CRITICAL THERAPEUTICS INC
Form 10-Q
November 10, 2005

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

þ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For The Quarterly Period Ended September 30, 2005
or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the Transition Period from ___to ___

Commission File Number: 000-50767
Critical Therapeutics, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**04-3523569**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
60 Westview Street **Lexington, Massachusetts** (Address of Principal Executive Offices)	**02421** (Zip Code)

(781) 402-5700
(Registrant s Telephone Number, Including Area Code)

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

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

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

As of November 7, 2005, the registrant had 34,123,190 shares of Common Stock, $0.001 par value per share, outstanding.

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PART I. Financial Information

Item 1. Financial Statements

CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)

in thousands	September 30, 2005	December 31, 2004
Assets:		
Current assets:		
Cash and cash equivalents	$ 55,206	$ 11,980
Amount due under collaboration agreement	439	16
Short-term investments	42,080	66,849
Inventory	1,309	
Prepaid expenses and other	2,028	1,851
Total current assets	101,062	80,696
Fixed assets, net	3,438	2,205
Other assets	167	213
Total assets	$ 104,667	$ 83,114
Liabilities and Stockholders Equity:		
Current liabilities:		
Current portion of long-term debt and capital lease obligation	$ 896	$ 837
Accounts payable	4,652	4,218
Accrued expenses	5,423	2,741
Revenue deferred under collaboration agreements	5,963	8,543
Total current liabilities	16,934	16,339
Long-term debt and capital lease obligation, less current portion	1,133	1,367
Stockholders equity:		
Preferred stock, par value $0.001; authorized 5,000,000 shares; no shares issued and outstanding		
Common stock, par value $0.001; authorized 90,000,000 shares; issued and outstanding 34,080,604 and 24,085,481 shares at September 30, 2005 and December 31, 2004, respectively	34	24
Additional paid-in capital	182,124	130,374
Deferred stock-based compensation	(4,450)	(6,101)
Accumulated deficit	(90,930)	(58,527)
Accumulated other comprehensive loss	(178)	(362)
Total stockholders equity	86,600	65,408
Total liabilities and stockholders equity	$ 104,667	$ 83,114

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

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
in thousands except share and per share data	**2005**	**2004**	**2005**	**2004**
Revenue under collaboration agreements	$ 1,335	$ 1,886	$ 4,125	$ 3,472
Operating expenses:				
Research and development	8,873	6,037	22,188	16,677
Sales and marketing	4,049	288	7,042	599
General and administrative	3,103	2,443	8,777	6,717
Total operating expenses	16,025	8,768	38,007	23,993
Operating loss	(14,690)	(6,882)	(33,882)	(20,521)
Other income (expense):				
Interest income	794	327	1,619	690
Interest expense	(61)	(29)	(140)	(84)
Total other income	733	298	1,479	606
Net loss	(13,957)	(6,584)	(32,403)	(19,915)
Accretion of dividends and offering costs on preferred stock				(2,209)
Net loss available to common stockholders	($13,957)	($6,584)	($32,403)	($22,124)
Net loss per share available to common stockholders	($0.41)	($0.28)	($1.17)	($1.91)
Basic and diluted weighted-average common shares outstanding	33,976,026	23,638,852	27,664,953	11,574,494

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

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CRITICAL THERAPEUTICS, INC. AND SUBSIDIARY
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)

	Nine Months Ended September 30,	
in thousands	**2005**	**2004**
Cash flows from operating activities:		
Net loss	($32,403)	($19,915)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	566	944
Amortization of premiums on short-term investments	791	555
Loss on disposal of fixed assets		278
Stock-based compensation expense	1,983	2,080
Forgiveness of notes receivable		185
Changes in assets and liabilities:		
Amount due under collaboration agreement	(423)	1,554
Inventory	(1,309)	
Prepaid expenses and other	(177)	(1,147)
Other assets	46	259
Accounts payable	434	718
Accrued expenses	2,682	(1,739)
Revenue deferred under collaboration agreements	(2,580)	(1,988)
Net cash used in operating activities	(30,390)	(18,216)
Cash flows from investing activities:		
Purchases of fixed assets	(1,674)	(1,844)
Proceeds from sales and maturities of short-term investments	55,423	28,150
Purchases of short-term investments	(31,261)	(98,172)
Net cash provided by (used in) investing activities	22,488	(71,866)
Cash flows from financing activities:		
Net proceeds from private placement of common stock	51,362	
Proceeds from exercise of stock options	66	143
Net proceeds from the initial public offering of common stock		37,817
Net proceeds from issuance of convertible preferred stock		28,050
Proceeds from long-term debt		1,412
Repayments of long-term debt and capital lease obligation	(300)	(442)
Net cash provided by financing activities	51,128	66,980
Net increase (decrease) in cash and cash equivalents	43,226	(23,102)
Cash and cash equivalents at beginning of period	11,980	40,078
Cash and cash equivalents at end of period	$ 55,206	$ 16,976

Supplemental disclosures of cash flow information:		
Cash paid during the period for interest	$ 140	$ 84
Non-cash investing and financing activities:		
Fixed assets acquired under capital lease obligation	$ 125	$ 0
Adjustment to deferred stock-based compensation for services to be performed	$ 332	($91)
Unrealized gain (loss) on investments	$ 184	($252)
Conversion of redeemable convertible preferred stock into common stock	$ 0	$ 81,802
Dividends forfeited on preferred stock conversion into common stock	$ 0	$ 5,313
Accretion of dividends and offering costs on preferred stock	$ 0	$ 2,209
Settlement of accrued licensing fee with common stock	$ 0	$ 485

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

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

(1) Basis of Presentation

The accompanying unaudited condensed consolidated financial statements include the accounts of Critical Therapeutics, Inc. and its subsidiary (the Company), and have been prepared in accordance with accounting principles generally accepted in the United States of America for interim financial information and with Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States of America for complete financial statements. The Company believes that all adjustments, consisting of normal recurring adjustments, considered necessary for a fair presentation, have been included. The information included in this quarterly report on Form 10-Q should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and footnotes thereto included in the Company s annual report on Form 10-K for the year ended December 31, 2004 filed with the Securities and Exchange Commission, or SEC.

