

CRITICAL THERAPEUTICS INC

Form 424B5

October 27, 2006

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The information contained in this prospectus supplement and the accompanying prospectus is not complete and may be changed. The registration statement filed with the Securities and Exchange Commission relating to these securities has been declared effective. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-136910**

**Preliminary Prospectus Supplement Dated October 26, 2006 Subject to Completion
(To Prospectus Dated September 11, 2006)**

**1 Shares of Common Stock
Warrants to Purchase 1 Shares of Common Stock**

Critical Therapeutics, Inc. is offering up to 1 shares of its common stock and warrants to purchase up to 1 shares of its common stock. The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase 1 shares of common stock, at an exercise price of \$ 1 per share of common stock. Each unit will be sold at a negotiated price of \$ 1 . Units will not be issued or certificated. The shares of common stock and warrants are immediately separable and will be issued separately.

Our common stock is quoted on The Nasdaq Global Market under the symbol CRTX. On October 25, 2006, the last reported sale price of our common stock on The Nasdaq Global Market was \$2.63 per share.

Investing in our securities involves significant risks. See Risk Factors beginning on page S-6 of this prospectus supplement.

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

We are offering these shares of common stock and warrants to purchase common stock on a best efforts basis primarily to institutional investors. We have retained Lazard Capital Markets LLC to act as placement agent in connection with this offering.

| | Per Unit | Maximum Offering Amount |
|----------------------------------|-----------------|--|
| Public offering price | \$ 1 | \$ 1 |
| Placement agent's fees | \$ 1 | \$ 1 |
| Proceeds, before expenses, to us | \$ 1 | \$ 1 |

We estimate the total expenses of this offering, excluding the placement agent's fees, will be approximately \$ 1 . Because there is no minimum offering amount required as a condition to closing in this offering, the actual offering amount, the placement agent's fees and net proceeds to us, if any, in this offering may be substantially less than the total maximum offering amounts set forth above. Placement agent's fees relating to units, if any, sold to certain of our existing stockholders will be sold at the same public offering price per unit, but the placement agent's fee payable by us will be 50% of the placement agent's fees for units sold to other purchasers. We are not required to sell any specific number or dollar amount of the units offered in this offering, but the placement agent will use its best efforts to arrange for the sale of all of the units offered. Pursuant to an escrow agreement among us, the placement agent and an escrow agent, some or all of the funds received in payment for the units sold in this offering will be wired to an interest bearing escrow account and held until we and the placement agent notify the escrow agent that this offering has closed, indicating the date on which the units are to be delivered to the purchasers and the proceeds are to be delivered to us.

Lazard Capital Markets

The date of this prospectus supplement is October 1, 2006

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of our common stock and warrants to purchase common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We are offering to sell, and seeking offers to buy, shares of our common stock and warrants to purchase common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the common stock and warrants to purchase common stock in certain jurisdictions may be restricted by law. Persons

outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and warrants to purchase common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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SUMMARY

This summary highlights selected information about us and this offering. This information is not complete and does not contain all the information you should consider before investing in the securities offered pursuant to this prospectus. You should carefully read this entire prospectus, including the Risk Factors section of this prospectus, which begins on page S-6 and the financial statements and the other information incorporated by reference, before making an investment decision.

About Critical Therapeutics, Inc.

Our Business

Critical Therapeutics, Inc. is a biopharmaceutical company focused on the discovery, development and commercialization of products designed to treat respiratory, inflammatory and critical care diseases linked to the body's inflammatory response. Our marketed product is ZYFL[®], an immediate-release tablet formulation of zileuton, which the U.S. Food and Drug Administration, or FDA, approved in 1996 for the prevention and chronic treatment of asthma in adults and children 12 years of age or older. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO and other formulations of zileuton for multiple diseases and conditions. We began selling ZYFLO in the United States in October 2005, and are developing a controlled-release formulation of zileuton, or zileuton CR, and an intravenous formulation of zileuton. In connection with the restructuring described below, in October 2006, we determined to focus our resources, including the proceeds from this offering, on these formulations.

We are currently developing zileuton CR, a tablet designed to be taken twice daily, two tablets per dose. We have submitted a New Drug Application, or NDA, for zileuton CR that was accepted for filing by the FDA as of September 29, 2006. Under the Prescription Drug User Fee Act, or PDUFA, guidelines, the PDUFA date for our NDA is May 31, 2007, which is the date by which we expect to receive an action letter from the FDA on this filing. If we receive regulatory approval on a timely basis, we expect to launch zileuton CR in the second half of 2007. We are currently exploring strategic alternatives for the marketing and sale of zileuton CR if approved and plan to pursue a co-promotion arrangement with a third party with respect to the marketing and sale of zileuton CR. If we are unable to enter into a co-promotion arrangement or other strategic alternative with a third party on terms that are favorable to us, we may determine to market and sell zileuton CR independently.

In addition, we are developing an intravenous formulation of zileuton 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 safety, tolerability and pharmacokinetics of the intravenous formulation of zileuton in patients with asthma. We plan to initiate a Phase IIb clinical trial in 2007 with our intravenous formulation of zileuton in asthma patients, while continuing to seek a co-development arrangement for this product candidate.

We are also developing other product candidates to regulate the excessive inflammatory response that can damage vital internal organs and, in the most severe cases, result in multiple organ failure and death. 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. on preclinical development of monoclonal antibodies directed toward a cytokine called HMGB1, or high mobility group box protein 1, which we believe may be an important target for the development of products to treat inflammation-mediated diseases. In addition, we are collaborating with Beckman Coulter, Inc. on the development of a diagnostic directed toward measuring HMGB1 in the bloodstream. In connection with the restructuring, we have determined to seek to enter into collaboration arrangements with respect to

our other product candidates and do not plan to conduct any clinical studies on these product candidates prior to entering into such arrangements.

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Recent Developments

Restructuring

In October 2006, we determined to focus our resources on the commercialization of zileuton CR and on the clinical development of the intravenous formulation of zileuton 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 plan to eliminate 63 positions. The planned headcount reduction reflects a downsizing of our sales force that markets ZYFLO®. We plan to retain a respiratory sales force of approximately 18 representatives who will be focused on continued promotion to prescribing physicians within the major metropolitan markets across the United States and increasing prescriptions from our existing base of prescribers. The planned headcount reductions also include 20 employees in our research and development group. In addition, as a result of our new strategy, our Chief Scientific Officer, Walter Newman, Ph.D., resigned effective October 31, 2006. Following completion of the restructuring, which we expect to complete by December 31, 2006, we expect to have approximately 58 employees.

We believe that the feedback from physicians to date indicates that ZYFLO®'s current dosing regimen of four times daily will continue to make it difficult to gain broad acceptance in the asthma market. With the twice-daily formulation, we expect increased usage by prescribing physicians while offering patients another treatment option for their asthma.

We plan to take the following steps to prepare for the commercialization of zileuton CR:

- conduct clinical studies in preparation for commercial launch to build zileuton CR's market position following approval;

- pursue a co-promotion arrangement to expand our promotional resources to both respiratory specialists, allergists and pulmonologists, and primary care physicians;

- implement a publication strategy that includes the presentation of data from the pivotal studies of zileuton CR at major medical conferences and in various scientific and medical journals; and

- initiate a clinical trial to evaluate a life-cycle extension strategy to enhance the intellectual property position of zileuton and provide for possible development opportunities in other inflammatory conditions.

We are also completing certain preclinical work in our alpha-7 program through a small team of scientists. Following completion of this work, we plan to seek a collaborator for our alpha-7 nicotinic receptor agonist program and do not currently plan to conduct clinical trials with the alpha-7 program without entering into such an arrangement. In collaboration with MedImmune, Inc., we expect to continue to support the development of HMGB1 antibodies for chronic and acute inflammatory diseases.

Based on our operating plans and the anticipated effects of the restructuring, we believe that our available cash and cash equivalents and anticipated cash received from product sales and anticipated payments received under collaboration agreements, together with the proceeds we receive from this offering, will be sufficient to fund anticipated levels of operations into the second half of 2008.

In connection with the implementation of our restructuring plan, we expect to record charges of approximately \$3.4 million in the fourth quarter of 2006 related to employee severance benefits, outplacement services, automobile

lease termination fees and impairment of assets. With respect to the headcount reductions to be implemented in the fourth quarter of 2006, we expect to incur charges associated with severance benefits of approximately \$1.6 million. In addition, as a result of these headcount reductions, we expect to record in the fourth quarter of 2006 an automobile lease termination fee of \$252,000, an outplacement service fee of \$28,000 and an impairment charge of approximately \$1.5 million for laboratory equipment, computer equipment and furniture and fixtures for which the future use is currently uncertain. We expect to record these restructuring charges as \$204,000 of general and administrative expense, \$2.2 million of research and development expense and \$1.0 million of sales and marketing expense.

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Consulting Agreement with M. Cory Zwerling.

On October 25, 2006, we entered into a consulting agreement with M. Cory Zwerling, one of our directors, under which Mr. Zwerling agreed to provide us services related to commercial sales, marketing and business development initiatives and other such related projects as mutually agreed upon by us and Mr. Zwerling. Under the consulting agreement, we have agreed to pay Mr. Zwerling \$1,800 per day and granted Mr. Zwerling an option to purchase 200,000 shares of our common stock under our 2004 Stock Incentive Plan. This option has an exercise price of \$2.63 per share, and will vest in 36 equal monthly installments commencing on November 25, 2006. In addition, 50% of the then unvested options will vest upon a change of control or specified transactions as set forth in the consulting agreement. We have also agreed to pay Mr. Zwerling \$49,000 for consulting performed prior to October 25, 2006. The consulting agreement has a term of twelve months and automatically renews on a month-to-month basis. We may terminate the consulting agreement upon three business days prior written notice to Mr. Zwerling. Mr. Zwerling may terminate the consulting agreement upon thirty days prior written notice.

Separation Agreement with Walter Newman, Ph.D.

