s sale or potential sale of DEY could lead to a slower launch of PERFOROMIST, negatively impact retail sales of PERFOROMIST and limit the amount of any co-promotion fee that we are entitled to receive from DEY.

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

We are subject to minimum purchase obligations under our supply agreements with our third-party manufacturers, which require us to buy inventory of the zileuton active pharmaceutical ingredient, or API, and tablet cores for ZYFLO CR. If ZYFLO CR does not achieve the level of demand we anticipate, we may not be able to use the inventory we are required to purchase. As of December 31, 2007, we had $5.6 million in inventory, consisting primarily of tablet cores and API. Based on our current expectations regarding demand for ZYFLO CR, we expect that our inventory levels could increase substantially in the future as a result of our minimum purchase obligations under our supply agreements with third-party manufacturers and orders we have submitted to date. Significant differences between our current estimates and judgments and future estimated demand for our products and the useful life of inventory may result in significant charges for excess inventory or purchase commitments in the future. If we are required to recognize charges for excess inventories, it could have a material adverse effect on our financial condition and results of operations in the period in which we recognize charges for excess inventory.

In the quarter ended December 31, 2007, we reserved for four batches of ZYFLO CR tablet cores which can not be released into our commercial supply chain due to issues associated with their manufacture. We cannot assure you that we will not have similar manufacturing issues in producing ZYFLO CR in the future. If we are unable to manufacture or release ZYFLO CR on a timely and consistent basis, if we fail to maintain an adequate inventory of zileuton API or ZYFLO CR core tablets, if our inventory were to be destroyed or damaged, or if our inventory were to reach its expiration date, patients might not have access to ZYFLO CR, our reputation and our brand could be harmed and physicians may be less likely to prescribe ZYFLO CR 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 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;
- pricing and cost effectiveness;
- the ability to be produced in commercial quantities at acceptable costs;

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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.

An element of our strategy is to develop and commercialize product candidates that address large unmet medical needs. We seek to do so through:

preclinical studies to evaluate product candidates;

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

In addition, subject to having sufficient cash and other resources to develop or commercialize additional products, we may seek to in-license or acquire product candidates or approved products. However, 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. 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.

If we are unable to develop suitable potential product candidates through our preclinical studies, 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 CR, PERFOROMIST 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 CR 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 CR. Many established therapies currently command large market shares in the asthma market, including Merck & Co., Inc. s Singulair®, GlaxoSmithKline plc s Advair® and

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inhaled corticosteroid products. In addition, we may face competition from pharmaceutical companies seeking to develop new drugs for the asthma market. For example, in June 2007, AstraZeneca commercially launched in the United States Symbicort®, a twice-daily asthma therapy combining budesonide, an inhaled corticosteroid, and formoterol, a long-acting beta2-agonist.

In the COPD market, PERFOROMIST and zileuton, if we are able to develop it as a treatment for COPD, will face intense competition. COPD patients are currently treated primarily with a number of medications that are indicated for COPD, asthma, or both COPD and asthma. The primary products used to treat COPD are anticholinergics, long-acting beta-agonists and combination long-acting beta-agonists and inhaled corticosteroids. These medications are delivered in various device formulations, including metered dose inhalers, dry powder inhalers and by nebulization. Lung reduction surgery is also an option for COPD patients.

Many therapies for COPD are already well established in the respiratory marketplace, including GlaxoSmithKline s Advair® and Serevent® and Spiriva®, a once-daily muscarinic antagonist from Boehringer Ingleheim GmbH and Pfizer. In April 2007, Sepracor began marketing a direct competitor to PERFOROMIST called Brovana®. Brovana is an isomer of formoterol that is delivered in a nebulized formulation. DEY has sued Sepracor for infringement of DEY s patents, and Sepracor has counterclaimed. Other novel approaches are also in development.

We are also developing an injectable formulation of zileuton, or zileuton injection, for use in the hospital emergency department for the treatment of acute asthma attacks. We may face intense competition from companies seeking to develop new drugs for use in severe acute asthma attacks. For example, Merck & Co., Inc. is conducting clinical trials of an intravenous formulation of its product Singulair®.

If our therapeutic programs directed toward the body s inflammatory response result in commercial products, such products will compete predominantly with therapies that have been approved for diseases such as rheumatoid arthritis, like Amgen, Inc. s Enbrel®, Johnson & Johnson s Remicade®, Bristol-Myers Squibb Company s Orencia®, Abbott Laboratories Humira® and Rituxan® marketed by Biogen Idec Inc. and Genentech, Inc., and diseases such as sepsis, like Eli Lilly and Company s Xigris®. 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.

Our competitors products may be safer, more effective, more convenient 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 are unable to retain key personnel and hire additional qualified personnel, we may not be able to achieve our goals.

Our success depends in large part on our ability to attract, retain and motivate qualified management and commercial personnel. We are highly dependent on the principal members of our executive management team. The loss of the services of any one or more of the members of our executive management team 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 the members of our executive management team.

On March 2, 2008, Frank E. Thomas resigned as our President and Chief Executive Officer effective March 31, 2008 and as a member of our board of directors effective March 2, 2008. On March 4, 2008, we announced that our board of directors appointed Trevor Phillips, Ph.D. as President and Chief Executive Officer effective April 1, 2008 and elected Dr. Phillips as a member of our board of directors effective March 4, 2008. Dr. Phillips currently serves as our Chief Operating Officer and Senior Vice President of Operations. In addition to Dr. Phillips, we also depend, in particular, on the continuing services of Thomas P. Kelly, our Chief Financial Officer and Senior Vice President of Finance and Corporate Development, and other members of our executive management team. Since June 1, 2006, we have experienced significant turnover on our executive management team, with five executive officers, including Mr. Thomas, leaving our company and one executive officer joining our company. If we are unsuccessful in transitioning our smaller executive management team to compensate for the loss of Mr. Thomas and these other executives, the achievement of our research, financial, development and commercialization objectives could be significantly delayed or may not occur. In addition, our focus on transitioning to our new management team could divert our management s attention from other business concerns. Furthermore, if we decide to recruit new executive personnel, we will incur additional costs.

Recruiting and retaining qualified commercial personnel, in addition to our executive management team, will also be critical to our success. Any 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. These demands may require us to hire additional 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 have experienced turnover in our sales and marketing team. For example, we have experienced an increase in the number of voluntary resignations of our sales and marketing personnel after we publicly announced in November 2007 that we are in the process of reviewing a range of strategic alternatives that could result in potential changes to our current business strategy and future operations. If we are not successful in our efforts to retain qualified sales and marketing personnel, our ability to market and sell ZYFLO CR and our ability to deliver our required level of promotional detailing under our co-promotion agreements with DEY would be impaired.

We have also experienced turnover on our board of directors. For example, we have had eight directors leave our board and three directors join our board since June 1, 2006. We currently have four directors serving on our board. If our board were to fail to satisfy the requirements of relevant rules and regulations of the Securities and Exchange Commission, or SEC, and The NASDAQ Stock Market, relating to director independence or membership on board committees, this could result in the delisting of our common stock from the NASDAQ Stock Market or could adversely affect investors confidence in our company and our ability to access the capital markets. If we are unable to attract and retain qualified directors, the achievement of our corporate objectives could be significantly delayed or may not occur.

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We identified a material weakness in our internal control over financial reporting for the second quarter and third quarter of 2007. If we fail to achieve and maintain effective internal control over financial reporting, we could face difficulties in preparing timely and accurate financial reports, which could result in a loss of investor confidence in our reported results and a decline in our stock price.

