CRITICAL THERAPEUTICS INC
Form S-3
June 24, 2005

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As filed with the Securities and Exchange Commission on June 24, 2005

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT UNDER
THE SECURITIES ACT OF 1933

CRITICAL THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**04-3523569**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)

60 Westview Street

Lexington, Massachusetts 02421
(781) 402-5700
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant s Principal Executive Offices)

Paul D. Rubin, M.D.
President and Chief Executive Officer
Critical Therapeutics, Inc.
60 Westview Street
Lexington, Massachusetts 02421
(781) 402-5700
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies to:

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Vice President of Legal Affairs and Secretary
Critical Therapeutics, Inc.
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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date hereof.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. ý

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨ _____

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨ _____

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ¨

CALCULATION OF REGISTRATION FEE

Title Of Each Class Of Securities To Be Registered	Amount To Be Registered(1)	Proposed Maximum Offering Price Per Share(2)	Proposed Maximum Aggregate Offering Price(2)	Amount Of Registration Fee
Common Stock, $0.001 par value per share	13,426,103	$5.99	$80,422,357	$9,466

(1) Consists of (a) 9,945,261 shares of common stock that Critical Therapeutics, Inc. issued to investors in a private placement in June 2005, (b) 3,480,842 additional shares of common stock issuable upon the exercise of warrants that Critical Therapeutics, Inc. issued to investors in the private placement in June 2005 and (c) an indeterminate number of additional shares of common stock as may from time to time be issued with respect to the foregoing securities as a result of stock splits, stock dividends, reclassifications, recapitalizations, combinations or similar events, which shares shall be deemed registered hereunder pursuant to Rule 416 under the Securities Act of 1933, as amended (the Securities Act).

(2) Estimated solely for purposes of calculating the registration fee pursuant to Rule 457(c) under the Securities Act, based upon the average of the high and low price per share of the common stock as reported on the Nasdaq National Market on June 20, 2005.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling stockholders named in this prospectus are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated June 24, 2005

PROSPECTUS

CRITICAL THERAPEUTICS, INC.

13,426,103 SHARES OF COMMON STOCK

This prospectus relates to resales of shares of our common stock, including shares of common stock issuable upon the exercise of warrants, that we issued to the selling stockholders identified in this prospectus in a private placement in June 2005. We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders. We have agreed to pay certain expenses in connection with the registration of the shares and to indemnify the selling stockholders against certain liabilities.

The selling stockholders identified in this prospectus, or their pledgees, donees, transferees or other successors-in-interest, may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices.

Our common stock is traded on the Nasdaq National Market under the symbol CRTX. On June 23, 2005, the closing sale price of our common stock on Nasdaq was $6.60 per share. You are urged to obtain current market quotations for the common stock.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 3.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 24, 2005.

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We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. The selling stockholders are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock.

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PROSPECTUS SUMMARY

This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, especially the risks of investing in our common stock discussed under Risk Factors.

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 through the regulation of the body s inflammatory response. The inflammatory response occurs within the body s immune system following a stimulus such as infection or trauma. Our most advanced product is ZYFLO® Filmtab®, a tablet formulation of zileuton, which the U.S. Food and Drug Administration, or FDA, approved in 1996 for the prevention and chronic treatment of asthma. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO and other formulations of zileuton for multiple diseases and conditions. We have transferred the manufacturing production of ZYFLO to new manufacturing sites, and subject to FDA approval of these sites, we expect to begin selling ZYFLO in the United States in the fourth quarter of 2005.

We also are developing products 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.

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 telephone number at that address is (781) 402-5700 and our Internet address is www.crtx.com. The information on our Internet website is not incorporated by reference in this prospectus, and you should not consider it to be a part of this document. Our website 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 logo and ZYFLO® are trademarks or service marks of Critical Therapeutics. Filmtab® is a registered trademark of the Abbott Group of Companies. Other tradenames and trademarks appearing in this prospectus are the property of their respective owners.

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THE OFFERING

Common stock offered by selling stockholders	13,426,103 shares of our common stock, including 3,480,842 shares issuable upon the exercise of warrants, held by the selling stockholders are being offered by this prospectus. All of the shares offered are being sold by the selling stockholders.
Use of proceeds	We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders. However, upon any exercise for cash of the warrants described herein, the selling stockholders will pay us the exercise price of the warrants.
Nasdaq National Market symbol	CRTX

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below before purchasing our common stock. The risks and uncertainties described below are not the only ones facing our company. Additional risks and uncertainties may also impair our business operations. If any of the following risks actually occur, our business, financial condition or results of operations would likely suffer. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock.

Risks Relating to Our Business

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

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

Despite being approved by the FDA since 1996, ZYFLO has not achieved broad market acceptance. In the 12-month period ending September 2003, only 1,700 physicians prescribed the product. We may have difficulty expanding the prescriber and patient base for ZYFLO if physicians view the product as outdated or less effective than other products on the market. In addition, ZYFLO requires four-times-a-day dosing, which some physicians and patients may find inconvenient compared to other available asthma therapies that require dosing only once or twice daily.