Walter Newman, Ph.D., our Senior Vice President of Research and Development and Chief Scientific Officer, has resigned from his positions, effective October 31, 2006. In connection with Dr. Newman's departure, we entered into a separation agreement with Dr. Newman on October 25, 2006, which is revocable by Dr. Newman for a period of seven days. Under the separation agreement, we agreed to pay Dr. Newman the following lump sum amounts in November 2006 pursuant to the employment agreement we entered into with Dr. Newman on December 21, 2004:

\$269,500, representing Dr. Newman's annual base salary; and

\$67,375, representing 10/12 of Dr. Newman's maximum cash bonus for 2006.

We also agreed that, for a period of up to twelve months, we would reimburse Dr. Newman for 80% of the premiums for continued health coverage for Dr. Newman and his dependents and for the cost of the premiums for life insurance and disability insurance for Dr. Newman. In addition, under the separation agreement, we agreed to accelerate 50% of Dr. Newman's unvested stock options as of October 31, 2006.

Preliminary Results for the Quarter Ended September 30, 2006

Our financial statements for the quarter ended September 30, 2006 are not yet available. Our preliminary expectations with respect to our results discussed below are based upon management estimates and are subject to quarterly review procedures and final recommendations and adjustments. Actual operating results may differ from our expectations, and those differences may be material.

We expect to recognize revenue from product sales, net of any discounts and rebates, of approximately \$1.9 million in the third quarter of 2006. We had approximately \$40.2 million in cash, cash equivalents and short-term investments at September 30, 2006, compared to \$82.8 million as of December 31, 2005. In addition, we anticipate our net cash expenditures for the quarter ended September 30, 2006 to be approximately \$12.0 million.

The foregoing discussion of our expectations regarding our results for the third quarter of 2006 is not necessarily indicative of expected future results following this offering.

Risks Associated with Our Business

Our business is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this summary. We have incurred significant operating losses in each year since our inception in July 2000. As of June 30, 2006, we had an accumulated deficit of approximately \$136.8 million. We expect to incur substantial losses for at least the next several years. We have not generated the level of revenues from the sales of ZYFLO that we anticipated, and we may not be able to successfully launch zileuton CR if it is approved. We have not received approval for zileuton CR and if this product candidate is not approved on a timely basis or at all, it would have a material adverse effect on our business, financial condition and results of operations. In addition, our operating results may be harmed if our restructuring plans and cost reduction measures do not achieve the anticipated results or cause undesirable consequences.

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Corporate Information

We were incorporated in Delaware on July 14, 2000. Our principal executive offices are located at 60 Westview Street, Lexington, Massachusetts 02421, our general telephone number at that address is (781) 402-5700 and our web site is located at www.crtx.com. The information on, or that can be accessed through, our web site is not incorporated by reference in this prospectus, and you should not consider it to be a part of this prospectus. Our web site address is included as an inactive textual reference only. Unless the context otherwise requires, references in this prospectus to Critical Therapeutics, we, us, and our refer to Critical Therapeutics, Inc.

Critical Therapeutics, Critical Therapeutics circular logo design[®], CRTX, CT2 and ZYFLO[®] are trademarks or service marks of Critical Therapeutics, Inc. Other trade names and trademarks appearing or incorporated by reference in this prospectus are the property of their respective owners.

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The Offering

| | |
|---|--|
| Common stock offered by us | 1 shares |
| Common stock to be outstanding after the offering | 1 shares |
| Warrants | Warrants to purchase 1 shares of common stock will be offered in this offering. The warrants will be exercisable on or before October 1, 2011 at an exercise price of \$ 1 per share of common stock. This prospectus also relates to the offering of the shares of common stock issuable upon exercise of the warrants. |
| Use of proceeds | We intend to use the proceeds from this offering to fund our efforts to obtain FDA approval for zileuton CR, to prepare for commercial launch of zileuton CR, to fund development of our intravenous formulation of zileuton and for other general corporate purposes. See Use of Proceeds on page S-31. |
| Risk factors | See Risk Factors beginning on page S-6 for a discussion of factors you should consider carefully before deciding to invest in our common stock and warrants to purchase our common stock. |
| The Nasdaq Global Market symbol | CRTX |

The number of shares of our common stock that will be outstanding immediately after the offering is based on 34,474,799 shares outstanding as of October 25, 2006. The number of outstanding shares excludes:

3,480,842 shares issuable as of October 25, 2006 upon the exercise of warrants outstanding prior to this offering, at a weighted average exercise price of \$6.58 per share;

1 shares issuable upon the exercise of warrants to be issued in this offering, at an exercise price of \$ 1 per share;

2,587,505 shares issuable upon the exercise of outstanding options that had vested as of October 25, 2006, at a weighted average exercise price of \$4.60 per share; and

4,505,949 shares issuable upon the exercise of outstanding options that had not vested as of October 25, 2006, at a weighted average exercise price of \$5.11 per share.

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RISK FACTORS

Risks Relating to Our Business

Our business depends heavily on obtaining approval for and the commercial success of zileuton CR.

ZYFLO is our only commercial product and it has not achieved broad market acceptance. Other than zileuton CR, our product candidates are in early clinical, preclinical and research stages of development and are a number of years away from commercialization. Our NDA for zileuton CR was accepted for filing by the FDA as of September 29, 2006. Under PDUFA guidelines, the PDUFA date for our NDA is May 31, 2007, which is the date by which we expect to receive an action letter from the FDA on this filing. If zileuton CR is not approved on a timely basis or at all, it would have a material adverse effect on our business, financial condition and results of operations. If approved for sale, we expect zileuton CR would account for a significant portion of our revenues for the foreseeable future, and that sales of ZYFLO would decline as patients converted to zileuton CR.

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 zileuton CR is not approved and commercially successful, we may be forced to find additional sources of funding earlier than we anticipated. If we are not successful in obtaining additional funding on acceptable terms, we may be forced to significantly delay, limit or eliminate one or more of our research, development or commercialization programs.

If we do not obtain the regulatory approvals or clearances required to market and sell zileuton CR, our business may be unsuccessful.

We may not market zileuton CR in the United States, Europe or any other country without marketing approval from the FDA or the equivalent foreign regulatory agency. We have submitted an NDA to the FDA for zileuton CR, which was accepted for filing as of September 29, 2006. Abbott Laboratories conducted the pivotal clinical trials on zileuton CR before we in-licensed the product candidate. We are relying on the results of these prior pivotal clinical trials to support our NDA. If the data at the clinical sites do not pass FDA audits, we could be required to repeat some or all of the clinical trials, which would lead to unanticipated costs and delays. 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 the controlled-release zileuton tablets that we have manufactured is similar to the pharmacokinetic profile of the controlled-release zileuton 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 zileuton CR in volunteers under both fed and fasting conditions. We believe that the results of the bioavailability studies are sufficient to allow us to bridge to the results of Abbott's prior clinical trials to support our NDA filing. The FDA has confirmed that this is a significant review issue. If the FDA disagrees with our conclusions regarding the sufficiency of the results from the bioavailability studies, we could be required to conduct additional clinical trials to support our NDA, which could lead to unanticipated costs and delays or to the termination of our program for zileuton CR. If we do not receive required regulatory approval or clearance to market zileuton CR, our ability to generate product revenues and achieve profitability, our reputation and our ability to raise additional capital will be materially impaired.

If zileuton CR is not approved for sale or the market is not receptive to it, 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 zileuton CR, if it is approved for sale, will depend upon its acceptance by the medical community, third-party payors and patients. Physicians will prescribe zileuton 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. If approved, we

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believe that the primary advantage of zileuton CR over ZYFLO would relate to a more convenient dosing schedule, but this advantage may not result in broad market acceptance of zileuton CR, and the difficulties we have had with ZYFLO may be equally applicable to zileuton CR.

Despite being approved by the FDA since 1996, ZYFLO, our first marketed zileuton product, has not achieved broad market acceptance. In the 12-month period ending September 2003, only 1,700 physicians prescribed the product. During the period between our commercial launch of ZYFLO in October 2005 through the week ending June 30, 2006, prescription data for ZYFLO indicates that approximately 2,400 physicians prescribed the product. For the six months ended June 30, 2006, we recorded revenue from the sale of ZYFLO of only \$2.8 million. We have had 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 four times per day, which some physicians and patients may find inconvenient compared to other available asthma therapies that require dosing only once or twice daily. In addition, if patients do not comply with the dosing schedule and take less than the prescribed number of tablets, our sales of zileuton CR would be limited and our revenues would be adversely effected.

Market perceptions about the safety of ZYFLO may limit the market acceptance of zileuton 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, a protein. In clinical trials for zileuton CR, 1.94% of the patients taking zileuton CR in the three-month efficacy trial and 2.6% of the patients taking zileuton CR in the six-month safety trial experienced ALT levels greater than or equal to three times the level normally seen in the bloodstream. Because ZYFLO can elevate liver enzyme levels, periodic liver function tests are recommended for patients taking ZYFLO, and given the results of the zileuton CR clinical trials these periodic liver function tests are likely to be advisable for patients taking zileuton CR. Some physicians and patients may perceive liver function tests as inconvenient or indicative of safety issues, which could make them reluctant to prescribe or accept ZYFLO and other zileuton product candidates, including zileuton CR. As a result, many physicians may have negative perceptions about the safety of ZYFLO and other zileuton product candidates, including zileuton CR, which could limit their commercial acceptance. The absence of ZYFLO from the market prior to our commercial launch in October 2005 may have exacerbated any negative perceptions about ZYFLO if physicians believe the absence of ZYFLO from the market was related to safety or efficacy issues.

The position of ZYFLO in managed care formularies, which are lists of approved products developed by managed care organizations, has also made it more difficult to expand the current market share for this product. As a result of a lack of a sustained sales and marketing effort prior to our commercial launch in October 2005, in many instances ZYFLO had been relegated to a third-tier status, which typically requires the highest co-pay for patients. We expect zileuton CR to have third-tier status as well.

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

If we do not have an adequate marketing and sales infrastructure and presence following our October 2006 restructuring, our ability to market and sell our products will be impaired.