In connection with the preparation of our financial statements for the second quarter of 2007, we identified a material weakness in our internal control over financial reporting as discussed in Item 9A of this annual report on Form 10-K and as previously reported in our quarterly reports on Form 10-Q for the quarters ended June 30, 2007 and September 30, 2007. As a result of this material weakness, our management concluded that our disclosure controls and procedures were not effective as of either June 30, 2007 or September 30, 2007. We implemented steps to remedy the material weakness and our management provided an unqualified assessment of our internal controls over financial reporting for the year ended December 31, 2007. Any failure or difficulties in maintaining these procedures and controls could cause us to fail to meet our periodic reporting obligations or result in our inability to prevent or detect material misstatements in our financial statements. It is possible that our management may not be able to provide an unqualified assessment of our internal control over financial reporting or disclosure controls and procedures in the future, or be able to provide quarterly certifications that our disclosure controls and procedures are effective. It is also possible that we may identify additional significant deficiencies or material weaknesses in our internal control over financial reporting in the future. Any material weakness, or any remediation thereof that is ultimately unsuccessful, could cause investors to lose confidence in the accuracy and completeness of our financial statements, which in turn could harm our business, lead to a decline in our stock price and restrict our ability to raise additional funds needed for the growth of our business.

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;

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;

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state food and drug laws, pharmacy acts and state pharmacy board regulations, which govern the 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.

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.

If our past or present operations are found to be in violation of any of the laws described above or other laws or 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 in November 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 CR in the market could be harmed.

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, Nevada, New Mexico, Vermont and West Virginia, as well as the District of Columbia have enacted legislation requiring pharmaceutical

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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, a California statute effective July 1, 2005 requires pharmaceutical companies to adopt and post on their public web site a comprehensive compliance program that complies 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, Nevada, 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.

Recently enacted legislation may make it more difficult and costly for us to obtain regulatory approval of our product candidates and to produce, market and distribute our existing products.

On September 27, 2007, President Bush signed into law the Food and Drug Administration Amendments Act of 2007, or the FDAAA. The FDAAA grants a variety of new powers to the FDA, many of which are aimed at assuring drug safety and monitoring the safety of drug products after approval. Under the FDAAA, companies that violate the new law are subject to substantial civil monetary penalties. While we expect the FDAAA to have a substantial effect on the pharmaceutical industry, the extent of that effect is not yet known. As the FDA issues regulations, guidance and interpretations relating to the new legislation, the impact on the industry, as well as our business, will become more clear. The new requirements and other changes that the FDAAA imposes may make it more difficult, and likely more costly, to obtain approval of new pharmaceutical products and to produce, market and distribute existing products.

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 CR and our other 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 and had approximately 80 employees as of December 31, 2007. 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 become applicable to us 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

registered public 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 have implemented do not comply with all of the relevant rules and regulations of the SEC and The

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NASDAQ Stock Market, we may be subject to sanctions or investigation by regulatory authorities, including the SEC or The NASDAQ Stock 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 and could result in the delisting of our common stock from the NASDAQ Stock Market. 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 the payment rate or reimbursement could result in decreased use or sales of our products.

Our sales of ZYFLO CR are, and any future sales of our product candidates will be, 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. For example, the Medicare Prescription Drug Improvement and Modernization Act of 2003, or the MMA, was signed into law in December 2003. Legislative or administrative acts that reduce reimbursement for our products could adversely impact our business. In addition, we believe that private insurers, such as 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 our product candidates, including ZYFLO CR, and current reimbursement policies for marketed products may change at any time.

The MMA established a prescription drug benefit that became effective in 2006 for all Medicare beneficiaries. We cannot be certain that ZYFLO CR, or any of our product candidates still in development, 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 CR 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 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 are in the

development stage, we do not know the level of reimbursement, if any, we will receive for those product candidates if they are successfully developed. If the reimbursement we receive for any of our product candidates is inadequate in light of our development and

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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.

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 CR, ZYFLO or one or more of our other 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 CR and ZYFLO and clinical trial liability claims for our product candidates. We may seek additional product liability insurance prior to marketing any of our other product candidates still in development. 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.

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 our product candidates under development, our business may be unsuccessful.

Neither we nor any of our collaborators may market any of our products or our product candidates under development in the United States, Europe or in any other country without marketing approval from the FDA or the equivalent foreign regulatory agency. ZYFLO CR is currently our only commercial product and can only be marketed in the United States.

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.

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 the required regulatory approval or clearance to market any of our 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

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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.

For example, in March 2006, we announced that we had discontinued a Phase II clinical trial of ethyl pyruvate, which we refer to as CTI-01, a small molecule product candidate that we had been developing for prevention of complications that can occur in patients after cardiopulmonary bypass, a procedure commonly performed during heart surgery. After reviewing the final data from the trial, we decided to discontinue further development of CTI-01. We subsequently terminated, effective in February 2007, the license agreements between us and the University of Pittsburgh and Xanthus Pharmaceuticals, Inc., formerly Phenome Sciences, Inc., related to patent rights related to CTI-01 controlled by University of Pittsburgh and Xanthus.

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 would 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;
- 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;

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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 preclinical 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 seasonality of the disease, 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. Delays in patient enrollment and the related increase in costs also could cause us to decide to discontinue a clinical trial prior to completion of the trial.

For example, in March 2008, we discontinued our Phase IV clinical trial for ZYFLO CR designed to generate data in the current patient treatment setting because of patient enrollment that was significantly slower than we had anticipated. We initiated the trial in July 2007 and had enrolled only approximately 25% of the patients prior to discontinuing the trial. We had planned to use data from this trial to support ZYFLO CR s market position and we may have increased difficulty promoting ZYFLO CR to physicians without this data.

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 products and 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 products and 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 ZYFLO CR, tablet cores and API and 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.

As part of the approval of the NDA for ZYFLO CR in May 2007, the FDA required us to conduct a pediatric clinical trial of ZYFLO CR as a post-approval commitment and report the results to the FDA by June 2010. If we do not successfully begin and complete this clinical trial in the time required by the FDA, our ability to market and sell ZYFLO CR may be hindered, and our business may be harmed as a result.

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Numerous proposals have been made in recent months and years to impose new requirements on drug approvals, expand post-approval requirements, and restrict sales and promotional activities. For example, a new drug application, or NDA, requires that an applicant submit risk evaluation and minimization plans to monitor and address potential safety issues for products upon approval, and federal legislation has been proposed that would require all new drug applicants to submit risk evaluation and minimization plans to monitor and address potential safety issues for products upon approval, grant the FDA the authority to impose risk management measures for marketed products and to mandate labeling changes in certain circumstances, and establish new requirements for disclosing the results of clinical trials. Additional measures have also been proposed to address perceived shortcomings in the FDA s handling of drug safety issues, and to limit pharmaceutical company sales and promotional practices that some see as excessive or improper. If these or other legal or regulatory changes are enacted, it may become more difficult or burdensome for us to obtain extended or new product approvals, and our current approvals may be restricted or subject to onerous post-approval requirements. Such changes may increase our costs and adversely affect our operations. The ability of us or our partners to commercialize approved products successfully may be hindered, and our business may be harmed as a result.

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 adversely 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 adversely affect our ability to develop, market and sell our product candidates successfully and could harm our reputation and hinder 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 DEY to jointly promote and market ZYFLO CR. This co-promotion arrangement may not be successful.

We are relying on DEY to jointly promote and market ZYFLO CR. ZYFLO CR is our only commercially marketed product. Our ability to generate meaningful near-term revenues from product sales is substantially dependent on the success of our co-promotion arrangement with DEY. DEY initiated promotional detailing activities for ZYFLO CR in September 2007 after initiating promotional detailing for ZYFLO in April 2007. We cannot predict if DEY s promotional detailing activities will have a meaningful impact on our revenues from ZYFLO CR.