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

Until we obtain regulatory approval of our supplemental new drug application, or sNDA, for ZYFLO, the product will not be commercially available. The absence of ZYFLO from the market could exacerbate any negative perceptions about ZYFLO if physicians believe the absence of ZYFLO from the market is related to safety or efficacy issues.

The position of ZYFLO in managed care formularies, which are lists of products approved by managed care organizations, may also make it difficult to expand the current market for this product. As a result of a lack of a sustained sales and marketing effort, ZYFLO has been removed from some formularies or relegated to third-tier status, which requires the highest co-pay for patients. In addition, ZYFLO may be removed from some managed

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care formularies as a result of the absence of ZYFLO from the market until we obtain regulatory approval of our related sNDA.

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

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

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

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

We intend to independently launch and market ZYFLO, the controlled-release formulation of zileuton and other of our product candidates where we believe the target physician market can be effectively reached by our planned sales and marketing force. We intend to have a sales force of approximately 80 personnel by the time of our expected launch of ZYFLO in the fourth quarter of 2005. We believe that the aggregate sales and marketing costs to launch ZYFLO, including the cost of the sales force, will be approximately $7.0 million in 2005. We are currently establishing distribution capabilities and have limited sales and marketing capabilities. We may not be able to attract, hire and train qualified sales and marketing personnel to build a significant or successful sales force. If we are not successful in our efforts to develop an internal sales force, our ability to independently launch and market our product candidates, including ZYFLO and the controlled-release formulation of zileuton, will be impaired.

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

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

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

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- 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; and
- the extent and success of our sales and marketing efforts.

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

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

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

- internal research programs;
- sponsored research programs with academic and other research institutions and individual doctors, chemists and researchers; and
- in-licensing or acquisition of product candidates or approved products for the critical care market.

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

- the research methodology used may not be successful in identifying potential product candidates; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be effective products.

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

acquiring suitable product candidates or approved products include the following:

- we may be unable to license or acquire the relevant technology on terms that would allow us to make an appropriate return from the product;
- companies that perceive us as a competitor may be unwilling to assign or license their product rights to us; and
- we may be unable to identify suitable products or product candidates within our areas of expertise.

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

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

The development and commercialization of new drugs is highly competitive. We will face competition with respect to the development of product candidates and for any products that we commercialize in the future from pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies, companies selling low-cost generic substitutes, academic institutions, government agencies or research institutions. A number of large pharmaceutical and biotechnology companies currently market and sell products to treat asthma that will compete with ZYFLO and the controlled-release formulation of zileuton, if approved. Many established therapies currently command large market shares in the mild to moderate asthma market, including Merck & Co., Inc. s Singulair® and GlaxoSmithKline plc s Advair®. We will also face competition from other pharmaceutical companies seeking to develop drugs for the severe asthma market. The severe asthma market is currently served by the therapies developed for mild to moderate asthma and oral and injectable steroid treatments. One product, Xolair®, developed jointly by Novartis AG, Genentech, Inc. and Tanox, Inc., was approved in 2004 for severe allergic asthma and has established a strong sales base.

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

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

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

- significantly greater financial, technical and human resources than we have and may be better equipped to discover, develop, manufacture and commercialize products;
- more extensive experience than we have in conducting preclinical studies and clinical trials, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products;
- competing products that have already received regulatory approval or are in late-stage development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

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

products, or obtain more effective patent protection, than we are able to. Accordingly, our competitors may commercialize products more rapidly or effectively than we are able to, which would adversely affect our competitive position, the likelihood that our product candidates will achieve initial market acceptance and our ability to generate meaningful revenues from our product candidates. Even if our product candidates achieve

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initial market acceptance, competitive products may render our products obsolete or noncompetitive. If our product candidates are rendered obsolete, we may not be able to recover the expenses of developing and commercializing those product candidates.

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

In order to evolve from a company primarily engaged in research and development to one involved in the commercialization of product candidates, we will need to expand our administrative and operational infrastructure. As we advance our product candidates through clinical trials, we will need to expand our development, regulatory and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various collaborators, suppliers and other third parties. Our need to manage our operations and growth will require us to continue to improve our operational, financial and management controls, our reporting systems and our procedures in the United States and the other countries in which we operate. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner, or we may discover deficiencies in existing systems and controls that could expose us to an increased risk of incurring financial or accounting irregularities or fraud.