In October 2006, we determined to reduce the size of our sales force to 18. Previously, we reduced the size of our sales force as part of the cost reduction program that we announced in May 2006. In addition, our Senior Vice President of Sales and Marketing resigned in June 2006, and our Vice President of Sales resigned in July 2006.

Despite these changes, we plan to continue to market and sell ZYFLO directly through our internal sales force. Because of the reduced size of our sales force, our sales of ZYFLO may decrease. In addition, due to our difficulty in achieving market acceptance of ZYFLO since its commercial launch in

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October 2005, the reduction in the size of our sales force, and the resignations of our Senior Vice President of Sales and Marketing and Vice President of Sales, it may be difficult for us to retain qualified sales and marketing personnel and maintain an effective sales force.

We plan to pursue a co-promotion arrangement with a third party with respect to the marketing and sales of zileuton CR. If we are unable to enter into a co-promotion arrangement on terms that are favorable to us, we may determine to market and sell zileuton CR independently.

If we independently launch and market zileuton CR, we would need to rebuild our sales force, which would involve significant expenses. In addition, we may not be able to attract, hire, train and retain qualified sales and marketing personnel to rebuild the sales force. If we are not successful in our efforts to build this sales force, our ability to independently launch and market zileuton CR would be impaired.

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

We purchased quantities of raw materials and supplies of ZYFLO tablets in connection with the commercial launch of ZYFLO. These purchases were made consistent with our forecasts of inventory levels of ZYFLO that we based on our estimate of expected customer orders in combination with limited historical information regarding actual sales. Because product demand for ZYFLO has been less than we anticipated, our inventory levels of the active pharmaceutical ingredient for ZYFLO have been higher than anticipated. In addition, we are subject to minimum purchase obligations under our supply agreements with our third-party manufacturers, which could require us to buy additional inventory. We plan to use a portion of the active pharmaceutical ingredient manufactured for ZYFLO in order to manufacture zileuton CR. If ZYFLO demand does not increase or approval and commercial launch of zileuton CR is delayed, we may not be able to reduce these inventories or use the additional inventory we are required to acquire. 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 unnecessary 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 during the period in which we recognize charges for excess inventory.

If we fail to maintain an adequate inventory of ZYFLO, zileuton's active pharmaceutical ingredient, or API, or zileuton CR, if it is approved, or if our inventory were to be destroyed or damaged or reached its expiration date, patients may not have access to our products, our reputation and our brand could be harmed and physicians may be less likely to prescribe our products in the future.

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 in the critical care market. We seek to do so through:

internal research programs;

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

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

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

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

the time, money and other resources that we devote to our research programs may not be adequate, including as a result of the May 2006 and October 2006 cost reduction programs; or

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

In addition, subject to having sufficient resources, cash and otherwise, 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 in the critical care market. These established companies may have a competitive advantage over us due to their size, cash resources or greater clinical development and commercialization capabilities. Other factors that may prevent us from licensing or otherwise acquiring suitable product candidates or approved products include the following:

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

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

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

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

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

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

The development and commercialization of new drugs is highly competitive. We will face competition with respect to the development of product candidates and for ZYFLO, zileuton CR, if approved, and any other products that we commercialize in the future from pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies, companies selling low-cost generic substitutes, academic institutions, government agencies or research institutions. A number of large pharmaceutical and biotechnology companies currently market and sell products to treat asthma that compete with ZYFLO and will compete with, if approved for sale, zileuton CR. Many established therapies currently command large market shares in the mild to moderate asthma market, including Merck & Co., Inc.'s Singulair®, GlaxoSmithKline plc's Advair® and inhaled corticosteroid products. We will also face competition in the severe asthma market. The severe asthma market is currently served by the therapies developed for mild to moderate asthma, as these therapies (Singulair®, Advair® and inhaled corticosteroids) are used in combination or add-on therapies in severe asthma, along with oral and injectable steroid treatments. One product, Xolair®, developed jointly by Novartis AG, Genentech, Inc. and Tanox, Inc., was approved in 2004 for severe allergic asthma and had U.S. sales of \$320.6 million in 2005. In addition, we may face competition from pharmaceutical companies seeking to develop new drugs for the asthma market. For example, in July 2006, AstraZeneca announced the approval of Symbicort®, a twice-daily asthma therapy combining budesonide, an inhaled corticosteroid, and formoterol, a beta2-agonist, that is expected to compete in the moderate and severe asthma markets. AstraZeneca has stated it expects to launch Symbicort® in mid-2007.

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

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

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

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

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

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

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

We will face competition based on the safety and effectiveness of our products, the timing and scope of regulatory approvals, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. Our competitors may develop or commercialize more effective, safer or more affordable products, or obtain more effective patent protection, than we are able to. Accordingly, our competitors may

commercialize products more rapidly or effectively than we are able to, which would adversely affect our competitive position, the likelihood that our product candidates will achieve initial market acceptance and our ability to generate meaningful revenues from our product candidates. Even if our product candidates achieve initial market acceptance, competitive products may render our products obsolete or noncompetitive. If our product candidates are rendered obsolete, we may not be able to recover the expenses of developing and commercializing those product candidates.

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Our operating results may be harmed if our restructuring plans and cost reduction measures do not achieve the anticipated results or cause undesirable consequences.

In May 2006, we implemented cost reduction measures and in the fourth quarter of 2006 we will be implementing additional cost reduction measures, which have included or will include, among other things, significant workforce reductions. Because of the nature and extent of the restructuring actions we have taken and are taking, we may have difficulty marketing and promoting ZYLFLO or zileuton CR, if approved. If we fail to achieve the desired results of our cost reduction measures, we may suffer material harm to our business.

Our cost reduction initiatives may yield unintended consequences, such as attrition beyond our planned reduction in workforce, reduced employee morale and reduced support from physicians. As a result of these factors, our employees may seek alternate employment. Attrition beyond our planned reduction in workforce could have a material adverse effect on our financial performance. In addition, as a result of these cost reduction programs and the reduction in our workforce, we face an increased risk of employment litigation.

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

We depend on the principal members of our management and scientific staff, including Frank E. Thomas, our President, Dana Hilt, M.D., our Chief Medical Officer and Senior Vice President of Clinical Development, and Trevor Phillips, Ph.D., our Chief Operating Officer and Senior Vice President of Operations. The loss of any of these individuals' services would diminish the knowledge and experience that we, as an organization, possess and might significantly delay or prevent the achievement of our research, development or commercialization objectives and could cause us to incur additional costs to recruit replacement executive personnel. We do not maintain key person life insurance on any of these individuals or any of our other scientific and management staff.

In June 2006, Paul D. Rubin, M.D. stepped down from his position as our President and Chief Executive Officer and resigned from our board of directors and Frederick Finnegan resigned from his position as our Senior Vice President of Sales and Marketing. In July 2006, Anne M. Fields resigned from her position of Vice President of Sales. We have not yet determined the impact that the departure of these executives may have on our ability to achieve our research, development and commercialization objectives. In October 2006, Walter Newman, Ph.D., resigned from his position as our Chief Scientific Officer and Senior Vice President of Research and Development. We put in place a new management structure, with a smaller management team that does not include a chief executive officer or a chief scientific officer, and have promoted individuals already employed by us to assume additional responsibilities. If we are unable to successfully transition our management staff to compensate for the loss of these executives, the achievement of our research, development and commercialization objectives could be significantly delayed or prevented. In addition, our focus on transitioning to our new management structure could divert our management's attention from other business concerns. Furthermore, if we decide to recruit new executive personnel, we will incur additional costs.

Our success depends in large part on our ability to attract and retain qualified scientific and management personnel. 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 management and scientific personnel and will require our existing management personnel to develop additional expertise. We face intense competition for personnel. As we transition to our new management structure, we may have difficulty attracting and retaining personnel. The failure to retain and attract personnel or to develop such expertise could delay or halt the research, development, regulatory approval and commercialization of our product candidates.

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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;

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

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

If our past or present operations are found to be in violation of any of the laws described above or other 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

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

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

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

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

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

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

The development, manufacturing, pricing, marketing, sales and reimbursement of ZYFLO, zileuton 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 expect to have approximately 50 employees after the completion of our October 2006 restructuring. 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

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requirements, it is possible that we may not be in compliance with all potentially applicable regulations. If we fail to comply with any of these regulations, we could be subject to a range of regulatory actions, including significant fines, litigation or other sanctions. Any action against us for a violation of these regulations, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management's attention and harm our reputation.

As a publicly traded company, we are subject to significant legal and regulatory requirements, including the Sarbanes-Oxley Act of 2002 and related regulations, some of which have either only recently been adopted or are subject to change. For example, we are incurring additional expenses and devoting significant management time and attention to evaluating our internal control systems in order to allow our management to report on, and our 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 implement do not comply with all of the relevant rules and regulations of the Securities and Exchange Commission, or SEC, and The Nasdaq Global Market, we may be subject to sanctions or investigation by regulatory authorities, including the SEC or The Nasdaq Global Market. This type of action could adversely affect our financial results or investors' confidence in our company and our ability to access the capital markets. If we fail to develop and maintain adequate controls and procedures, we may be unable to provide the required financial information in a timely and reliable manner, which could cause a decline in our stock price.

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

Our sales of ZYFLO are, and sales of our product candidates including zileuton CR 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. The Medicare Prescription Drug Improvement and Modernization Act of 2003, or the MMA, was signed into law in December 2003. We cannot predict the full impact of the MMA and its regulatory requirements on our business. However, legislative or administrative acts that reduce reimbursement for our products could adversely impact our business. In addition, we believe that private insurers, such as managed care organizations, or MCOs, may adopt their own reimbursement reductions in response to legislation. Any reduction in reimbursement for our products could materially harm our results of operations. In addition, we believe that the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of our products, which may adversely impact our product sales. Furthermore, when a new drug product is approved, governmental and private reimbursement for that product, and the amount for which that product will be reimbursed, are uncertain. We cannot predict the availability or amount of reimbursement for ZYFLO or our product candidates, including zileuton CR, and current reimbursement policies for marketed products may change at any time.