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After September 27, 2010, DEY may terminate the co-promotion agreement with six-months, advance written notice. In addition, DEY has the right to terminate the co-promotion agreement with two-months, prior written notice if ZYFLO CR cumulative net sales for any four consecutive calendar quarters after commercial launch of ZYFLO CR are less than $25 million. Each party has the right to terminate the co-promotion agreement upon the occurrence of a material uncured breach by the other party. Both we and DEY have agreed to use diligent efforts to promote the applicable products in the United States during the term of the co-promotion agreement. In particular, both we and DEY have agreed to provide a minimum number of details per month for ZYFLO CR. We also rely on DEY to provide the support of its managed care group to negotiate contracts and engage in other activities with third-party payors for favorable managed care access. This managed care support includes advice and logistical support to us regarding our managed care strategy.

If DEY were to terminate or breach the co-promotion agreement, and we were unable to enter into a similar co-promotion agreement with another qualified party in a timely manner or devote sufficient financial resources or capabilities to independently promoting and marketing ZYFLO CR, our sales of ZYFLO CR would be limited and we would not be able to generate significant revenues from product sales. In addition, DEY may choose not to devote time, effort or resources to the promotion and marketing of ZYFLO CR beyond the minimum required by the terms of the co-promotion agreement. DEY is a subsidiary of Mylan Inc. Mylan acquired DEY in October 2007 as part of its acquisition of Merck KGaA s generic business, of which DEY was a part. We cannot predict what impact Mylan s acquisition of DEY may have on our co-promotion arrangement with DEY. For example, in February 2008, Mylan announced that it is pursuing strategic alternatives for DEY, including the potential sale of the business. Any decision by DEY or Mylan not to devote sufficient resources to the co-promotion arrangement or any future reduction in efforts under the co-promotion arrangement, including as a result of the sale or potential sale of DEY by Mylan, would limit our ability to generate significant revenues from product sales. Furthermore, if DEY does not have sufficient sales capabilities, as a result of difficulty retaining or hiring sales representatives following Mylan s announcement that it is pursuing strategic alternatives for DEY or otherwise, then DEY may not be able to meet its minimum detailing obligations under the co-promotion agreement.

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, Inc., a wholly-owned subsidiary of AstraZeneca PLC, 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 prior to October 2005, when we commercially launched ZYFLO, were 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 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

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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, curtailment or termination of our HMGB1 program could significantly harm our future prospects.

Our license agreement with Beckman Coulter generally is terminable by Beckman Coulter 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.

In June 2007, AstraZeneca PLC completed its acquisition of MedImmune and MedImmune became a wholly-owned subsidiary of AstraZeneca. We cannot predict what impact this transaction may have on our HMGB1 collaboration with MedImmune. If MedImmune does not devote sufficient time and resources to our collaboration or changes the focus of its programs, it could delay or prevent the achievement of clinical, regulatory and commercial milestones and prevent us from realizing the potential commercial benefits of the collaboration.

We intend to enter into collaboration agreements with other parties in the future that relate to our other product candidates, and we are likely to have similar risks with regard to any such future collaborations.

IMI may not be successful in developing a product under the patent rights and know-how that we licensed to IMI relating to the mechanical and electrical stimulation of the vagus nerve.

We have licensed to Innovative Metabolics, Inc., or IMI, patent rights and know-how relating to the mechanical and electrical stimulation of the vagus nerve. IMI is an early-stage company. We are not involved in IMI s efforts to develop and commercialize a medical device based on the intellectual property that we licensed to IMI. We will

receive additional payments under the IMI license only if IMI is successful in achieving full regulatory approval of such a device or receives a royalty, fee or other payment from a third party in connection with a sublicense of its rights under our license agreement.

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We rely on third parties to manufacture and supply the zileuton API, ZYFLO CR and our product candidates. We expect to continue to rely on these sole source suppliers 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 commercialize ZYFLO CR, develop product candidates, apply for regulatory approvals and commercialize our product candidates, we need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities. We expect to continue to rely on third parties for production of the zileuton API, commercial supplies of ZYFLO CR and preclinical and clinical supplies of our product candidates. These third parties are currently our sole source suppliers, and we expect to continue to rely on them for these purposes for the foreseeable future.

We have contracted with Shasun Pharma Solutions Ltd. for commercial production of the zileuton API, subject to specified limitations, through December 31, 2010. Zileuton API is used in our FDA-approved oral zileuton product, ZYFLO CR, as well as in our zileuton injection product candidate. Our only source of supply for zileuton API is Shasun, which manufactures the zileuton API in the United Kingdom. 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 zileuton API could be disrupted or delayed if a batch is discontinued or damaged, if the manufacturing sites are damaged, or if local health and safety regulations require a third-party manufacturer to implement additional safety procedures or cease production. In addition, there is only one qualified supplier of a chemical known as 2-ABT, which is one of the starting materials for zileuton, and if that manufacturer stops manufacturing 2-ABT, is unable to manufacture 2-ABT or is unwilling to manufacture 2-ABT on commercially reasonable terms or at all, Shasun may be unable to manufacture API for us.

We have contracted with SkyePharma PLC, through its subsidiary Jagotec AG, for the manufacture of core tablets for ZYFLO CR for commercial sale. Our only source of supply for the core tablets of ZYFLO CR is SkyePharma, which manufactures them in France. The manufacture of the core tablets for ZYFLO CR could be disrupted or delayed if one or more batches are discontinued or damaged or if the manufacturing site were damaged or destroyed. In January 2007, following a decision to concentrate on oral and pulmonary products, SkyePharma announced that it had reached an agreement for the sale of its injectable business. If SkyePharma sells all or a part of its remaining business or the manufacturing site for the core tablets of ZYFLO CR, our ability to produce ZYFLO CR may be impaired.

We have contracted with Patheon Pharmaceuticals Inc. to coat and package the core tablets of ZYFLO CR for commercial supplies. Patheon is currently our only source of finished ZYFLO CR tablets. The manufacture of the finished ZYFLO CR tablets could be disrupted or delayed if one or more batches are discontinued or damaged or if the manufacturing site were damaged or destroyed.

We are dependent upon Shasun, 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. For example, during the quarter ended March 31, 2008, one of our contract manufacturers failed to meet our manufacturing specifications relating to certain manufacturing batches of ZYFLO CR. 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 meet commercial demands for ZYFLO CR;

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

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

we may be delayed in submitting applications for regulatory approvals for our product candidates.

If Shasun, Patheon or SkyePharma experiences any significant difficulties in their respective manufacturing processes for our products including the zileuton API, ZYFLO CR core tablets or finished

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product for ZYFLO CR, we could experience significant interruptions in the supply of ZYFLO CR. Our inability to coordinate the efforts of our third-party manufacturing partners, or the lack of capacity or the scheduling of manufacturing sufficient for our needs at our third-party manufacturing partners, could impair our ability to supply ZYFLO CR at required levels. Such an interruption could cause us to incur substantial costs and impair our ability to generate revenue from ZYFLO CR may be adversely affected.

The zileuton API is manufactured in United Kingdom by Shasun, and we either store the zileuton API at a Shasun warehouse, ship the zileuton API either directly to a contract manufacturer or to a third-party warehouse. For the manufacture of ZYFLO CR, we ship zileuton API to France for manufacturing of core tablets by SkyePharma and we ship core tablets from France to the United States to be coated, packaged and labeled at Patheon. While in transit, our zileuton API and ZYFLO CR core tablets, each shipment of which is of significant value, could be lost or damaged. Moreover, at any time after shipment from Shasun, our zileuton API, which is stored in the United States at Patheon or at third-party warehouse, or our ZYFLO CR core tablets, which are stored at Patheon prior to coating and packaging, and our finished ZYFLO CR products, which are stored at our third-party logistics provider, Integrated Commercialization Solutions, Inc., or ICS, could be lost or suffer damage, which would render them unusable. We have attempted to take appropriate risk mitigation steps and to obtain transit insurance. However, depending on when in the process the zileuton API, ZYFLO CR core tablets or finished product is lost or damaged, we may have limited recourse for recovery against our manufacturers or insurers. As a result, our financial performance could be impacted by any such loss or damage to our zileuton API, ZYFLO CR core tablets or finished product.