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

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

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

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

The development, manufacturing, pricing, sales and reimbursement of our product candidates, together with our general operations, are subject to extensive regulation by federal, state and other authorities within the United States and numerous entities outside of the United States. We are a relatively small company with 93 employees as of June 20, 2005, the majority of whom joined us in 2004 and 2005. We rely heavily on third parties to conduct many

important functions. Further, as a publicly traded company we are subject to significant legal and regulatory requirements, including the Sarbanes-Oxley Act of 2002 and regulations promulgated thereunder, some of which have either only recently been adopted or are subject to change. While we have developed and instituted a corporate compliance program based on what we believe are the current best practices and continue to update the program in response to newly implemented and changing regulatory requirements, it is possible that we may not be in compliance with all potentially applicable regulations. If we fail to comply with any of these regulations we could be subject to a range of regulatory actions, including significant fines, litigation, the suspension or termination of

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clinical trials, the failure to approve a product candidate, restrictions on our products or manufacturing processes, withdrawal of products from the market or other sanctions.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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adequate coverage against potential losses, damages, penalties or costs relating to accidental contamination or injury as a result of hazardous, controlled or radioactive materials.

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

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

Neither we nor any of our collaborators may market any of our products in the United States, Europe or in any other country without marketing approval from the FDA or the equivalent foreign regulatory agency. Although ZYFLO has been approved by the FDA, we are required to submit a sNDA with the FDA for ZYFLO because we have changed the manufacturing process and transferred the manufacturing production for the active pharmaceutical ingredient, or API, of zileuton and the immediate-release ZYFLO finished product from Abbott to contract manufacturing sites. We submitted our sNDA for ZYFLO on March 31, 2005. The FDA may not approve our sNDA on a timely basis or at all.

We expect to submit a new drug application, or NDA, to the FDA for the controlled-release formulation of zileuton in the first half of 2006. At present, we are conducting production campaigns and assessing performance of the manufactured tablets, prior to initiation of bioavailability trials in healthy volunteers designed to confirm that our manufactured tablets behave similarly in the body to the tablets that had been manufactured by Abbott. During the transition from pilot scale manufacture to commercial scale, our tablets manufactured at commercial scale exhibited dissolution profiles that were slower than those manufactured at pilot scale. We believe we have isolated the source of this issue and have recently produced commercial scale tablets that have shown a similar dissolution profile to the pilot scale tablets. We are currently targeting to complete the registration batches and to initiate stability testing in the third quarter of 2005. We believe that any significant variability in product performance or delay in manufacturing could further delay the submission of the NDA.

In May 2005, we held a pre-NDA meeting with the FDA for the controlled-release formulation of zileuton, during which the FDA informed us that new review guidance issued in April 2005 limits its ability to accept additional data during the NDA review process. Our strategy has been to file the NDA with six months of stability data and provide additional stability data during the NDA review period. We will continue to work with the FDA to explore what options may be available to us regarding a submission based on an initial six months of stability data. If the FDA requires nine or twelve months of stability data in the original NDA, this could delay our NDA submission for the product candidate beyond the first half of 2006.

Abbott conducted all of the preclinical and clinical trials on the controlled-release formulation of zileuton before we in-licensed the product candidate. We intend to rely on the results of these prior pivotal clinical trials to support our NDA for this product candidate. If the FDA does not permit us to rely on the prior clinical data or if the data is not available at the clinical sites for required FDA audits, we would be required to repeat some or all of the clinical trials, which would lead to unanticipated costs and delays. Problems with the previous trials, such as incomplete, outdated or otherwise unacceptable data, could cause our NDA to be delayed or rejected.

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

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

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

All of our product candidates remain subject to regulatory approval or clearance, and all of our product candidates other than ZYFLO are still in development and remain subject to clinical testing. In order to obtain regulatory approvals or clearances for the commercial sale of our product candidates, we and our collaborators will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our product candidates. We may not be able to obtain authority from the FDA, institutional review boards or other regulatory agencies to commence or complete these clinical trials. If permitted, such clinical testing may not prove that our product candidates are safe and effective to the extent necessary to permit us to obtain marketing approvals or clearances from regulatory authorities. One or more of our product candidates may not exhibit the expected therapeutic results in humans, may cause harmful side effects or have other unexpected characteristics that may delay or preclude regulatory approval or clearance or limit commercial use if approved or cleared. Furthermore, we, one of our collaborators, institutional review boards, or regulatory agencies may hold, suspend or terminate clinical trials at any time if it is believed that the subjects or patients participating in such trials are being exposed to unacceptable health risks or for other reasons.

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

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

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

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

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

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays or the inability to obtain required approvals from institutional review boards or other governing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling patients and volunteers into clinical trials;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- the need to repeat clinical trials as a result of inconclusive or negative results or poorly executed testing;

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

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

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

the placement of a clinical hold on a trial.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis will be subject to a number of factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, 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 review. If we fail to comply with continuing U.S. and applicable foreign regulations, we could lose those approvals and the sale of our product candidates could be suspended.

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

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

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

product seizures;

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voluntary or mandatory recalls;

suspension of review or refusal to approve pending applications;

voluntary or mandatory patient or physician notification;

withdrawal of product approvals;

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

restrictions on applying for or obtaining government bids;

fines;

restrictions on importation of our product candidates;

injunctions; and

civil and criminal penalties.