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

patient reimbursement constraints, restrictions on access to certain products, and bulk purchasing of drugs.

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If we succeed in bringing products in addition to ZYFLO to the market, these products may not be considered cost effective and reimbursement to the patient may not be available or sufficient to allow us to sell our product candidates on a competitive basis to a sufficient patient population. Because our product candidates other than zileuton CR are in the development stage, we are unable at this time to determine the cost-effectiveness of these product candidates. We may need to conduct expensive pharmacoeconomic trials in order to demonstrate their cost-effectiveness. Sales of prescription drugs are highly dependent on the availability and level of reimbursement to the consumer from third-party payors, such as government and private insurance plans. These third-party payors frequently require that drug companies provide them with predetermined discounts or rebates from list prices, and third-party payors are increasingly challenging the prices charged for medical products. Because our product candidates other than zileuton CR are in the development stage, we do not know the level of reimbursement, if any, we will receive for those product candidates if they are successfully developed. If the reimbursement we receive for any of our product candidates is inadequate in light of our development and other costs, our ability to realize profits from the affected product candidate would be limited. If reimbursement for our marketed products changes adversely or if we fail to obtain adequate reimbursement for our other current or future products, health care providers may limit how much or under what circumstances they will prescribe or administer them, which could reduce use of our products or cause us to reduce the price of our products.

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

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

In addition, because ZYFLO was previously marketed by Abbott prior to our licensing it, the rebate that we are required to pay to Medicaid for prescriptions filled by patients covered under a Medicaid program could be substantial. The calculation of the Medicaid rebate is based on the initial pricing set by Abbott with adjustments for inflation each year. Since the price set by Abbott for ZYFLO is below the price we are currently charging, we are subject to a Medicaid rebate of greater than 75% of our selling price. Based on historical prescribing patterns since our launch in October 2005, our Medicaid business has represented less than 5% of total ZYFLO prescriptions. However, if the Medicaid portion of our ZYFLO sales were to increase such that Medicaid represented a larger than expected percentage of the mix of sales for ZYFLO, the increased level of rebates could have a material adverse effect on our financial condition and results of operations.

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

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and marketing and sale of drugs. If the use of ZYFLO, zileuton CR 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 and clinical trial liability claims for our product candidates. We may seek additional product liability insurance prior to marketing zileuton CR or any of our other product candidates. However, our insurance may not provide adequate coverage

against potential liabilities. Furthermore, product liability and clinical trial insurance is becoming increasingly expensive. As a result, we may be unable to

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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.

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

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

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

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

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

If we do not obtain the regulatory approvals or clearances required to market and sell our product candidates under development, our business may be unsuccessful.

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

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 required regulatory approval or clearance to market zileuton CR or any of our other product candidates under development, our ability to generate product revenue and achieve profitability, our reputation and our ability to raise additional capital will be materially impaired.

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

Our product candidates are still in development and remain subject to clinical testing and regulatory approval or clearance. In order to obtain regulatory approvals or clearances for the commercial sale of our product candidates, we and our collaborators will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our product candidates. We may not be able to obtain authority from the FDA, institutional review boards or other regulatory agencies to commence or complete these clinical trials. If permitted, such clinical testing may not prove that our product candidates are safe and effective to the extent necessary to permit us to obtain marketing approvals or clearances from regulatory authorities. One or more of our product candidates may not exhibit the expected therapeutic results in humans, may cause harmful side effects or have other unexpected characteristics that may delay or preclude submission and

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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 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. We discontinued the trial after routine testing revealed some swelling in the butyl rubber stoppers used to seal the vials that stored the drug. We determined that the durability of the stopper could have affected the integrity of clinical supplies of the product candidate at the trial sites. We are analyzing the safety and efficacy data from the patients who received our drug before we discontinued the trial. After reviewing the final data from the trial, we plan to assess if there is an opportunity to continue development of CTI-01 with a collaborative partner or to out-license CTI-01.

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

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

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

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

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

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

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

If we or our third-party manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell

our product candidates successfully and could harm our reputation and lead to less market acceptance of our product candidates. These enforcement actions include:

product seizures;

voluntary or mandatory recalls;

suspension of review or refusal to approve pending applications;

voluntary or mandatory patient or physician notification;

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withdrawal of product approvals;

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

restrictions on applying for or obtaining government bids;

finances;

restrictions on importation of our product candidates;

injunctions; and

civil and criminal penalties.

Risks Relating to Our Dependence on Third Parties

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

We are relying on MedImmune to fund the development of and to commercialize product candidates in our HMGB1 program. We are relying on Beckman Coulter to fund the development and to commercialize diagnostics in our HMGB1 program. All of our revenues for the years ended December 31, 2003 and 2004 were derived from fees paid to us by MedImmune. Our revenues for the year ended December 31, 2005 and the six months ended June 30, 2006 were derived from fees paid to us by MedImmune and Beckman Coulter under our collaboration agreements with them and revenue from the sale of ZYFLO beginning in the fourth quarter of 2005; however, a significant portion of our revenues for the year ended December 31, 2005 and the six months ended June 30, 2006 continued to be derived from our collaboration agreements with MedImmune and Beckman Coulter. Additional payments due to us under the collaboration agreements with MedImmune and Beckman Coulter are generally based on our achievement of specific development and commercialization milestones that we may not meet. In addition, the collaboration agreements entitle us to royalty payments that are based on the sales of products developed and marketed through the collaborations. These future royalty payments may not materialize or may be less than expected if the related products are not successfully developed or marketed or if we are forced to license intellectual property from third parties. Accordingly, we cannot predict if our collaborations with MedImmune and Beckman Coulter will continue to generate revenues for us.

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

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

Our license agreement with Beckman Coulter relating to diagnostic assays for HMGB1 will terminate if Beckman Coulter does not exercise its option to continue the license by a future date. In addition, Beckman Coulter has the right to terminate the license agreement on 90-days written notice. Each party has the right to

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terminate the license agreement upon the occurrence of a material uncured breach by the other party. If Beckman Coulter were to terminate or breach our arrangement, and we were unable to enter into a similar agreement with another qualified third party in a timely manner or devote sufficient financial resources or capabilities to continue development and commercialization on our own, the development and commercialization of a diagnostic based on the detection of HMGB1 likely would be delayed, curtailed or terminated.

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

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

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

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

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

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

We rely on third parties to manufacture and supply the zileuton API, ZYFLO and our product candidates. We expect to continue to rely on 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 develop product candidates, apply for regulatory approvals and commercialize products, we need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities. We currently rely on third parties for production of the zileuton API and zileuton CR and commercial supplies of ZYFLO and the production of our product candidates for preclinical and clinical testing purposes. 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, 2009. 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. 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, Sumitomo is currently the only qualified supplier of a chemical known as 2-ABT one of the starting materials for zileuton, and if Sumitomo stops manufacturing, 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 ZYFLO and zileuton CR.

We have contracted with Patheon Pharmaceuticals Inc. for the manufacture of commercial supplies of ZYFLO tablets. We have contracted with Patheon for a technology transfer program to enable Patheon to coat

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and package the core tablets of zileuton CR for clinical trials and regulatory review, and, subject to negotiation of a commercial manufacturing agreement, commercial supplies.

We have contracted with SkyePharma PLC, through its subsidiary Jagotec AG, for the manufacture of tablets of zileuton CR for clinical trials, regulatory review and, subject to negotiation of a commercial manufacturing agreement, commercial supplies. SkyePharma announced that it was the target of an unsolicited acquisition bid in November 2005. SkyePharma subsequently announced that it had retained an investment bank to consider strategic options, including the sale of the company. In February 2006, SkyePharma announced a new senior management team and the conclusion of its strategic review, deciding to concentrate on oral and pulmonary products and divest its injectable business. The sale of SkyePharma as a whole or in parts may impact our ability to produce zileuton CR or to enter into a manufacturing agreement.

We have not secured a long-term commercial supply arrangement for any of our product candidates other than the zileuton API. The manufacturing process for our product candidates is an element of the FDA approval process. We will need to contract with manufacturers who can meet the FDA requirements, including current Good Manufacturing Practices, on an ongoing basis. As part of obtaining regulatory approval for zileuton CR, we are required to engage a commercial manufacturer to produce registration and validation batches of the drug consistent with regulatory approval requirements. In addition, if we receive the necessary regulatory approval for our product candidates, we also expect to rely on third parties, including our collaborators, to produce materials required for commercial production. We may experience difficulty in obtaining adequate manufacturing capacity or timing for our needs. If we are unable to obtain or maintain contract manufacturing of these product candidates, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our product candidates.

We are dependent upon Shasun Pharma Solutions, Patheon and SkyePharma as sole providers, and will be dependent on any other third parties who manufacture our product candidates, to perform their obligations in a timely manner and in accordance with applicable government regulations. For example, during the quarter ended June 30, 2006, one of our contract manufacturers failed to meet our manufacturing specifications relating to certain manufacturing batches of ZYFLO. If third-party manufacturers with whom we contract fail to perform their obligations, we may be adversely affected in a number of ways, including the following:

- we may not be able to initiate or continue clinical trials of our product candidates that are under development;
- we may be delayed in submitting applications for regulatory approvals for our product candidates;
- we may be required to cease distribution or issue recalls; and
- we may not be able to meet commercial demands.

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

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

We rely on third parties to distribute ZYFLO to pharmacies. We have contracted with Integrated Commercialization Services, Inc., or ICS, a third-party logistics company, to warehouse ZYFLO and distribute it to three primary

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

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rely on RxHope to administer our patient assistance program and to distribute ZYFLO to physicians and other prescribers who are authorized under state law to receive and dispense samples.