We may not be able to enter into alternative supply arrangements at commercially acceptable rates, if at all. If we were required to change manufacturers for the zileuton API or ZYFLO CR tablet cores or coating, 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. In addition, we would be required to conduct additional clinical bioequivalence trials to demonstrate that ZYFLO CR manufactured by the new manufacturer is equivalent to ZYFLO CR manufactured by our current manufacturer. Any delays associated with the verification of a new manufacturer or conducting additional clinical bioequivalence trials could adversely affect our production schedule or increase our production costs.

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. 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 develop and commercialize our product candidates successfully.

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

We rely on third parties to distribute ZYFLO CR to pharmacies. We have contracted with ICS, a third-party logistics company, to warehouse and distribute ZYFLO CR to three primary wholesalers, AmerisourceBergen Corporation, Cardinal Health and McKesson Corporation, and a number of smaller wholesalers. ICS is our exclusive supplier of commercial distribution logistics services. The wholesalers in turn distribute to chain and independent pharmacies. Sales to AmerisourceBergen Corporation, Cardinal Health and McKesson Corporation collectively accounted for at least 95% of our annual billings for ZYFLO CR and ZYFLO during 2007. The loss of any of these wholesaler customers accounts or a material reduction in their purchases could harm our business, financial condition and results of operations.

We rely on Phoenix Marketing Group LLC to distribute product samples to our sales representatives, who in turn distribute samples to physicians and other prescribers who are authorized under state law to receive

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and dispense samples. We rely on RxHope to administer our patient assistance program and to distribute samples of ZYFLO CR 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 ICS, 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, we lack the resources and experience to establish any of these functions and we do not intend to establish these functions in the foreseeable future. If we were 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, the distribution of ZYFLO CR could be delayed or interrupted, which would damage 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 CR 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 may seek to enter into additional collaboration agreements with pharmaceutical or biotechnology companies to fund all or part of the costs of drug development and commercialization of product candidates. For example, we have determined to seek to enter into collaboration arrangements with respect to the development of our alpha-7 product candidates and our zileuton injection product candidate. We face, and will continue to face, significant competition in seeking appropriate collaborators. Moreover, collaboration agreements are complex and time consuming to negotiate, document and implement. 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 develop or 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.

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Risks Relating to Intellectual Property and Licenses

If we or our licensors are not able to obtain and enforce patent and other intellectual property protection for our discoveries or discoveries we have in-licensed, 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, develop or license 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. The composition of matter patent for zileuton in the United States will expire in December 2010. The patent for ZYFLO CR, which relates only to the controlled-release technology used to control the release of zileuton, will expire in June 2012. We are exploring strategies to extend and expand the patent protection for our zileuton products, but we may not be able to obtain additional patent protection.

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, and because even patent applications for which no request for non-publication is made are not published until approximately 18 months after filing, 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 such patent applications of others. There may also be prior art that may prevent allowance of our patent applications or enforcement of our or our licensors issued patents.

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

Our confidentiality agreements with our current and potential collaborators, employees, consultants, strategic partners, outside scientific collaborators and sponsored researchers and other advisors may not effectively prevent disclosure of our confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. 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.

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Litigation regarding patents, patent applications and other proprietary rights is expensive and time consuming. If we are unsuccessful in litigation or other adversarial proceedings concerning patents or patent applications, 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 patent applications could take place in the United States or foreign courts or in the United States or foreign patent offices or other administrative agencies. Proceedings involving our patents or patent applications could result in adverse decisions regarding:

- the patentability of our applications, 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 or to bring such 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.

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

- incur substantial monetary damages, potentially including treble damages, if we are found to have willfully infringed on such parties patent rights;
- encounter significant delays in bringing our product candidates to market; or
- be precluded from participating in the manufacture, use or sale of our products or methods of treatment.

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

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

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

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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 our zileuton products, our 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.

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 $37.0 million in the year ended December 31, 2007 and $48.8 million in the year ended December 31, 2006. As of December 31, 2007, we had an accumulated deficit of approximately $191.4 million. For the year ended December 31, 2007, we recorded $11.0 million of revenue from the sale of ZYFLO and ZYFLO CR 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. We expect that the losses that we incur will fluctuate from quarter to quarter and that these fluctuations may be substantial. We will need to generate significant revenues to achieve profitability. Until we are able to generate such revenues, we will not be profitable and 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 support ongoing sales and marketing efforts for ZYFLO CR and to fund the development of our other product candidates. Our funding requirements will depend on numerous factors, including:

- the ongoing costs of marketing ZYFLO CR;
- the scope, costs and results of our clinical trials on ZYFLO CR and zileuton injection;
- the amount and timing of sales and returns of ZYFLO CR and ZYFLO;
- the costs of ongoing sales, marketing and manufacturing activities for ZYFLO CR;
- the time and costs involved in preparing, submitting, obtaining and maintaining regulatory approvals for our other product candidates;
- the timing, receipt and amount of milestone and other payments, if any, from DEY, MedImmune, Beckman Coulter, IMI or future collaborators or licensees;
- the timing, receipt and amount of sales and royalties, if any, from our product candidates;

continued progress in our research and development programs, as well as the magnitude of these programs, including milestone payments to third parties under our license agreements;

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

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

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

our ability to establish and maintain additional collaborative or co-promotion arrangements; and

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the ongoing time and costs involved in 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 DEY and MedImmune, sales of ZYFLO CR and ZYFLO represent our only sources of cash flow and revenue. We believe that our ability to access external funds will depend upon market acceptance of ZYFLO CR, 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 successfully commercialize ZYFLO CR. Based on our current 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 into the second quarter of 2009.

For the year ended December 31, 2007, our net cash used for operating activities was $14.4 million, and we had minimal capital expenditures. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional products or 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.

As a result of our recurring losses from operations, accumulated deficit and our expectation that we will incur substantial additional operating costs for the foreseeable future, as discussed in Note 1 to our consolidated financial statements, there is substantial doubt about our ability to continue as a going concern. Our ability to continue as a going concern will require us to obtain additional financing to fund our operations. We have prepared our financial statements on the assumption that we will continue as a going concern, which contemplates the realization of assets and discharge of liabilities in the normal course of business. Doubt about our ability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees.

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 those 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. For example, our reserve for potential returns for ZYFLO CR and ZYFLO is based on our historical experience of product returns for ZYFLO and other factors that could significantly impact expected returns. 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.

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Risks Relating to Our Common Stock

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

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

If we fail to continue to meet all applicable continued listing requirements of The NASDAQ Global Market and NASDAQ determines to delist our common stock, the market liquidity and market price of our common stock could decline.

Our common stock is listed on The NASDAQ Global Market. In order to maintain that listing, we must satisfy minimum financial and other continued listing requirements. For example, NASDAQ rules require that we maintain a minimum bid price of $1.00 per share for our common stock. Between January 1, 2008 and March 20, 2008, the closing bid price per share of our common stock has ranged from $0.72 to $1.38. As of March 20, 2008, the closing bid price per share of our common stock was $0.72. If the closing bid price per share of our common stock falls below $1.00 for a period of 30 consecutive business days, we could be subject to delisting. In addition, to retain our listing on The NASDAQ Global Market we must maintain either minimum stockholders equity of $10.0 million or an aggregate market value of our common stock of $50.0 million. We may not continue to meet the minimum bid price requirement under NASDAQ rules or the other applicable continued listing requirements for The NASDAQ Global Market.

If we fail to continue to meet all applicable continued listing requirements of The NASDAQ Global Market in the future and NASDAQ determines to delist our common stock or transfer our listing from The NASDAQ Global Market to The NASDAQ Capital Market, a trading market for smaller companies, an active trading market for our common stock may not be sustained and the market price of our common stock could decline. If an active trading market for our common stock is not sustained, it will be difficult for our stockholders to sell shares of our common stock without further depressing the market price of our common stock or at all. A delisting of our common stock also could make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees.