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

We are relying on MedImmune, Inc. to fund the development of and to commercialize product candidates in our high mobility group box protein 1, or HMGB1, program. We are relying on Beckman Coulter, Inc. 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, and all of our revenues for the quarter ended March 31, 2005 were derived from fees paid to us by MedImmune and Beckman Coulter, under collaboration agreements. We expect that until we generate revenue from the sale of ZYFLO, all of our revenues will continue to be derived from our collaboration agreements with MedImmune and Beckman Coulter. Additional payments due to us under the collaboration agreements with MedImmune and Beckman Coulter are generally based on our achievement of specific development and commercialization milestones that we may not meet. In addition, the collaboration agreements entitle us to royalty payments that are based on the sales of products developed and marketed through the collaborations. These future royalty payments may not materialize or may be less than expected if the related products are not successfully developed or marketed or if we are forced to license intellectual property from third parties. Accordingly, we cannot predict if our collaborations with MedImmune and Beckman Coulter will continue to generate revenues for us.

Our collaboration agreement with MedImmune generally is terminable by MedImmune at any time upon six-months notice 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.

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

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

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

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

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

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

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

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

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

Only a limited number of manufacturers have the capability to supply us with zileuton, and we have not secured a long-term commercial supply arrangement for any of our product candidates, other than the controlled-release formulation of zileuton and the zileuton API. The manufacturing process for our product candidates is an element of the FDA approval process and we will need to contract with manufacturers who can meet the FDA requirements, including current Good Manufacturing Practices, on an ongoing basis. As part of obtaining regulatory approval for

ZYFLO and the controlled-release formulation of zileuton, we are required to engage a commercial manufacturer to produce registration and validation batches of the drug consistent with regulatory approval requirements. Rhodia Pharma Solutions has produced the validation batches of API. We are dependent upon Rhodia Pharma Solutions, SkyePharma and Patheon, and will be dependent on any other third parties who manufacture our product candidates, to perform their obligations in a timely manner and in accordance with applicable government

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regulations. In addition, if we receive the necessary regulatory approval for our product candidates, we also expect to rely on third parties, including our collaborators, to produce materials required for commercial production. We may experience difficulty in obtaining adequate manufacturing capacity or timing for our needs. If we are unable to obtain or maintain contract manufacturing of these product candidates, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our product candidates.

The manufacturing process for the zileuton API involves an exothermic reaction that generates heat and, if not properly controlled by the safety and protection mechanisms in place at the manufacturing sites, could result in unintended combustion of the product. The manufacture of the API could be disrupted or delayed if a batch is destroyed or damaged or if local health and safety regulations require a third-party manufacturer to implement additional safety procedures or cease production.

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

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

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

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

- we may be required to expend our own funds to advance the product candidate to commercialization;
- revenue from product sales could be delayed; or
- we may elect not to commercialize the product candidate.

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

For product candidates with large target physician markets, we plan to rely significantly on sales, marketing and distribution arrangements with third parties. For example, we plan to rely on MedImmune for the commercialization of any anti-HMGB1 products that we develop, and we plan to rely on Beckman Coulter for the commercialization of

any diagnostic based on HMGB1 or its antibodies. We may not be successful in entering into additional marketing arrangements in the future and, even if successful, we may not be able to enter into these

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arrangements on terms that are favorable to us. In addition, we may have limited or no control over the sales, marketing and distribution activities of these third parties. If these third parties are not successful in commercializing the products covered by these arrangements, our future revenues may suffer.

Risks Relating to Intellectual Property and Licenses

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

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

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

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

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

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

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

applications could result in adverse decisions regarding:

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

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

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

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

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

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

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

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

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

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

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

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

We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary for our business. In fact, we acquired the rights to each of our product candidates under licenses with third parties. These licenses impose various development, commercialization, funding, royalty, diligence and other obligations on us. If

we breach these obligations, our licensors may have the right to terminate the licenses or render the licenses non-exclusive, which would result in our being unable to 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 $9.1 million in the three months ended March 31, 2005 and $7.5 million in the three months ended March 31, 2004. As of March 31, 2005, we had an accumulated deficit of approximately $67.6 million. We expect that we will continue to incur substantial losses for at least the next several years as we spend significant amounts to fund research, development and commercialization of our product candidates and to enhance our core technologies. We expect that the losses that we incur will fluctuate from quarter to quarter and that these fluctuations may be substantial. We will need to generate significant revenues to pay these costs and achieve profitability. Until we are able to generate such revenues, we will need to raise substantial additional capital to fund our operations.

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

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

- the costs and timing of the commercial launch of ZYFLO, if and when it is approved by regulatory authorities;
- the costs and timing of the development, regulatory submission and approval and the commercial launch of the controlled-release formulation of zileuton, if and when it is approved by regulatory authorities;
- the scope and results of our clinical trials;
- advancements of other product candidates into development;
- potential acquisition or in-licensing of other products or technologies;
- the time and costs involved in preparing, submitting and obtaining regulatory approvals;
- the timing, receipt and amount of milestone and other payments, if any, from MedImmune, Beckman Coulter or future collaborators;

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

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

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the cost of manufacturing, marketing and sales activities;

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

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

our ability to establish and maintain additional collaborative arrangements.