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

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

Our drug development programs and potential commercialization of our product candidates will require substantial additional cash to fund expenses to be incurred in connection with these activities. We may seek to enter into additional collaboration agreements with pharmaceutical companies to fund all or part of the costs of drug development and commercialization of product candidates. For example, we have determined to seek to enter into a collaboration arrangement with respect to the development of alpha-7 and do not plan to proceed with development without entering into such arrangement. We may not be able to enter into future collaboration agreements, and the terms of the collaboration agreements, if any, may not be favorable to us. If we are not successful in efforts to enter into a collaboration arrangement with respect to a product candidate, we may not have sufficient funds to develop any of our product candidates internally. If we do not have sufficient funds to develop our product candidates, we will not be able to bring these product candidates to market and generate revenue. In addition, our inability to enter into collaboration agreements could delay or preclude the development, manufacture and/or commercialization of a product candidate and could have a material adverse effect on our financial condition and results of operations because:

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

revenue from product sales could be delayed; or

we may elect not to commercialize the product candidate.

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

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

revenues may suffer.

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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 2010. The patent for zileuton CR will expire in 2012 and relates to the controlled-release technology used to control the release of zileuton. 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.

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

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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.

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.

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

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

Risks Relating to Our Financial Results and Need for Additional Financing

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

We have experienced significant operating losses in each year since our inception in 2000. We had net losses of \$31.2 million in the six months ended June 30, 2006 and \$47.1 million in the year ended December 31, 2005. As of June 30, 2006, we had an accumulated deficit of approximately \$136.8 million. For the six months ended June 30, 2006, we recorded \$2.8 million of revenue from the sale of ZYFLO and have not recorded revenue from any other product. We expect that we will continue to incur substantial losses for the foreseeable future as we spend significant amounts to fund our research, development and commercialization efforts. 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 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 obtain regulatory approval for zileuton CR, to support the anticipated commercial launch of zileuton CR, to fund additional clinical trials and pilot studies on zileuton CR and to fund the development of our other product candidates. Our funding requirements will depend on numerous factors, including:

- the costs and timing of the development, regulatory submission and approval and the commercial launch of zileuton CR, if and when it is approved by regulatory authorities;
- the scope and results of our clinical trials on zileuton CR;
- if approved, the amount and timing of sales of zileuton CR;
- the scope and results of our clinical trials on the intravenous formulation of zileuton;
- the amount and timing of the May 2006 and October 2006 cost reduction programs;
- the timing, receipt and amount of sales from ZYFLO;
- the costs of ongoing sales and marketing for ZYFLO;

advancements of other product candidates into development;

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

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

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

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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 cost of manufacturing, marketing and sales activities;

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

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

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

our ability to establish and maintain additional collaborative arrangements; and

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

Other than payments that we receive from our collaborations with MedImmune and Beckman Coulter, we expect that sales of ZYFLO will represent our only source of revenue until we commercially launch zileuton CR if it is approved. We believe that our ability to access external funds will depend upon the regulatory status of zileuton CR, market acceptance of zileuton CR, if approved, market acceptance of ZYFLO, the success of our other preclinical and clinical development programs, the receptivity of the capital markets to financings by biopharmaceutical companies, our ability to enter into additional strategic collaborations with corporate and academic collaborators and the success of such collaborations.

The extent of our future capital requirements is difficult to assess and will depend largely on our ability to obtain regulatory approval for and successfully commercialize zileuton CR and to sell ZYFLO. Based on our operating plans, we believe that our available cash and cash equivalents and anticipated cash received from product sales and anticipated payments received under collaboration agreements, together with the proceeds we receive from this offering, will be sufficient to fund anticipated levels of operations into the second half of 2008. Our operating plans assume the effective implementation of the May 2006 and October 2006 cost reductions.

For the six months ended June 30, 2006, our net cash used for operating activities was \$29.9 million, and we had capital expenditures of \$321,000. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we may need to raise additional external funds through collaborative arrangements and public or private financings. Additional financing may not be available to us on acceptable terms or at all. In addition, the terms of the financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our then-existing stockholders will result. If we are unable to obtain funding on a timely basis, we may be required to significantly delay, limit or eliminate one or more of our research, development or commercialization programs, which could harm our financial condition and operating results. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products which we would otherwise pursue on our own.

If the estimates we make, or the assumptions on which we rely, in preparing our financial statements prove inaccurate, our actual results may vary from 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. 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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Changes in or interpretations of accounting rules and regulations, such as expensing of employee stock options, could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for business and market practices of biopharmaceutical companies are subject to review, interpretation and guidance from relevant accounting authorities, including the SEC. For example, a new accounting rule, which became effective for us on January 1, 2006, requires us to record stock-based compensation expense for the fair value of stock options granted to employees. We rely heavily on stock options to compensate existing employees and attract new employees. Adoption of the new accounting rule on stock-based compensation expense is expected to increase net losses or reduce net income in future periods. Because we are now required to expense stock options, we may reduce our reliance on stock options as a compensation tool. If we reduce our reliance on stock options, it may be more difficult for us to attract and retain qualified employees. If we do not reduce our reliance on stock options, our reported losses would increase. Although we believe that our accounting practices are consistent with current accounting pronouncements, changes to or interpretations of accounting methods or policies in the future may require us to reclassify, restate or otherwise change or revise our financial statements.

Risks Relating to Our Common Stock

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

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

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 regulatory status of zileuton CR;

if approved, the amount and timing of sales of zileuton CR;

the amount and timing of sales of ZYFLO;

the timing of operating expenses, including selling and marketing expenses and the costs of maintaining a direct sales force;

the availability and timely delivery of a sufficient supply of ZYFLO;

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

the amount and timing of product returns for ZYFLO;

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

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

production problems occurring at our third party manufacturers;

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the results of regulatory reviews relating to the development or approval of our product candidates; and
general and industry-specific economic conditions that may affect our research and development expenditures.

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

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

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

the regulatory status of zileuton CR;
if approved, the amount and timing of sales of zileuton CR;
our operating results, including the amount and timing of sales of ZYFLO;
our licensing and collaboration agreements and the products or product candidates that are the subject of those agreements;
the results of discovery, preclinical studies and clinical trials by us or our competitors;
the acquisition of technologies, product candidates or products by us or our competitors;
the development of new technologies, product candidates or products by us or our competitors;
regulatory actions with respect to our product candidates or products or those of our competitors; and
significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors.

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 September 30, 2006, our directors, executive officers and 10% or greater stockholders, together with their affiliates, to our knowledge, beneficially owned, in the aggregate, approximately 50.2% 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, our anti-takeover provisions include provisions in our by-laws providing that stockholders' meetings may be called only by the president or the majority of the board of directors and a provision in our certificate of incorporation providing that our stockholders may not take action by written consent.

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

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

Investors in this offering will pay a much higher price than the book value of our stock.

If you purchase common stock in this offering, you will incur an immediate and substantial dilution in net tangible book value of \$ 1 per share, after giving effect to the sale by us of 1 units in this offering at the public offering price of \$ 1 per unit. In the past, we have issued options to acquire common stock at prices significantly below this offering price. To the extent these outstanding options are ultimately exercised, you will incur additional dilution.

Because our management will have broad discretion over the use of the net proceeds from this offering, you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

We intend to use the net proceeds from this offering to fund our efforts to obtain FDA approval for zileuton CR, to prepare for commercial launch of zileuton CR, to fund development of the intravenous formulation of zileuton and for other general corporate purposes, therefore, our management will have broad discretion as to the use of the offering proceeds. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for our company.

There is no public market for the warrants to purchase common stock in this offering.

There is no established public trading market for the warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply for listing the warrants on any securities exchange or for quotation on the Nasdaq. Without an active market, the liquidity of the warrants will be limited.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we incorporate by reference include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For purposes of these statutes, any statement contained herein or therein, other than a statement of historical fact, may be a forward-looking statement. For example, we may, in some cases, use words such as anticipate, believe, could, estimate, expect, intend, may, plan, project, should, will,

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would or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the factors referred to above under the heading Risk Factors. These important factors include the factors that we identify in the documents that we incorporate by reference in this prospectus. 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. You should consider these factors and the other cautionary statements made in this prospectus or the documents we incorporate by reference as being applicable to all related forward-looking statements wherever they appear in this prospectus or the documents incorporated by reference. We do not assume, and specifically disclaim, any obligation to do so, whether as a result of new information, future events or otherwise.

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USE OF PROCEEDS

We estimate that our net proceeds from the sale of securities offered pursuant to this prospectus, excluding the proceeds, if any, from the exercise of the warrants issued in this offering, will be approximately \$ 1 million if we sell the maximum number of units, after deducting the placement agent fees and all estimated offering expenses that are payable by us.

We currently intend to use the net proceeds from the sale of the units;

to fund our efforts to obtain FDA approval for zileuton CR;

to prepare for commercial launch of zileuton CR;

to fund development of the intravenous formulation of zileuton CR; and

for other general corporate purposes.

We cannot estimate precisely the allocation of the net proceeds from this offering among these uses. The amount that we actually expend for these purposes may vary significantly depending upon numerous factors including the costs and timing of the development, regulatory submission and approval of zileuton CR, the costs of the commercial launch of zileuton CR, if and when it is approved by regulatory authorities, the amount and timing of sales of ZYFLO, and the progress of our research, drug discovery and development programs.

Pending the application of the net proceeds, we intend to invest the net proceeds in short-term investment grade and U.S. government securities.

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Our net tangible book value as of June 30, 2006 was \$45.7 million, or \$1.34 per share of common stock based on 34,237,790 shares of our common stock outstanding as of June 30, 2006. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, and dividing this amount by the number of shares of common stock outstanding.

After giving effect to the sale of an estimated 8.0 million units in this offering at an assumed public offering price of \$2.69 per unit and after deducting estimated placement agent's fees and estimated offering expenses, our net tangible book value as of June 30, 2006 would have been \$65.2 million, or \$1.54 per share of common stock. This represents an immediate increase in net tangible book value of \$0.20 per share to our existing shareholders and an immediate dilution in net tangible book value of \$1.09 per share to new investors. Our net tangible book value calculation assumes:

no exercise of outstanding options to purchase our common stock or warrants to purchase shares of our common stock; and

no exercise of the warrants offered hereby.