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 CR;
- 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 CR;

the amount of rebates, discounts and chargebacks to wholesalers, Medicaid and managed care organizations related to ZYFLO CR;

the amount and timing of product returns for ZYFLO CR and ZYFLO;

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

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 that 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 CR;

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.

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 29, 2008, our directors, executive officers and 10% or greater stockholders, together with their affiliates, to our knowledge, beneficially owned, in the aggregate, approximately 24.3% of our outstanding common stock. As a result, our directors, executive officers and 10% or greater stockholders, together with their affiliates, if acting together, may have the ability to affect 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.

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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, anti-takeover provisions to which we are subject include provisions in our by-laws providing that stockholders meetings may be called only by our president or the majority of our 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 sublease approximately 11,298 square feet of office space in Lexington, Massachusetts. The sublease expires on February 28, 2009, and we have an option to extend the term of the sublease for an additional six months. We believe our facilities are sufficient to meet our needs for the foreseeable future.

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 fourth quarter of the year ended December 31, 2007.

EXECUTIVE OFFICERS OF THE REGISTRANT

Our executive officers, their ages and their positions as of March 19, 2008 are as follows:

Name	Age	Position
Frank E. Thomas	38	President and Chief Executive Officer

Trevor Phillips, Ph.D.	46	Chief Operating Officer and Senior Vice President of Operations and Director
Thomas P. Kelly	37	Chief Financial Officer and Senior Vice President of Finance and Corporate Development
Scott B. Townsend, J.D.	41	Senior Vice President of Legal Affairs, General Counsel and Secretary
Jeffrey E. Young	35	Vice President of Finance, Chief Accounting Officer and Treasurer

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Frank E. Thomas has served as our President since June 2006 and as our Chief Executive Officer since December 2006. Mr. Thomas served as a member of our board of directors from June 2006 until March 2008. On March 2, 2008, Mr. Thomas resigned as our President and Chief Executive Officer effective March 31, 2008 and as a member of our board of directors effective March 2, 2008. Mr. Thomas served as our Chief Financial Officer from April 2004 to June 2006, as our Treasurer from May 2004 to June 2006, as our Senior Vice President of Finance from December 2004 until June 2006 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.

Trevor Phillips, Ph.D. has served as our Chief Operating Officer since November 2003 and as our Senior Vice President of Operations since December 2004. On March 4, 2008, we announced that our board of directors appointed Dr. Phillips as our President and Chief Executive Officer effective April 1, 2008 and elected Dr. Phillips as a member of our board of directors effective March 4, 2008. Dr. Phillips served as our Secretary from March 2004 to September 2004, as our Treasurer from September 2003 to May 2004 and as our Vice President of Operations from October 2002 to December 2004. From November 2001 to September 2002, Dr. Phillips served as Senior Program Director for Sepracor, Inc., a pharmaceutical company. From October 1999 to November 2001, Dr. Phillips served as Director of Drug Development, Strategy and Planning for Scotia Holdings plc, a biotechnology company. From March 1997 to October 1999, Dr. Phillips served as a Senior Manager, Strategic Planning for Accenture Ltd. (formerly known as Andersen Consulting), a management consulting company. From March 1990 to March 1997, Dr. Phillips served in a variety of positions, including Director of Strategic Direction, for GlaxoWellcome plc, a pharmaceutical company. Dr. Phillips holds a B.Sc. in Microbiology from the University of Reading, a Ph.D. in Microbial Biochemistry from the University of Wales and an M.B.A. from Henley Management College.

Thomas P. Kelly has served as our Chief Financial Officer and Senior Vice President of Finance and Corporate Development since August 2007. From July 2003 to August 2007, Mr. Kelly served as a principal in life sciences investment banking at Canaccord Adams, Inc., an investment banking firm. From June 1998 to July 2002, Mr. Kelly served as vice president of life sciences investment banking at Robertson Stephens, Inc., an investment banking firm. From September 1996 to June 1998, Mr. Kelly served as an associate with Foley, Hoag & Eliot LLP, a law firm. Mr. Kelly holds a B.S. in Foreign Service from Georgetown University and a J.D. from The University of Chicago School of Law.

Scott B. Townsend, J.D. has served as our Senior Vice President of Legal Affairs since March 2007, as our Secretary since September 2004 and as our General Counsel since June 2006. Mr. Townsend served as our Vice President of Legal Affairs from August 2004 to March 2007. 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.

Jeffrey E. Young has served as our Vice President of Finance, Chief Accounting Officer and Treasurer since June 2006. Mr. Young served as our Senior Director of Finance from April 2006 to June 2006 and as our Director of Financial Planning and Analysis from April 2005 to March 2006. From March 2003 to April 2005, Mr. Young served in a variety of finance positions with PerkinElmer, Inc., a life and analytical science and photonic instrument

company, including most recently as Senior Manager of Consolidation and Technical Accounting. From September 1996 to March 2003, Mr. Young was employed by the registered public accounting firm PricewaterhouseCoopers LLP, including as a manager from 2000 to March 2003. Mr. Young is a certified public accountant and holds a B.S. in Business Administration from Georgetown University.

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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 trades on the NASDAQ Global Market under the symbol CRTX. Prior to July 2006, our common stock traded on the NASDAQ National Market. The following table sets forth, for the periods indicated, the high and low sales prices for our common stock on the NASDAQ Stock Market.

Year Ended December 31, 2007	**High**	**Low**
First Quarter (from January 1 to March 31)	$ 2.59	$ 1.50
Second Quarter (from April 1 to June 30)	$ 3.23	$ 1.60
Third Quarter (from July 1 to September 30)	$ 2.51	$ 1.71
Fourth Quarter (from October 1 to December 31)	$ 2.52	$ 1.27

Year Ended December 31, 2006	**High**	**Low**
First Quarter (from January 1 to March 31)	$ 7.20	$ 4.92
Second Quarter (from April 1 to June 30)	$ 5.43	$ 3.37
Third Quarter (from July 1 to September 30)	$ 4.14	$ 2.15
Fourth Quarter (from October 1 to December 31)	$ 2.79	$ 1.52

On March 20, 2008, the closing price per share of our common stock as reported on the NASDAQ Global market was $0.72, and we had approximately 125 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.

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

Not applicable.

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Stock Performance Graph

The stock performance graph below compares the cumulative total stockholder return for our common stock with the cumulative total return of the NASDAQ Composite Index, the NASDAQ Biotechnology Index, which we refer to as the NASDAQ Biotech Index, and the American Stock Exchange Biotechnology Index, which we refer to as the AMEX Biotech Index. The comparison assumes the investment of $100.00 on May 27, 2004, the date our common stock was first publicly traded, in each of our common stock, the NASDAQ Composite Index, the NASDAQ Biotech Index and the AMEX Biotech Index and assumes the reinvestment of dividends.

The graph below and related information shall not be deemed soliciting material or filed with the Securities and Exchange Commission or otherwise subject to the liabilities of Section 18 of the Exchange Act, nor shall such information be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent we specifically request that such information be treated as soliciting material or specifically incorporate such information by reference into a document filed under the Securities Act or the Exchange Act.