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

The extent of our future capital requirements is difficult to assess and will depend largely on our ability to obtain regulatory approval for and successfully commercialize ZYFLO and the controlled-release formulation of zileuton. Based on our operating plans, we believe that our available cash and cash equivalents and anticipated cash received from product sales and anticipated payments received under collaboration agreements will be sufficient to fund anticipated levels of operations until the middle of 2007.

For the three months ended March 31, 2005, our net cash used for operating activities was $10.1 million and we had capital expenditures of $527,000. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we will need to raise additional external funds through collaborative arrangements and public or private financings. Additional financing may not be available to us on acceptable terms or at all. In addition, the terms of the financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our then-existing stockholders will result. If we are unable to obtain funding on a timely basis, we may be required to significantly delay, limit or eliminate one or more of our research, development or commercialization programs, which could harm our financial condition and operating results. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products which we would otherwise pursue on our own.

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

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

Risks Relating to Our Common Stock

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

The market price of our common stock may fluctuate significantly in response to factors that are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. The

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market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of our common stock.

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

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

- achievement of, or the failure to achieve, milestones under our development agreement with MedImmune, our license agreement with Beckman Coulter and, to the extent applicable, other licensing and collaboration agreements;
- the results of ongoing and planned clinical trials of our product candidates;
- production problems occurring at our third party manufacturers;
- the results of regulatory reviews relating to the approval of our product candidates; and
- general and industry-specific economic conditions that may affect our research and development expenditures.

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

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

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

- our licensing and collaboration agreements and the products or product candidates that are the subject of those agreements;
- the results of discovery, preclinical studies and clinical trials by us or our competitors;
- the acquisition of technologies, product candidates or products by us or our competitors;
- the development of new technologies, product candidates or products by us or our competitors;
- regulatory actions with respect to our product candidates or products or those of our competitors; and
- significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors.

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 June 20, 2005, our directors, executive officers and 5% or greater stockholders, together with their affiliates, to our knowledge, beneficially owned, in the aggregate, approximately 65% of our outstanding common stock. As a

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result, our directors, executive officers and 5% or greater stockholders, together with their affiliates, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

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

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

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

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

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

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

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

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SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus includes and incorporates forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Any statements contained or incorporated in this prospectus regarding the progress and timing of our drug development program and related trials and the efficacy of our product candidates, our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management, other than statements of historical facts, are forward-looking statements made under the provisions of The Private Securities Litigation Reform Act of 1995. We may, in some cases, use words such as anticipate, believe, could, estimate, expect, intend, project, should, will, would or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including our critical accounting estimates and risks relating to: the results of preclinical studies and clinical trials with respect to our products under development and whether such results will be indicative of results obtained in later clinical trials; the timing and success of submission, acceptance and approval of regulatory filings; our heavy dependence on the commercial success of ZYFLO and the controlled-release formulation of zileuton; our ability to obtain the substantial additional funding required to conduct our research, development and commercialization activities; our dependence on our strategic collaboration with MedImmune, Inc.; and our ability to obtain, maintain and enforce patent and other intellectual property protection for our discoveries and product candidates. We have included these and other important factors in the cautionary statements included or incorporated in this prospectus, particularly under the heading Risk Factors, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. 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. Any such forward-looking statements represent management s views as of the date of the document in which such forward-looking statement is contained. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, whether as a result of new information, future events or otherwise. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

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USE OF PROCEEDS

We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders.

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq National Market listing fees and fees and expenses of our counsel and our accountants.

A portion of the shares covered by this prospectus are issuable upon exercise of warrants to purchase common stock. Upon any exercise for cash of the warrants, the selling stockholders will pay us the exercise price of the warrants. The cash exercise price of the warrants is $6.58 per share. The warrants are also exercisable on a cashless basis. We will not receive any cash payment from the selling stockholders upon any exercise of the warrants on a cashless basis.

SELLING STOCKHOLDERS

The shares of common stock being sold by the selling stockholders consist of:

· 9,945,261 shares of our common stock that we issued to the selling stockholders in a private placement in June 2005; and

· 3,480,842 shares of our common stock issuable upon exercise of warrants to purchase common stock that we issued to the selling stockholders in connection with their purchase of shares of our common stock in the private placement.

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

The actual number of shares of common stock covered by this prospectus, and included in the registration statement of which this prospectus forms a part, includes additional shares of common stock that may be issued with respect to the shares of common stock or the warrants described herein as a result of stock splits, stock dividends, reclassifications, recapitalizations, combinations or similar events.

The following table sets forth, to our knowledge, information about the selling stockholders as of June 20, 2005.