The following table illustrates this per share dilution:

| | | |
|---|---------|---------|
| Assumed public offering price per share | | \$ 2.63 |
| Net tangible book value per share as of June 30, 2006 | \$ 1.34 | |
| Increase per share attributable to new investors | 0.20 | |
| Net tangible book value per share after this offering | | 1.54 |
| Dilution per share to new investors | | \$ 1.09 |

A \$0.25 increase (decrease) in the assumed public offering price of \$2.69 per unit would increase (decrease) the net tangible book value by \$1.9 million, the net tangible book value per share after this offering by \$0.04 per share and the dilution in net tangible book value per share to investors in this offering by \$0.21 per share, assuming that the number of units offered by us, as set forth above, remains the same and after deducting the estimated placement agent's fees and offering expenses payable by us.

New investors that purchase common stock upon exercise of warrants may experience dilution depending on our net tangible book value at the time of exercise.

In the discussion and table above, we assume no exercise of outstanding options. As of October 25, 2006, there were 7,093,454 shares of common stock reserved for issuance upon exercise of outstanding options with a weighted average exercise price of \$4.92 per share. To the extent that any of these outstanding options are exercised, there may be further dilution to new investors.

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DESCRIPTION OF SECURITIES WE ARE OFFERING

In this offering, we are offering a maximum of 1 units, consisting of 1 shares of common stock and warrants to purchase 1 shares of common stock. Each unit consists of one share of common stock and warrants to purchase 1 shares of common stock at an exercise price of \$ 1 per share. This prospectus also relates to the offering of shares of our common stock upon exercise, if any, of the warrants.

Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption Description of Capital Stock starting on page 4.

Warrants

The material terms and provisions of the warrants being offered pursuant to this prospectus are summarized below.

Exercisability. The warrants will be exercisable at any time prior to 3:30 p.m. Eastern Time on October 1, 2011. The warrants will be exercisable, at the option of each holder, upon the surrender of the warrants to us and the payment in cash by the holder of the exercise price of the shares being acquired upon exercise of the warrants.

Exercise Price. The exercise price per share of common stock purchasable upon exercise of the warrants is \$ 1 per share of common stock being purchased. The exercise price is subject to appropriate adjustment in the event of stock dividends, stock splits, stock combinations, reclassifications or similar events affecting our common stock. We may at any time reduce the exercise price per share of common stock purchasable upon exercise of the warrants to any amount deemed appropriate by our board of directors, for any length of time.

Transferability. The warrants may be transferred at the option of the warrant holder upon surrender of the warrants to the warrant agent with the appropriate instruments of transfer.

Effect of Merger, Consolidation or Sale of Assets. If we consummate any consolidation or merger into another corporation in which our common stock is converted into or exchanged for other securities or property, the holder of any warrants will thereafter receive upon exercise of the warrants, the securities or property to which a holder of the number of shares of common stock then deliverable upon the exercise or conversion of such warrants would have been entitled upon such consolidation or merger. A sale of all or substantially all our assets for consideration consisting primarily of securities shall be deemed a consolidation or merger.

Table of Contents**PLAN OF DISTRIBUTION**

We are offering the units through a placement agent. Subject to the terms and conditions contained in the placement agent agreement dated October 1, 2006, Lazard Capital Markets LLC has agreed to act as the placement agent for the sale of up to 1 units. The placement agent is not purchasing or selling any units by this prospectus, nor is it required to arrange for the purchase or sale of any specific number or dollar amount of units, but has agreed to use best efforts to arrange for the sale of all 1 units.

The placement agent agreement provides that the obligations of the placement agent and the investors are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of certain opinions, letters and certificates from our counsel, our independent auditors and us.

Confirmations and definitive prospectuses will be distributed to all investors who agree to purchase the units, informing investors of the closing date as to such units. We currently anticipate that closing of the sale of 1 units will take place on or about October 1, 2006. Investors will also be informed of the date and manner in which they must transmit the purchase price for their units.

On the scheduled closing date, the following will occur:

we will receive funds in the amount of the aggregate purchase price; and

Lazard Capital Markets LLC will receive the placement agent's fee in accordance with the terms of the placement agent agreement.

We will pay the placement agent a commission equal to 6% of the gross proceeds of the sale of units, except that we will pay the placement agent a commission equal to 3% of the gross proceeds of the sale of units, if any, to specified existing investors. We may also reimburse the placement agent for certain legal expenses incurred by them. In no event will the total amount of compensation paid to the placement agent and other securities brokers and dealers upon completion of this offering exceed 8% of the gross proceeds of the offering. The estimated offering expenses payable by us, in addition to the placement agent's fee of \$ 1, are approximately \$ 1, which includes legal, accounting and printing costs and various other fees associated with registering and listing the common stock. After deducting certain fees due to the placement agent and our estimated offering expenses, we expect the net proceeds from this offering to be approximately \$ 1 million if the maximum number of units is sold.

The following table provides information regarding the amount of commission to be paid to the placement agent by us based on a public offering price of \$ 1 per unit:

| | Per Unit | Total |
|------------------------|-----------------|--------------|
| Placement agent's fees | \$ 1 | \$ 1 |

Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith. We also have retained Lazard Frères & Co. LLC to provide us with certain financial advisory services unrelated this offering, for which it may receive customary fees.

We have agreed to indemnify the placement agent and Lazard Frères & Co. LLC against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and

warranties contained in the placement agent agreement. We have also agreed to contribute to payments the placement agent and Lazard Frères & Co. LLC may be required to make in respect of such liabilities.

We, along with our executive officers, directors and specified shareholders, have agreed to certain lock-up provisions with regard to future sales of our common stock for a period of 90 days after the offering as set forth in the placement agent agreement.

The placement agent agreement is included as an exhibit to our Current Report on Form 8-K that we will file with the SEC in connection with the consummation of this offering.

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The transfer agent for our common stock and for the warrants to purchase our common stock to be issued in this offering is Mellon Investor Services LLC.

Our common shares are traded on the Nasdaq Global Market under the symbol CRTX. The warrants to purchase common stock are not expected to be eligible for trading on any market.

The price per share of for the units and the exercise price for the warrants was determined based on negotiations with the purchasers and discussions with the placement agent.

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VALIDITY OF SECURITIES

The validity of the issuance of the securities offered by this prospectus will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Brown Raysman Millstein Felder & Steiner LLP, New York, New York is counsel for the placement agent in connection with this offering.

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\$40,000,000

CRITICAL THERAPEUTICS, INC.

**Common Stock
Preferred Stock
Debt Securities
Warrants**

We may from time to time issue up to \$40,000,000 aggregate principal amount of common stock, preferred stock, debt securities and warrants. We may sell these securities to or through underwriters, directly to investors or through agents. We will specify the terms of the securities, and the names of any underwriters or agents, in supplements to this prospectus.

Our common stock is listed on The Nasdaq Global Market and traded under the symbol CRTX.

Investing in our securities involves significant risks. See Risk Factors on page 2.

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

This prospectus may not be used to consummate sales of securities unless it is accompanied by a prospectus supplement.

Prospectus dated September 11, 2006.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, we may from time to time sell common stock, preferred stock, debt securities or warrants, or any combination of these securities, in one or more offerings up to a total dollar amount of \$40,000,000. We have provided to you in this prospectus a general description of the securities we may offer. Each time we sell securities under this shelf registration process, we will provide a prospectus supplement that will contain specific information about the terms of the offering. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus or any prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

As permitted by the rules and regulations of the SEC, the registration statement, of which this prospectus forms a part, includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or at the SEC's offices described below under the heading Where You Can Find Additional Information.

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SUMMARY

Critical Therapeutics, Inc.

Critical Therapeutics, Inc. is a biopharmaceutical company focused on the discovery, development and commercialization of products designed to treat respiratory, inflammatory and critical care diseases linked to the body's inflammatory response. Our marketed product is ZYFLO[®], an immediate-release tablet formulation of zileuton, which the U.S. Food and Drug Administration, or FDA, approved in 1996 for the prevention and chronic treatment of asthma in adults and children 12 years of age or older. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO and other formulations of zileuton for multiple diseases and conditions. We began selling ZYFLO in the United States in October 2005. In addition to asthma, we believe that zileuton has potential therapeutic benefits in a range of other diseases and conditions, such as acute asthma exacerbations and chronic obstructive pulmonary disease, known as COPD. We are currently incurring costs to expand our applications of zileuton through development of additional formulations, including controlled-release and intravenous formulations. In July 2006, we submitted a New Drug Application for the twice-daily, controlled-release tablet formulation of zileuton to the FDA.

We are also developing product candidates to regulate the excessive inflammatory response that can damage vital internal organs and, in the most severe cases, result in multiple organ failure and death. The inflammatory response occurs following stimuli such as infection or trauma. Our research programs and 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. on preclinical development of monoclonal antibodies directed toward a cytokine called HMGB1, or high mobility group box protein 1, which we believe may be an important target for the development of products to treat inflammation-mediated diseases. In addition, we are collaborating with Beckman Coulter, Inc. on development of a diagnostic directed toward measuring HMGB1 in the bloodstream.

Corporate Information

We were incorporated in Delaware on July 14, 2000. Our principal executive offices are located at 60 Westview Street, Lexington, Massachusetts 02421, our general telephone number at that address is (781) 402-5700 and our web site is located at www.crtx.com. The information on, or that can be accessed through, our web site is not incorporated by reference in this prospectus or any prospectus supplement, and you should not consider it to be a part of this prospectus or any prospectus supplement. Our web site address is included as an inactive textual reference only. Unless the context otherwise requires, references in this prospectus to Critical Therapeutics or the Company, we, us, and our refer to Critical Therapeutics, Inc.

Critical Therapeutics[™], Critical Therapeutics circular logo design[®], CRTX[™], CT2[™] and ZYFLO[®] are trademarks or service marks of Critical Therapeutics, Inc. Other trade names and trademarks appearing or incorporated by reference in this prospectus or in any prospectus supplement are the property of their respective owners.