Critical Therapeutics, Inc.
Performance Graph

04	**12/31/04**	**3/31/05**	**6/30/05**	**9/30/05**	**12/31/05**	**3/31/06**	**6/30/06**	**9/30/06**	**12/31/06**
39	$ 112.68	$ 95.63	$ 98.87	$ 132.68	$ 101.13	$ 71.69	$ 50.70	$ 33.80	$ 28.73
82	$ 110.06	$ 101.31	$ 104.42	$ 109.41	$ 112.40	$ 119.55	$ 111.18	$ 115.78	$ 124.06
34	$ 100.39	$ 84.99	$ 90.21	$ 102.56	$ 103.28	$ 109.94	$ 97.10	$ 98.61	$ 104.39
84	$ 105.72	$ 95.73	$ 109.64	$ 125.97	$ 132.26	$ 138.49	$ 128.96	$ 130.08	$ 146.51

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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 annual report on Form 10-K 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, 2007, 2006 and 2005 and the balance sheet data as of December 31, 2007 and 2006 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, 2004 and 2003 and the balance sheet data as of December 31, 2005, 2004 and 2003 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.

Effective January 1, 2006, we adopted SFAS 123(R), using the modified prospective method, which requires us to recognize compensation cost for granted, but unvested, awards, new awards and awards modified, repurchased, or cancelled after January 1, 2006 and granted after we became a public company. The amounts for prior periods do not include the impact of SFAS 123(R). In the notes to our consolidated financial statements included herein, we have provided pro forma disclosures for the year ended December 31, 2005 in accordance with SFAS 123 since that period has not been restated to conform to the 2007 and 2006 presentation.

	Year Ended December 31,				
	2007	2006	2005	2004	2003
	(In thousands, except share and per share data)				
Statements of Operations Data:					
Net product sales	$ 11,008	$ 6,647	$ 387	$	$
Revenue under collaboration and license agreements	1,861	6,431	5,837	4,436	1,021
Total revenues	12,869	13,078	6,224	4,436	1,021
Cost of products sold	4,233	2,222	514		
Research and development	21,655	26,912	29,959	25,578	17,458
Sales and marketing	12,193	18,284	13,671	1,199	
General and administrative	13,572	13,456	11,406	9,679	3,771
Restructuring charges		3,498			
Total costs and expenses	51,653	64,372	55,550	36,456	21,229
Operating loss	(38,784)	(51,294)	(49,326)	(32,020)	(20,208)
Interest income	2,020	2,726	2,427	1,098	191

Interest expense	(209)	(214)	(191)	(172)	(93)
Net loss	(36,973)	(48,782)	(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	$ (36,973)	$ (48,782)	$ (47,090)	$ (33,303)	$ (22,374)
Net loss per common share: Basic and diluted	$ (0.87)	$ (1.37)	$ (1.61)	$ (2.28)	$ (33.99)
Weighted-average basic and diluted shares outstanding	42,580,884	35,529,048	29,276,243	14,631,371	658,204

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	As of December 31,				
	2007	2006	2005	2004	2003
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 33,828	$ 49,038	$ 82,811	$ 78,829	$ 40,078
Working capital	26,380	47,738	70,005	64,357	25,218
Total assets	44,924	58,182	91,819	83,114	45,054
Long-term debt, net of current portion		421	1,489	1,367	720
Redeemable convertible preferred stock					51,395
Accumulated deficit	(191,372)	(154,399)	(105,617)	(58,527)	(27,433)
Total stockholders equity (deficit)	17,091	49,906	72,247	65,408	(24,851)

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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 the related notes included 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 the Risk Factors section of this report.

Summary

Critical Therapeutics, Inc. is a biopharmaceutical company focused on the development and commercialization of products designed to treat respiratory, inflammatory and critical care diseases linked to the body s inflammatory response. Our marketed product is ZYFLO CR, an extended-release formulation of zileuton, which the FDA approved in May 2007 for the prevention and chronic treatment of asthma in adults and children 12 years of age or older. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO CR, ZYFLO and other formulations of zileuton for multiple diseases and conditions. We began selling ZYFLO CR in the United States in September 2007. In January 2008, we requested and received from the FDA a waiver from the requirement to provide six-months notice to cease manufacturing of the immediate-release formulation of zileuton. As a result, we ceased manufacturing and supplying ZYFLO to the market in February 2008. In addition, we are developing an injectable formulation of zileuton, or zileuton injection.

In November 2007, we announced that we are in the process of reviewing a range of strategic alternatives that could result in potential changes to our current business strategy and future operations. As part of this process, we are considering alternatives to our current business strategy designed to maximize the value of our commercial organization and product development programs. We have engaged an investment bank to advise us this process. As a result of this process, we could determine to:

- engage in one or more potential transactions, such as the sale or divestiture of certain of our assets, the merger or sale of our company, or other strategic transactions; or

- continue to operate our business in accordance with our existing business strategy.

Pending any decision to change strategic direction, we are continuing our commercial and development activities in accordance with our existing business strategy with an increased focus on managing our cash position. We cannot assure you that our evaluation of strategic alternatives will lead to a change in our current business strategy or future operations, or result in one or more transactions. If we decide to pursue an alternative strategy or engage in a strategic transaction, the descriptions of our strategy, future operations and financial position, future revenues, projected costs and prospects and the plans and objectives of management in this Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this annual report on Form 10-K may no longer be applicable. Because of the significant uncertainty regarding our future plans, the forward-looking statements contained herein do not reflect the impact of a potential change to our existing business strategy.

On March 13, 2007, we entered into an agreement with Dey, L.P., or DEY, a subsidiary of Mylan Inc., under which we and DEY agreed to jointly promote ZYFLO and ZYFLO CR. Under the co-promotion agreement, DEY paid us a non-refundable upfront payment of $3.0 million upon signing the co-promotion agreement, a milestone payment of $4.0 million following approval by the FDA of the NDA for ZYFLO CR and a milestone payment of $5.0 million following our commercial launch of ZYFLO CR. Under the co-promotion agreement, we record all quarterly net sales

of ZYFLO CR and ZYFLO, after third-party royalties, up to $1.95 million and pay DEY a commission on quarterly net sales of ZYFLO CR and ZYFLO, after third-party royalties, in excess of $1.95 million.

On June 25, 2007, we entered into a definitive agreement with DEY to jointly promote DEY s product PERFOROMIST™ (formoterol fumarate) Inhalation Solution, or PERFOROMIST, for the treatment of chronic

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obstructive pulmonary disease, or COPD. Under the agreement, DEY granted us a right and license or sublicense to promote and detail PERFOROMIST in the United States, together with DEY. In October 2007, after expanding our sales force to over 40 representatives, we announced that we commercially launched PERFOROMIST with DEY. Under the agreement, DEY pays us a commission on retail sales of PERFOROMIST above a specified baseline.

In addition, we are developing zileuton injection initially for add-on use in emergency room or urgent care centers for acute asthma patients. In August 2006, we announced results from our Phase I/II clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of zileuton injection in patients with asthma. We initiated a Phase II clinical trial in October 2007 with zileuton injection in asthma patients.

We are also developing other product candidates directed towards reducing the potent inflammatory response that we believe is associated with the pathology, morbidity and, in some cases, mortality in many acute and chronic diseases. The inflammatory response occurs following stimuli such as infection or trauma. Our product candidates target the production and release into the bloodstream of proteins called cytokines that play a fundamental role in the body s inflammatory response.

We are collaborating with MedImmune, Inc., a subsidiary of AstraZeneca PLC, on the development of monoclonal antibodies directed toward a cytokine called high mobility group box protein 1, or HMGB1, which we believe may be an important target for the development of products to treat diseases mediated by the body s inflammatory response. In addition, we are collaborating with Beckman Coulter, Inc. on the development of a diagnostic directed toward measuring HMGB1 in the bloodstream.

We are conducting preclinical work in our alpha-7 program. We believe the successful development of a small molecule product candidate targeting the nicotinic alpha-7 cholinergic receptor, or 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 asthma and rheumatoid arthritis. Based on preclinical studies, we have selected a lead compound that is currently in development and which we are continuing to advance, with the goal of filing an investigational new drug application, or IND. In addition, we continue to seek collaborations with other pharmaceutical companies for our alpha-7 program. We have licensed to Innovative Metabolics, Inc., or IMI, patent rights and know-how relating to the mechanical and electrical stimulation of the vagus nerve. This license agreement specifically excludes from the licensed field pharmacological modulation of the alpha-7 receptor.