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission, or SEC, and includes voting or investment power with respect to shares of our common stock. Shares of common stock issuable upon exercise of warrants or stock options that are exercisable within 60 days after June 20, 2005 are deemed to be beneficially owned by the person holding the warrants or stock options for purposes of calculating the percentage ownership of that person but are not deemed outstanding for calculating the percentage ownership of any other person. Unless otherwise indicated below, to our knowledge, all persons named in this table have sole voting and investment power with respect to their shares of common stock, except to the extent authority is shared by

spouses under applicable law. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the person named below.

We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders might not sell any or all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements

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or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders.

	Shares of Common Stock Beneficially Owned Prior to Offering					Shares of Common Stock to be Beneficially Owned After Offering	
Name of Selling Stockholder(1)	Outstanding Shares	Shares Issuable Upon Exercise of Warrants	Total Number of Shares Beneficially Owned	Percentage of Common Stock Beneficially Owned	Number of Shares of Common Stock Being Offered	Total Number of Shares Beneficially Owned	Percentage of Common Stock Beneficially Owned
Abingworth Bioventures III A LP	164,891	57,712	222,603	*	222,603		
Abingworth Bioventures III B LP	100,656	35,229	135,885	*	135,885		
Abingworth Bioventures III C LP	60,294	21,103	81,397	*	81,397		
Abingworth Bioventures III Executives LP	2,628	920	3,548	*	3,548		
Abingworth Bioventures IV LP	514,566	75,991	590,557	1.7%	293,107	297,450	*
Abingworth Bioventures IV Executives LP	4,411	651	5,062	*	2,512	2,550	*
Advanced Technology Ventures VI, L.P.	427,315	60,037	487,352	1.4%	231,570	255,782	*
Advanced Technology Ventures VII, L.P.	2,554,802	359,696	2,914,498	8.5%	1,387,398	1,527,100	4.1%
Advanced Technology Ventures VII (B), L.P.	102,522	14,434	116,956	*	55,675	61,281	*
Advanced Technology Ventures VII (C), L.P.	49,279	6,938	56,217	*	26,761	29,456	*

ATV Entrepreneurs VI, L.P.	27,275	3,832	31,107	*	14,781	16,326	*
ATV Entrepreneurs VII, L.P.	15,225	2,144	17,369	*	8,269	9,100	*
Baker Bros. Investments, L.P.	31,098	3,879	34,977	*	14,961	20,016	*
Baker Bros. Investments II, L.P.	29,966	3,730	33,696	*	14,387	19,309	*
Baker Biotech Fund I, L.P.	245,184	38,427	283,611	*	148,218	135,393	*
Baker Biotech Fund II, L.P.	283,361	35,120	318,481	*	135,466	183,015	*
Baker Biotech Fund II (Z), L.P.	38,950	4,922	43,872	*	18,984	24,888	*
Baker Biotech Fund III, L.P.	247,524	32,694	280,218	*	126,105	154,113	*
Baker Biotech Fund III (Z), L.P.	47,466	6,253	53,719	*	24,119	29,600	*

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	Shares of Common Stock Beneficially Owned Prior to Offering					Shares of Common Stock to be Beneficially Owned After Offering	
Name of Selling Stockholder(1)	Outstanding Shares	Shares Issuable Upon Exercise of Warrants	Total Number of Shares Beneficially Owned	Percentage of Common Stock Beneficially Owned	Number of Shares of Common Stock Being Offered	Total Number of Shares Beneficially Owned	Percentage of Common Stock Beneficially Owned
14159, L.P.	18,890	2,712	21,602	*	10,461	11,141	*
Capital Ventures International(2)	182,482	63,869	246,351	*	246,351		
HealthCare Ventures VII, L.P.	1,094,891	383,212	1,478,103	4.3%	1,478,103		
H&Q Life Sciences Investors	456,205	159,672	615,877	1.8%	615,877		
Mediphase Venture Partners II Limited Partnership	273,723	95,803	369,526	1.1%	369,526		
MPM BioVentures II, L.P.	360,533	14,256	374,789	1.1%	54,986	319,803	*
MPM BioVentures II-QP, L.P.	3,267,091	129,181	3,396,272	9.9%	498,269	2,898,003	7.7%
MPM BioVentures GmbH & Co. Parallel- Beteiligungs KG	1,150,411	45,487	1,195,898	3.5%	175,451	1,020,447	2.7%
MPM Asset Management Investors 2001 LLC	67,841	2,682	70,523	*	10,346	60,177	*
OZ Master Fund, Ltd.	897,081	313,978	1,211,059	3.5%	1,211,059		
Fleet Maritime, Inc.	15,328	5,365	20,693	*	20,693		
Prospect Venture Partners III, L.P.	2,281,022	798,358	3,079,380	8.8%	3,079,380		
Special Situations Private Equity Fund L.P.	456,204	159,671	615,875	1.8%	615,875		
Special Situations Fund III, L.P.	456,205	159,672	615,877	1.8%	615,877		
	912,409	319,343	1,231,752	3.6%	1,231,752		

Steelhead Investments Ltd.(2)					
UBS O Connor LLC f/b/o O Connor PIPES Corporate Strategies Master Ltd.	182,482	63,869	246,351	*	246,351

* Less than one percent.