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RISK FACTORS

Investing in our securities involves significant risks. Please see the risk factors under the heading "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2006 on file with the SEC, which are incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any prospectus supplement. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the documents we incorporate by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For purposes of these statutes, any statement contained herein or therein, other than a statement of historical fact, may be a forward-looking statement. For example, we may, in some cases, use words such as anticipate, believe, could, estimate, expect, intend, may, plan, project, should, will, would or could to indicate uncertainty of future events or outcomes to identify these forward-looking statements. Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the factors referred to above under the heading "Risk Factors." These important factors include the factors that we identify in the documents that we incorporate by reference in this prospectus. 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. You should consider these factors and the other cautionary statements made in this prospectus, any prospectus supplement or the documents we incorporate by reference in this prospectus as being applicable to all related forward-looking statements wherever they appear in this prospectus, any prospectus supplement or the documents incorporated by reference. While we may elect to update forward-looking statements wherever they appear in this prospectus, any prospectus supplement or the documents incorporated by reference, we do not assume, and specifically disclaim, any obligation to do so, whether as a result of new information, future events or otherwise.

USE OF PROCEEDS

Unless otherwise provided in the applicable prospectus supplement, we currently intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, including sales and marketing expenses, clinical trial costs, research and development expenses, general and administrative expenses, and potential acquisition of, or investment in, companies, technologies, products or assets that complement our business. We will set forth in a prospectus supplement relating to a specific offering our intended use for the net proceeds received from the sale of securities in that offering. Pending the application of the net proceeds, we intend to invest the net proceeds in short-term investment grade and U.S. government securities.

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RATIO OF EARNINGS TO FIXED CHARGES

Our consolidated ratio of earnings to fixed charges for each of the periods indicated is set forth below.

| Six Months Ended June 30, 2006 | 2005 | Year Ended December 31, | | | |
|---|-------------|--------------------------------|-------------|-------------|-------------|
| | | 2004 | 2003 | 2002 | 2001 |

Ratio of earnings to fixed charges

We have computed the ratio of earnings to fixed charges set forth above by dividing pre-tax loss from continuing operations before fixed charges by fixed charges. Fixed charges are the sum of the following:

interest expense;

amortized premiums, discounts and capitalized expenses related to indebtedness; and

an estimate of the interest within rental expense.

Our earnings were insufficient to cover fixed charges by \$14.3 million for the six months ended June 30, 2006, \$46.8 million for the year ended December 31, 2005, \$33.0 million for the year ended December 31, 2004, \$22.2 million for the year ended December 31, 2003, \$5.9 million for the year ended December 31, 2002 and \$1.9 million for the year ended December 31, 2001.

As of the date of this prospectus, we have no shares of preferred stock outstanding and have not declared or paid any preferred stock dividends for the periods set forth above.

DILUTION

We will set forth in a prospectus supplement the following information regarding any material dilution of the equity interests of investors purchasing securities in an offering under this prospectus:

the net tangible book value per share of our equity securities before and after the offering;

the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers in the offering; and

the amount of the immediate dilution from the public offering price which will be absorbed by such purchasers.

THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where

applicable, about material U.S. federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may sell from time to time, in one or more offerings:

common stock;

preferred stock;

debt securities;

warrants to purchase any of the securities listed above; and

any combination of the foregoing securities.

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In this prospectus, we will refer to the common stock, preferred stock, debt securities and warrants collectively as securities. The total dollar amount of all securities that we may issue under this prospectus will not exceed \$40,000,000.

If we issue debt securities at a discount from their original stated principal amount, then, for purposes of calculating the total dollar amount of all securities issued under this prospectus, we will treat the initial offering price of the debt securities as the total original principal amount of the debt securities.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. For the complete terms of our common stock and preferred stock, please refer to our certificate of incorporation and bylaws, which are incorporated by reference into the registration statement, of which this prospectus forms a part. The terms of our common stock and preferred stock may also be affected by Delaware law.

Authorized Capital Stock

Our authorized capital stock consists of 90,000,000 shares of common stock, \$0.001 par value per share, and 5,000,000 shares of preferred stock, \$0.001 par value per share. As of August 22, 2006, we had 34,294,352 shares of common stock outstanding and no shares of preferred stock outstanding. All of our outstanding shares of common stock are duly authorized, validly issued, fully paid and non-assessable.

Common Stock

Voting

For all matters submitted to a vote of stockholders, each holder of common stock is entitled to one vote for each share registered in the stockholder's name. Our common stock does not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. An election of directors by our stockholders is determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

Dividends

Holders of common stock are entitled to share ratably in any dividends declared by our board of directors, subject to any preferential dividend rights of any outstanding preferred stock. Dividends consisting of shares of common stock may be paid to holders of shares of common stock. We have never declared or paid cash dividends on our capital stock. We do not intend to pay cash dividends in the foreseeable future.

Liquidation and Dissolution

If we are liquidated or dissolve, the holders of our common stock will be entitled to share ratably in all the assets that remain after we pay our liabilities, subject to the prior rights of any outstanding preferred stock.

Other Rights and Restrictions

Holders of our common stock do not have preemptive rights, and they have no right to convert their common stock into any other securities. Our common stock is not subject to redemption by us. Our certificate of incorporation and bylaws do not restrict the ability of a holder of common stock to transfer the stockholder's shares of common stock. When we issue shares of common stock under this prospectus, the shares will be fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

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Listing

Our common stock is listed on The Nasdaq Global Market under the symbol CRTX. On August 22, 2006, the last reported sale price for our common stock on The Nasdaq Global Market was \$3.57 per share. As of August 22, 2006 we had approximately 115 stockholders of record.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Mellon Investor Services LLC.

Preferred Stock

Our board of directors is authorized, subject to any limitations under our certificate of incorporation or prescribed by law, without further stockholder approval, to issue up to an aggregate of 5,000,000 shares of preferred stock. Our board of directors may establish the applicable and relative designations, number of authorized shares, dividend rates and terms, redemption or sinking fund provisions, conversion or exchange rates, anti-dilution provisions, voting rights, liquidation preferences and other terms, preferences and limitations of any series of preferred stock it determines to issue.

If we decide to issue any preferred stock pursuant to this prospectus, we will describe in a prospectus supplement the terms of the preferred stock, including, if applicable, the following:

the title of the series and stated value;

the number of shares of the series of preferred stock offered, the liquidation preference per share, if applicable, and the offering price;

the applicable dividend rate(s) or amount(s), period(s) and payment date(s) or method(s) of calculation thereof;

the date from which dividends on the preferred stock will accumulate, if applicable;

any procedures for auction and remarketing;

any provisions for a sinking fund;

any applicable provision for redemption and the price or prices, terms and conditions on which preferred stock may be redeemed;

any securities exchange listing;

any voting rights and powers;

whether interests in the preferred stock will be represented by depository shares;

the terms and conditions, if applicable, of conversion into shares of our common stock, including the conversion price or rate or manner of calculation thereof;

a discussion of any material U.S. federal income tax considerations;

the relative ranking and preference as to dividend rights and rights upon our liquidation, dissolution or the winding up of our affairs;

any limitations on issuance of any series of preferred stock ranking senior to or on a parity with such series of preferred stock as to dividend rights and rights upon our liquidation, dissolution or the winding up of our affairs; and

any other specific terms, preferences, rights, limitations or restrictions of such series of preferred stock.

Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of The Nasdaq Global Market. We may

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utilize these additional shares for a variety of corporate purposes, including for future public offerings to raise additional capital or facilitate corporate acquisitions or for payment as a dividend on our capital stock. The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a controlling interest in our company by means of a merger, tender offer, proxy contest or otherwise. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Delaware Law and Certificate of Incorporation and Bylaw Provisions

Anti-Takeover Provisions

We are subject to Section 203 of the General Corporation Law of Delaware. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a business combination with any interested stockholder for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger or consolidation involving us and the interested stockholder and the sale of more than 10% of our assets. In general, an interested stockholder is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders.

Staggered Board

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before the meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our chairman of the board, our president or chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority

of our outstanding voting securities.

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Super-Majority Voting

The General Corporation Law of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes which all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes which all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described in the prior two paragraphs.

Limitation of Liability and Indemnification of Officers and Directors

Our amended and restated certificate of incorporation contains provisions permitted under the General Corporation Law of Delaware relating to the liability of directors. The provisions eliminate a director's liability for monetary damages for a breach of fiduciary duty, except in circumstances involving wrongful acts, such as the breach of a director's duty of loyalty or acts or omissions that involve intentional misconduct or a knowing violation of law. Further, our amended and restated certificate of incorporation contains provisions to indemnify our directors and officers to the fullest extent permitted by the General Corporation Law of Delaware.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we indicate in a prospectus supplement, the terms of any debt securities we offer under that prospectus supplement may differ from the terms we describe below.

We will issue senior notes under a senior indenture, which we will enter into with a trustee to be named in the senior indenture. We will issue subordinated notes under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus forms a part. We use the term "indentures" to refer to both the senior indenture and the subordinated indenture. The indentures will be qualified under the Trust Indenture Act of 1939, or the Trust Indenture Act. We use the term "trustee" to refer to either the senior trustee or the subordinated trustee, as applicable.

The following summaries of material provisions of senior notes, subordinated notes and the indentures are subject to, and qualified in their entirety by reference to, the provisions of the indenture applicable to a particular series of debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

If we decide to issue any senior notes or subordinated notes pursuant to this prospectus, we will describe in a prospectus supplement the terms of the series of notes, including the following:

the title;

any limit on the amount that may be issued;

whether or not we will issue the series of notes in global form, and, if so, who the depository will be;
the maturity date;

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the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

whether or not the notes will be secured or unsecured, and the terms of any secured debt;

whether or not the notes will be senior or subordinated;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, and the price at which, we may, at our option, redeem the series of notes pursuant to any optional redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of notes;

whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;

whether we will be restricted from incurring any additional indebtedness;

a discussion of any material or special U.S. federal income tax considerations;

the denominations in which we will issue the series of notes, if other than denominations of \$2,000 and any integral multiple thereof; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of notes may be convertible into or exchangeable for common stock or other securities of ours. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of common stock or other securities of ours that the holders of the series of notes receive would be subject to adjustment.