In January 2007, we entered into an exclusive license agreement with IMI under which we licensed to IMI patent rights and know-how relating to the mechanical and electrical stimulation of the vagus nerve. In May 2007, under the agreement with IMI, we received an initial license fee of $500,000 in cash and IMI junior preferred stock valued at $500,000 in connection with IMI s first financing. However, under our license agreement with The Feinstein Institute for Medical Research, formerly known as The North Shore-Long Island Jewish Research Institute, or The Feinstein Institute, we were obligated to pay The Feinstein Institute $100,000 of this cash payment and IMI junior preferred stock valued at $100,000. We included in revenue under collaboration and license agreements in 2007 the $1.0 million total license fee that we received from IMI and included in research and development expenses the payments of $100,000 in cash and IMI junior preferred stock valued at $100,000 that we made to The Feinstein Institute. These amounts were recorded in the second quarter of 2007. In March 2008, we sold the remaining 400,000 shares of junior preferred stock to two investors, which had participated in IMI s first financing, for an aggregate purchase price of $400,000. The purchase price is subject to adjustment if these investors sell or receive consideration for these shares of junior preferred stock pursuant to an acquisition of IMI prior to February 1, 2009 at a price per share greater than they paid us. Under the license agreement, IMI also has agreed to pay us $1.0 million, excluding a $200,000 payment that we would be obligated to pay The Feinstein Institute, upon full regulatory approval of a licensed product by the FDA or a foreign counterpart agency and royalties based on a net sales of licensed products and methods by IMI and its affiliates.

In 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 $10.0 million in late

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2003 and $2.5 million in early 2004. In addition, MedImmune agreed to fund to us $125,000 in 2007, $1.0 million in 2006, $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 January 2005, we entered into a license agreement with Beckman Coulter relating to the development of diagnostic products for measuring HMGB1. In consideration for the license, Beckman Coulter paid us a product evaluation license fee of $250,000 in February 2005. In December 2006, Beckman Coulter elected to exercise its option for full development of a diagnostic test measuring HMGB1 in the bloodstream. This election triggered a $400,000 milestone payment, which we received in January 2007.

In May 2006, we announced a restructuring of our operations that was intended to better align costs with revenue and operating expectations. Related restructuring charges pertained to employee severance benefits, outplacement services, automobile lease termination fees and impairment of assets. In October 2006, we announced a second restructuring of our operations to focus our resources on the commercialization of ZYFLO CR and the clinical development of zileuton injection and to significantly reduce our net cash expenditures through lower spending on our existing sales force as well as on our discovery and research programs. As part of this new business strategy, we eliminated 60 positions, or approximately 50% of our workforce. The headcount reductions included 38 sales and marketing employees, 17 research and development employees and five general and administrative employees.

Since our inception, we have incurred significant losses each year. We had net losses of $37.0 million in the year ended December 31, 2007 and $48.8 million in the year ended December 31, 2006. As of December 31, 2007, we had an accumulated deficit of $191.4 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 CR and prepare for the potential commercial launch of our product candidates. Since our inception, we have raised proceeds to fund our operations through public offerings of common stock, private placements of equity securities, debt financings, the receipt of interest income, payments from our collaborators MedImmune and Beckman Coulter, license fees from IMI, payments from DEY under our zileuton co-promotion agreement and revenues from sales of ZYFLO and ZYFLO CR.

Recent Developments

On January 16, 2008, we entered into a sublease with Microbia Precision Engineering, Inc., or Microbia. We entered into the sublease in connection with our negotiated termination of our lease with ARE 60 WESTVIEW, LLC, or ARE, and the negotiation of a new lease between ARE and Microbia for the same premises. Pursuant to the terms of the sublease, we are subleasing from Microbia a portion of the current premises occupied by us in Lexington, Massachusetts totaling approximately 11,298 square feet effective March 1, 2008.

On March 2, 2008, Frank E. Thomas resigned as our President and Chief Executive Officer effective March 31, 2008 and as a member of our board of directors effective March 2, 2008. On March 4, 2008, we announced that our board of directors appointed Trevor Phillips, Ph.D. as our President and Chief Executive Officer effective April 1, 2008 and elected Dr. Phillips as a member of our board of directors effective March 4, 2008. Dr. Phillips currently serves as our Chief Operating Officer and Senior Vice President of Operations.

Financial Operations Overview

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 and license agreements with MedImmune and Beckman Coulter. In the fourth quarter of 2005, we began

selling, and recognizing revenue from ZYFLO. In September 2007, we began selling, and recognizing revenue from ZYFLO CR. In 2007, we also recorded license revenue from our license agreement with IMI.

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Cost of Products Sold. Cost of products sold consists of manufacturing, distribution and other costs related to our commercial products, ZYFLO and ZYFLO CR. In addition, it includes royalties to third parties related to ZYFLO and ZYFLO CR and any reserves established for excess or obsolete inventory. Most of our manufacturing and distribution costs are paid to third-party manufacturers. However, there are some internal costs included in cost of products sold, including salaries and expenses related to managing our supply chain and for certain quality assurance and release testing costs. We do not expect to record costs for manufacturing or distributing ZYFLO after February 2008, when we ceased manufacturing and supplying ZYFLO.

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, regulatory costs, including user fees paid to the FDA, milestone payments to third parties, costs related to the development of our approved new drug application, or NDA, for ZYFLO CR, 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, we record manufacturing expenses associated with a product as cost of products sold rather than as research and development expenses. We expense research and development costs and patent related costs as they are 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 clinical stage programs such as zileuton injection 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 portfolio will fluctuate depending primarily on the timing and outcomes of clinical trials, related manufacturing initiatives and milestone payments to third parties and the results of our decisions based on these outcomes. We expect to incur additional expenses over the next several years for clinical trials of ZYFLO CR and our product development candidates, including zileuton injection and alpha-7. We also expect manufacturing expenses for some programs included in research and development expenses to increase as we scale up production of zileuton injection for later stages of clinical development. We initiated a Phase IV clinical trial in July 2007 related to ZYFLO CR to examine its potential clinical benefits in the current patient treatment setting. In March 2008, we discontinued the trial because of patient enrollment that was significantly slower than we had anticipated. The costs of this trial will be included in research and development expenses. As a result of the FDA s approval of the NDA for ZYFLO CR in May 2007, we made milestone payments totaling $3.1 million and accrued at present value an additional $3.5 million related to milestone obligations due on the first and second anniversary of the FDA s approval. We included these milestone payments and accruals in research and development expenses in our results for the second quarter of 2007 and included the accretion of the discount related to the present value of the milestone obligations in interest expense.

Sales and Marketing Expenses. Sales and marketing expenses consist primarily of salaries and other related costs for personnel in sales, marketing, managed care and our sales operations functions as well as other costs related to ZYFLO CR and ZYFLO. We also incurred marketing and other costs related to our launch of ZYFLO CR in September 2007. Other costs included in sales and marketing expenses include sales and marketing cost related to our co-promotion and marketing agreement, cost of product samples of ZYFLO CR and ZYFLO, promotional materials, market research and sales meetings. We expect to continue to incur sales and marketing costs associated with enhancing our sales and marketing functions and maintaining our increased sales force to support ZYFLO CR. In addition, under our co-promotion agreement with DEY, we have deferred the $12.0 million in aggregate upfront and milestone payments that we received in 2007. We are amortizing these payments over the term of the agreement. The amortization of the upfront and milestone payments will offset some or all of the co-promotion fees paid to DEY for

promoting ZYFLO CR and ZYFLO in future periods under the agreement. We expect to record all ZYFLO CR sales generated by the combined sales force and record any co-promotion fees paid to DEY and the amortization of the upfront and

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milestone payments in sales and marketing. We do not expect to record sales and marketing expenses for ZYFLO after February 2008, when we ceased manufacturing and supplying ZYFLO.