(1) The term selling stockholders includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer.

(2) The selling stockholder is an affiliate of a broker-dealer. The selling stockholder has informed us that it purchased the shares offered by this prospectus in the ordinary course of its business and, at the time of such purchase, had no arrangement or understanding with any other persons regarding the distribution of the shares.

Relationships with Selling Stockholders

Jean George, a member of our board of directors, is a General Partner of Advanced Technology Ventures, which is affiliated with Advanced Technology Ventures VI, L.P., Advanced Technology Ventures VII, L.P.,

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Advanced Technology Ventures VII (B), L.P., Advanced Technology Ventures VII (C), L.P., ATV Entrepreneurs VI, L.P. and ATV Entrepreneurs VII, L.P.

Christopher Mirabelli, Ph.D., a member of our board of directors, is a General Partner of HealthCare Partners VII, L.P., the general partner of HealthCare Ventures VII, L.P. From July 2001 to August 2002, Dr. Mirabelli served as our acting non-employee president.

Nicholas Galakatos, Ph.D., a member of our board of directors, is a General Partner of MPM Capital, L.P., which is affiliated with MPM BioVentures II, L.P., MPM BioVentures II-QP, L.P., MPM BioVentures GmbH & Co. Parallel- Beteiligungs KG and MPM Asset Management Investors 2001 LLC.

Pursuant to the purchase agreements that we entered into in connection with the private placement in June 2005, we agreed, as promptly as reasonably practicable after the closing of the private placement, to take all actions reasonably necessary to provide for the election of James B. Tananbaum, M.D. to our board of directors as a Class II director. Dr. Tananbaum is a Managing Member of Prospect Management Co. III, L.L.C., the general partner of Prospect Venture Partners III, L.P.

Other than as set forth above, to our knowledge, no selling stockholder has held any position or office or otherwise had a material relationship with us within the past three years.

PLAN OF DISTRIBUTION

The shares covered by this prospectus may be offered and sold from time to time by the selling stockholders. The term selling stockholders includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then current market price or in negotiated transactions. The selling stockholders may sell their shares by one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an over-the-counter distribution in accordance with the rules of the Nasdaq National Market;
- in privately negotiated transactions; and
- in options transactions.

In addition, any shares that qualify for sale pursuant to Rule 144 may be sold under Rule 144 rather than pursuant to this prospectus.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with distributions of the shares or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the common stock in the course of hedging the positions they assume with selling stockholders. The selling stockholders may also sell the common stock short and redeliver the shares to close out such short positions. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to

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such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus, as supplemented or amended to reflect such transaction. The selling stockholders may also pledge shares to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged shares pursuant to this prospectus, as supplemented or amended to reflect such transaction.

In effecting sales, broker-dealers or agents engaged by the selling stockholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling stockholders in amounts to be negotiated immediately prior to the sale.

In offering the shares covered by this prospectus, the selling stockholders and any broker-dealers who execute sales for the selling stockholders may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. Any profits realized by the selling stockholders and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions.

In order to comply with the securities laws of certain states, if applicable, the shares must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

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

At the time a particular offer of shares is made, if required, a prospectus supplement will be distributed that will set forth the number of shares being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public.

We have agreed to indemnify the selling stockholders against certain liabilities, including certain liabilities under the Securities Act.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of:

- two years after the effective date of the registration statement;
- such time as all of the shares covered by this prospectus become eligible for resale pursuant to Rule 144(k) under the Securities Act of 1933, as amended, or any other rule of similar effect; and
- such time as all of the shares covered by this prospectus have been sold by the selling stockholders.

Our agreements with the selling stockholders also provide that under certain circumstances we may suspend the use of this prospectus in connection with sales of shares for up to 60 consecutive days and 90 days in the aggregate in any twelve-month period.

We will bear the expenses of preparing and filing the registration statement and all amendments and supplements to the registration statement and the prospectus.

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LEGAL MATTERS

The validity of the shares offered by this prospectus has been passed upon 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 incorporated in this prospectus by reference from our Annual Report on Form 10-K for the year ended December 31, 2004 have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference, and have been so incorporated in reliance upon the report 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 documents with the SEC. You may read and copy any document we file at the SEC s public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You should call 1-800-SEC-0330 for more information on the public reference room. Our SEC filings are also available to you on the SEC s Internet site at www.sec.gov.

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 our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC s Internet 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 updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the sale of all the shares covered by this prospectus.

(1) Our Annual Report on Form 10-K for the year ended December 31, 2004;

(2) Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2005;

(3) Our Current Report on Form 8-K filed with the SEC on January 12, 2005;

(4) Our Current Report on Form 8-K filed with the SEC on February 9, 2005;

(5) Our Current Report on Form 8-K filed with the SEC on June 7, 2005;

(6) Our Current Report on Form 8-K filed with the SEC on June 23, 2005;

(7) 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; and

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(8) 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.