Consolidation, Merger or Sale

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the notes, as appropriate.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of notes that we may issue:

if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;

if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;

if we fail to observe or perform any other covenant contained in the notes or the indentures, other than a covenant specifically relating to another series of notes, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding notes of the applicable series; and

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if we experience specified events of bankruptcy, insolvency or reorganization.

If an event of default with respect to notes of any series occurs and is continuing, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding notes of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, or premium, if any, on and accrued interest, if any, on the notes due and payable immediately.

The holders of a majority in principal amount of the outstanding notes of an affected series may waive any default or event of default with respect to the series and its consequences, except uncured defaults or events of default regarding payment of principal, or premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of notes, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding notes of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the notes of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the notes of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies, if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding notes of that series have made written request, and such holders have offered reasonable indemnity to the trustee to institute the proceeding as trustee; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding notes of that series other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of notes if we default in the payment of the principal of, or the premium, if any, or interest on, the notes.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters, including:

to fix any ambiguity, defect or inconsistency in the indenture; and

to change anything that does not materially adversely affect the interests of any holder of notes of any series.

In addition, under the indentures, we and the trustee may change the rights of holders of a series of notes with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding

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notes of each series that is affected. However, we and the trustee may only make the following changes with the consent of each holder of any outstanding notes affected:

extending the fixed maturity of the series of notes;

reducing the principal amount, the rate of interest or any premium payable upon the redemption of any notes; or

reducing the minimum percentage of notes, the holders of which are required to consent to any amendment.

Discharge

Each indenture provides that we can elect, under specified circumstances, to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the notes of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$2,000 and any integral multiple thereof. The indentures provide that we may issue notes of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, or DTC, or another depository named by us and identified in a prospectus supplement with respect to that series. See [Legal Ownership of Securities](#) for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the notes of any series can exchange the notes for other notes of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the notes may present the notes for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the notes that the holder presents for transfer or exchange, we will not require any payment for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any notes. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the notes of each series.

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If we elect to redeem the notes of any series, we will not be required to:

issue, register the transfer of, or exchange any notes of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any notes that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any notes so selected for redemption, in whole or in part, except the unredeemed portion of any notes we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care and skill as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given to it by the indentures at the request of any holder of notes unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any notes on any interest payment date to the person in whose name the notes, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest payment.

We will pay principal of and any premium and interest on the notes of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the trustee in The City of New York as our sole paying agent for payments with respect to notes of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the notes of a particular series. We will maintain a paying agent in each place of payment for the notes of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any notes which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the notes will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Notes

The subordinated notes will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated notes that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of

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warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, of which this prospectus forms a part.

General

We may issue warrants for the purchase of common stock, preferred stock or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate agreement. We may enter into a warrant agreement with a warrant agent. We will indicate the name and address and other information regarding the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

If we decide to issue warrants pursuant to this prospectus, we will specify in a prospectus supplement the terms of the series of warrants, including, if applicable, the following:

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

the date on and after which the warrants and the related securities will be separately transferable;

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

in the case of warrants to purchase common stock, the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreement and warrants may be modified;

a discussion of any material U.S. federal income tax considerations of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

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in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5:00 P.M. Eastern time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee maintain for this purpose as the **holders** of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names as **indirect holders** of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution

that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its nominee. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and

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we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which will in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depository participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

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if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security held by a depositary that represents one or any other number of individual securities. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under **Special Situations When a Global Security Will Be Terminated**. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above under **Legal Holders** ;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depositary in any way;

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

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financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

if the depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depository, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities being offered hereby in one or more of the following ways from time to time:

through agents to the public or to investors;

to one or more underwriters for resale to the public or to investors;

in at the market offerings, within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;

directly to investors in privately negotiated transactions; or

through a combination of these methods of sale.

The securities that we distribute by any of these methods may be sold, in one or more transactions, at:

a fixed price or prices, which may be changed;

market prices prevailing at the time of sale;

prices related to prevailing market prices; or
negotiated prices.

We will set forth in a prospectus supplement the terms of the offering of securities, including:

the name or names of any agents or underwriters;

the purchase price of the securities being offered and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

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any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;
the public offering price;
any discounts or concessions allowed or reallocated or paid to dealers; and
any securities exchanges on which such securities may be listed.

Underwriters

If we use underwriters for a sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. The underwriters will be obligated to purchase all the securities of the series offered if they purchase any of the securities of that series. We may change from time to time any initial public offering price and any discounts or concessions the underwriters allow or reallocate or pay to dealers. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement naming the underwriter the nature of any such relationship.

Agents

We may designate agents who agree to use their reasonable efforts to solicit purchases for the period of their appointment or to sell securities on a continuing basis.

Direct Sales

We may also sell securities directly to one or more purchasers without using underwriters or agents.

Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

Trading Markets and Listing of Securities

Unless otherwise specified in the applicable prospectus supplement, each class or series of securities will be a new issue with no established trading market, other than our common stock, which is listed on The Nasdaq Global Market. We may elect to list any other class or series of securities on any exchange, but we are not obligated to do so. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

Stabilization Activities

In connection with an offering, an underwriter may purchase and sell securities in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of securities than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional securities, if any, from us in the offering. If the underwriters have an over-allotment option to purchase additional securities from us, the underwriters may close out any covered short position by either exercising their over-allotment option or purchasing securities in the open market. In

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determining the source of securities to close out the covered short position, the underwriters may consider, among other things, the price of securities available for purchase in the open market as compared to the price at which they may purchase securities through the over-allotment option. Naked short sales are any sales in excess of such option or where the underwriters do not have an over-allotment option. The underwriters must close out any naked short position by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the securities in the open market after pricing that could adversely affect investors who purchase in the offering.

Accordingly, to cover these short sales positions or to otherwise stabilize or maintain the price of the securities, the underwriters may bid for or purchase securities in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to syndicate members or other broker-dealers participating in the offering are reclaimed if securities previously distributed in the offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. The impositions of a penalty bid may also affect the price of the securities to the extent that it discourages resale of the securities. The magnitude or effect of any stabilization or other transactions is uncertain. These transactions may be effected on The Nasdaq Global Market or otherwise and, if commenced, may be discontinued at any time.

VALIDITY OF SECURITIES

The validity of the issuance of the securities offered by this prospectus will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Partners of Wilmer Cutler Pickering Hale and Dorr LLP beneficially own 19,020 shares of our common stock.

EXPERTS

The financial statements and management's report on the effectiveness of internal control over financial reporting incorporated in this registration statement by reference from the Company's Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their reports, which are incorporated herein by reference, and have been so incorporated in reliance upon the reports of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other information with the SEC as required by the Exchange Act. You can find, copy and inspect information we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information about the public reference room. You can review our electronically filed reports, proxy and information statements on the SEC's web site at <http://www.sec.gov> or on our web site at <http://www.crtx.com>. Information included on our web site is not a part of this prospectus or any prospectus supplement.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and the securities, including exhibits and schedules. You can obtain a copy of the registration statement from the SEC at any address listed above or from the SEC's web site.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC requires us to incorporate into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that

information. The information incorporated by reference is considered to be part of this prospectus. Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically modifies and supersedes previously filed information

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including information in previously filed documents or reports that have been incorporated by reference in this prospectus, to the extent the new information differs from or is inconsistent with the old information. Any information so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We incorporate by reference, as of their respective dates of filing, the documents listed below that we have filed with the SEC and any documents that we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus:

our Annual Report on Form 10-K for the year ended December 31, 2005, as filed with the SEC on March 7, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated January 6, 2006, as filed with the SEC on January 6, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated February 9, 2006, as filed with the SEC on February 9, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated February 14, 2006, as filed with the SEC on February 15, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated March 15, 2006, as filed with the SEC on March 15, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated April 25, 2006, as filed with the SEC on April 27, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated April 26, 2006, as filed with the SEC on May 1, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated May 2, 2006, as filed with the SEC on May 2, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated May 4, 2006, as filed with the SEC on May 4, 2006 (SEC File No. 000-50767);

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2006, as filed with the SEC on May 10, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated June 23, 2006, as filed with the SEC on June 27, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated June 29, 2006, as filed with the SEC on June 30, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated July 10, 2006, as filed with the SEC on July 14, 2006 (SEC File No. 000-50767);

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our Current Report on Form 8-K dated July 18, 2006, as filed with the SEC on July 18, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated August 3, 2006, as filed with the SEC on August 3, 2006 (SEC File No. 000-50767);

our Current Report on Form 8-K dated August 23, 2006, as filed with the SEC on August 23, 2006 (SEC File No. 000-50767);

our Quarterly Report on Form 10-Q for the quarter ended June 30, 2006, as filed with the SEC on August 9, 2006 (SEC File No. 000-50767);

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the description of our common stock contained in our Registration Statement on Form 8-A dated May 19, 2004, including any amendments or reports filed for the purpose of updating that description; and

any other filings we make pursuant to the Exchange Act after the date of filing the initial registration statement and prior to effectiveness of the registration statement.

You may request a copy of these documents, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

Critical Therapeutics, Inc.

60 Westview Street

Lexington, Massachusetts 02421

Attention: Vice President of Investor and Media Relations

Telephone: (781) 402-5700

You should rely only on the information contained in this prospectus, including information incorporated by reference as described above, or any prospectus supplement or that we have specifically referred you to. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents or that any document incorporated by reference is accurate as of any date other than its filing date. You should not consider this prospectus to be an offer or solicitation relating to the securities in any jurisdiction in which such an offer or solicitation relating to the securities is not authorized. Furthermore, you should not consider this prospectus to be an offer or solicitation relating to the securities if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

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1 Shares of Common Stock
Warrants to Purchase 1 Shares of Common Stock

PRELIMINARY PROSPECTUS SUPPLEMENT

Lazard Capital Markets

October 1, 2006