General and Administrative Expenses. General and administrative expenses consist primarily of salaries and other related costs for personnel in executive, finance, accounting, legal, business development, information technology and human resource functions. Other costs included in general and administrative expenses include certain facility and insurance costs, including director and officer liability insurance, as well as professional fees for legal, consulting and accounting services.

Lease Abandonment.

In the third quarter of 2007, we ceased our in-house research activities to focus on the clinical development and commercialization aspects of our business. In accordance with SFAS No. 146, *Costs Associated with an Exit or Disposal Activity*, we recorded a liability of $360,000 related to a portion of the remaining obligations under our then operating lease that would expire in March 2009 at our facility in Lexington, Massachusetts that we ceased to use. The liability recorded was reduced by an estimated sublease rental income that we estimated could be reasonably obtained for the unused portion of the facility. In December 2007, we adjusted this estimated sublease income to reflect the negotiated termination of our operating lease and our sublease for the 11,298 square feet we currently occupy. This adjustment resulted in a $140,000 reduction to the abandonment charges. We recorded the abandonment charges in the third and fourth quarter of 2007 in our research and development expenses. As of December 31, 2007, the remaining obligation under the operating lease was $214,000, which is included in accrued expenses, and will be recognized over the two month period ending February 29, 2008.

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 our financial condition or operating performance is material.

Our significant accounting policies are more fully described in the notes to our consolidated financial statements included in this annual report on Form 10-K. 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, product returns, inventory, accrued expenses, short-term investments, stock-based compensation and income taxes described below fit the definition of critical accounting estimates.

Revenue Recognition. We sell ZYFLO CR and ZYFLO primarily to pharmaceutical wholesalers, distributors and pharmacies, which have the right to return purchased product. We commercially launched ZYFLO in October 2005

and ZYFLO CR in September 2007. In January 2008, we requested and received from the FDA a waiver from the requirement to provide six-months notice to cease manufacturing ZYFLO. As a result, we ceased manufacturing and supplying ZYFLO to the market in February 2008. We recognize revenue from product sales in accordance with Statement of Financial Accounting Standards No. 48, *Revenue Recognition When Right of Return Exists*, or SFAS No. 48, which requires the amount of future returns to be

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reasonably estimated. We recognize product sales net of estimated allowances for product returns, estimated rebates in connection with contracts relating to managed care, Medicaid, Medicare, and estimated chargebacks from distributors and prompt payment and other discounts.

Prior to the first quarter of 2007, we deferred the recognition of revenue on ZYFLO product shipments to wholesale distributors until units were dispensed through patient prescriptions as we were unable to reasonably estimate the amount of future product returns. Units dispensed are not generally subject to return. In the first quarter of 2007, based on our product return experience since we launched ZYFLO in October 2005, we began recording revenue upon shipment to third parties, including wholesalers, distributors and pharmacies, and providing a reserve for potential returns from these third parties as sufficient history existed to make such estimates. In connection with this change in estimate, we recorded an increase in net product sales in 2007 related to the recognition of revenue from product sales that had been previously deferred, net of an estimate for remaining product returns. This change in estimate totaled approximately $953,000 and was reported in our results for the first quarter of 2007. We recorded $2.3 million in net product sales of ZYFLO CR in the second half of 2007. We anticipate that the rate of return for ZYFLO CR will be comparable to the rate of return used for ZYFLO. As a result, we recognize revenue for sales of ZYFLO CR upon shipment to third parties and record a reserve for potential returns from these third parties based on our product returns experience with ZYFLO and other factors.

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 statements 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 adjusted from time to time for any delays or acceleration in the development of the product. 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 adjustment is limited to the cash received.

Under our license agreement with IMI, we included in revenue from collaboration and license agreements in the second quarter of 2007 a $1.0 million initial license fee that we received from IMI and included in research and development expenses a related $100,000 cash payment and IMI preferred stock payment valued at $100,000 that we made to The Feinstein Institute.

Product Returns. Consistent with industry practice, we offer customers the ability to return products during the six months prior to, and the 12-months after, the product expires. At the time of its commercial launch in October 2005, we began shipping ZYFLO with an expiration date of 12 months. Since our launch of ZYFLO, we have extended ZYFLO s expiration date from 12 months to 24 months as of December 31, 2007. In September 2007, we launched ZYFLO CR, which currently has an expiration date of 18 months. We anticipate that the rate of return for ZYFLO CR will be comparable to the rate of return for ZYFLO. We may adjust our estimate of product returns if we become aware of other factors that we believe could significantly impact our expected returns. These factors include our estimate of inventory levels of our products in the distribution channel, the shelf-life of the product shipped, competitive issues such as new product entrants and other known changes in sales trends. We evaluate this reserve on a quarterly basis, assessing each of the factors described above, and adjust the reserve accordingly. As a result of this ongoing evaluation, our product return reserve is $873,000 as of December 31, 2007, which is comprised of a product return reserve of approximately $696,000 for ZYFLO and $177,000 for ZYFLO CR. Our allowance for ZYFLO product returns includes $605,000 of product in our distribution channel that we did not expect to be dispensed through prescriptions in the first quarter of 2008 as a result of our decision to cease manufacturing and supplying ZYFLO in February 2008.

Inventory. Inventory is stated at the lower of cost or market value 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

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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. We determine the estimated useful life of our inventory based upon stability data of the underlying product stored at different temperatures or in different environments. As of December 31, 2007, inventory consists of zileuton active pharmaceutical ingredient, or API, which is raw material in powder form, 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 based upon anticipated product revenues. At December 31, 2007, we had an inventory reserve of $816,000. The inventory reserve includes $155,000 recorded in the second quarter of 2007, relating to the zileuton active pharmaceutical ingredient in certain batches of ZYFLO CR tablets that did not meet certain specifications, $54,000 recorded in the third quarter of 2007, relating to excess ZYFLO finished tablets that we believe will not be sold as a result of our recent launch of ZYFLO CR and our decision to cease manufacturing and supplying ZYFLO in February 2008 and $607,000 recorded in the fourth quarter of 2007, relating to certain batches which did not pass our manufacturing specifications with the manufacture of ZYFLO CR. As of December 31, 2007, we had $5.6 million in inventory. We expect that our inventory levels could grow substantially in future periods as a result of our minimum purchase obligations under our supply agreements with third-party manufacturers.

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, fees paid to contract manufacturers in connection with the production of clinical materials, license fees in connection with the achievement of milestones and restructuring charges.

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 and ZYFLO CR. In the event that our sales mix to certain third-party payors is different from our estimates, we may be required to pay higher or lower total rebates than we have estimated. In connection with service fees, our estimates are most affected by our understanding of the status and timing of services provided relative to the actual levels of services incurred by such service providers. The majority of our service providers invoice us monthly in arrears for services performed; however, certain service providers invoice us based upon milestones in the agreement. In the event that we do not identify certain costs 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.

Investments. 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. These investments are recorded at fair value and accounted for as available-for-sale securities. We record any unrealized gain (loss) during the year as an adjustment to stockholders equity unless we determine that the unrealized gain (loss) is not temporary. We adjust the original cost of debt securities for amortization of premiums and accretion of discounts to maturity. Because we have determined that the unrealized gain (loss) on our investments have been temporary, we have not recorded any impairment losses since inception.

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 of 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

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sale of the related security prior to the maturity of the underlying investment to minimize any losses. At December 31, 2007, we held $300,000 in auction rate securities. In February 2008, we were informed that there was insufficient demand at auction for these securities. As a result, this amount is currently not liquid and may not become liquid unless the issuer is able to refinance it. We have classified our investment in auction rate securities as a long-term investment and have included the amount in other assets on our balance sheet.