A statement contained in a document incorporated by reference into this prospectus shall be deemed to be modified or superceded for purposes of this prospectus to the extent that a statement contained in this prospectus, any prospectus supplement or in any other subsequently filed document which is also incorporated in this prospectus modifies or replaces such statement. Any statements so modified or superceded shall not be deemed, except as so modified or superceded, to constitute a part of this prospectus.

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: Investor Relations
Telephone: (781) 402-5700

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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

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

SEC registration fee	$ 9,466
Legal fees and expenses	$ 30,000
Accounting fees and expenses	$ 15,000
Miscellaneous expenses	$ 15,534
Total expenses.	$ 70,000

Item 15. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of Delaware allows a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. The Amended and Restated Certificate of Incorporation of Critical Therapeutics provides that, except to the extent that the General Corporation Law of Delaware prohibits the elimination or limitation of liability of directors for breach of fiduciary duty, no director of Critical Therapeutics shall be personally liable to Critical Therapeutics or its stockholders for monetary damages for any breach of fiduciary duty as a director.

Section 145 of the General Corporation Law of Delaware provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against amounts paid and expenses incurred in connection with an action or proceeding to which he is or is threatened to be made a party by reason of such position, if such person shall have acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal proceeding, if such person had no reasonable cause to believe his conduct was unlawful; provided that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the adjudicating court determines that such indemnification is proper under the circumstances.

The Amended and Restated Bylaws of Critical Therapeutics provide that:

Critical Therapeutics must indemnify its directors and officers to the fullest extent permitted by Delaware law;

Critical Therapeutics may indemnify its other employees and agents to the same extent that it indemnified its officers and directors, unless otherwise determined by its Board of Directors; and

Critical Therapeutics must advance expenses, as incurred, to its directors and executive officers in connection with a legal proceeding to the fullest extent permitted by Delaware law.

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The indemnification provisions contained in the Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws are not exclusive of any other rights to which a person may be entitled by law, agreement, vote of stockholders or disinterested directors or otherwise.

In addition, Critical Therapeutics maintains insurance on behalf of its directors and executive officers insuring them against liability asserted against them in their capacities as directors or officers or arising out of such status.

Item 16. Exhibits

EXHIBIT NUMBER	DESCRIPTION
4.1	Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767)).
4.2	Amended and Restated Bylaws of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767)).
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP.
23.1	Consent of Deloitte & Touche LLP.
23.2	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (Included in Exhibit 5.1 filed herewith).
24.1	Power of Attorney (See page II-4 of this registration statement).

Item 17. Undertakings.

Item 512(a) of Regulation S-K. The undersigned Registrant hereby undertakes:

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

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

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

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

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

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

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

Item 512(b) of Regulation S-K. The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant s annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

Item 512(h) of Regulation S-K. Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Lexington, Commonwealth of Massachusetts, on June 24, 2005.

CRITICAL THERAPEUTICS, INC.

By: /s/ Paul D. Rubin
Paul D. Rubin, M.D.
President and Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Critical Therapeutics, Inc., hereby severally constitute and appoint Paul D. Rubin, M.D., Frank E. Thomas and Trevor Phillips, Ph.D. and each of them singly, our true and lawful attorneys with full power to any of them, and to each of them singly, to sign for us and in our names in the capacities indicated below the registration statement on Form S-3 filed herewith and any and all pre-effective and post-effective amendments to said registration statement and generally to do all such things in our name and behalf in our capacities as officers and directors to enable Critical Therapeutics, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said registration statement and any and all amendments thereto.

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

Signature	Title	Date
/s/ Paul D. Rubin Paul D. Rubin, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	June 24, 2005
/s/ Frank E. Thomas Frank E. Thomas	Senior Vice President of Finance, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	June 24, 2005
/s/ Richard W. Dugan Richard W. Dugan	Director	June 24, 2005
/s/ Nicholas Galakatos Nicholas Galakatos, Ph.D.	Director	June 24, 2005
/s/ Jean George Jean George	Director	June 24, 2005

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Signature	Title	Date
/s/ Christopher Mirabelli Christopher Mirabelli, Ph.D.	Director	June 24, 2005
/s/ Christopher Walsh Christopher Walsh, Ph.D.	Director	June 23, 2005
/s/ H. Shaw Warren H. Shaw Warren, M.D.	Director	June 24, 2005
/s/ Robert H. Zeiger Robert H. Zeiger	Director	June 24, 2005

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EXHIBIT INDEX

EXHIBIT NUMBER	DESCRIPTION
4.1	Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767)).
4.2	Amended and Restated Bylaws of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (SEC File No. 000-50767)).
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP.
23.1	Consent of Deloitte & Touche LLP.
23.2	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (Included in Exhibit 5.1 filed herewith).
24.1	Power of Attorney (See page II-4 of this registration statement).