Operating results for the three- and nine-month periods ended September 30, 2005 and 2004 are not necessarily indicative of the results for the full year. Certain amounts in the condensed consolidated statement of operations and condensed consolidated statement of cash flows for the nine months ended September 30, 2004 have been reclassified to conform to current year presentation.

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates or assumptions. The more significant estimates reflected in these financial statements include certain judgments regarding revenue recognition, accrued expenses and valuation of stock-based compensation.

(2) Private Placement

On June 20, 2005, the Company sold an aggregate of 9,945,261 shares of its common stock at a price of $5.48 per share, together with warrants to purchase an aggregate of 3,480,842 shares of common stock, for a total purchase price of approximately $54.5 million. The sales were made to institutional and other accredited investors. The net proceeds from the private placement were approximately $51.4 million, after deducting placement agents fees and other offering costs of approximately $3.1 million.

The warrants issued in connection with the private placement have an exercise price per share of $6.58, with a five-year life and are fully vested and exercisable from June 20, 2005. The warrants may also be exercised on a cashless basis at the option of the warrant holder. The warrants have been included in permanent equity at their fair value of $9.2 million. The fair value of the warrants was determined using the Black-Scholes model with the following assumptions: dividend yield of 0%; estimated volatility of 58%; risk-free interest rate of 3.65% and a contractual life of five years.

(3) Revenue Recognition

The Company recognizes revenue in accordance with the Securities and Exchange Commission s Staff Accounting Bulletin No. 101, Revenue Recognition in Financial Statements (SAB 101), as amended by SEC Staff Accounting Bulletin No. 104 Revenue Recognition (SAB 104). Specifically, revenue is recognized when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable and collectibility is reasonably assured. The Company s revenue is currently derived exclusively from its collaboration agreements. These agreements provide for various payments, including research and development funding, license fees, milestone payments and royalties.

Revenue from research and development funding is recognized over the estimated performance period based on a proportional performance model. Under the proportional performance model, performance is measured as the percentage of cost incurred to date compared to the total costs estimated for the performance period. The amount of revenue recognized during each period represents the cumulative performance percentage of amounts received and due to the Company under the agreement less amounts previously recognized. The Company periodically reviews the

estimated performance period and total costs and, to the extent such estimates change, the impact of such change is recorded in operations at that time. If the Company s collaborators have the right to cancel the

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agreement at any time, the Company does not recognize revenues in excess of cumulative cash collections. Revenue from non-refundable, upfront license fees is recognized ratably over the commitment period. Deferred revenue consists of payments received in advance of revenue recognized under the agreement.

(4) Cash Equivalents and Short-Term Investments

The Company considers all highly-liquid investments with original maturities of 90 days or less when purchased to be cash equivalents.

Short-term investments consist primarily of U.S. government treasury and agency notes, corporate debt obligations, municipal debt obligations, auction rate securities and money market funds, each of investment-grade quality, which have an original maturity date greater than 90 days that mature or can be sold within one year. These securities are held until such time as the Company intends to use them to meet the ongoing liquidity needs to support its operations. These investments are recorded at fair value and accounted for as available-for-sale securities. The unrealized gain (loss) during the period is recorded as an adjustment to stockholders equity. The Company recorded $83,000 and $125,000 unrealized gain on investments during the three-month periods ended September 30, 2005 and 2004, respectively, and recorded $184,000 unrealized gain and $252,000 unrealized loss on investments during the nine-month periods ended September 30, 2005 and 2004, respectively. The cost of the debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. The amortization or accretion is included in interest income (expense) in the corresponding period. The Company has concluded that the unrealized gain (loss) on investments is temporary and therefore no impairment exists during the three- and nine-month periods ended September 30, 2005.

(5) Inventory

Inventory is stated at the lower of cost or market with cost determined under the first-in, first-out (FIFO) method. As of September 30, 2005, the Company held $1.3 million in raw material inventory to be used for commercial sales related to its October 2005 product launch of ZYFLO®, a tablet formulation of zileuton. The Company analyzes its inventory levels quarterly and writes-down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. Expired inventory is disposed of and the related costs are written off. As of September 30, 2005, there has been no adjustments to inventory related to impairment or expiry.

(6) Comprehensive Loss

Comprehensive loss is the total of net loss and all other non-owner changes in equity. The difference between net loss, as reported in the accompanying condensed consolidated statements of operations for the three and nine-month periods ended September 30, 2005 and 2004, and comprehensive loss is the unrealized gain (loss) on short-term investments for the period. Total comprehensive loss was $13.9 million and $6.5 million for the three-month periods ended September 30, 2005 and 2004, respectively, and $32.2 million and $20.2 million for the nine-month periods ended September 30, 2005 and 2004, respectively. The unrealized gain (loss) on investments is the only component of accumulated other comprehensive loss in the accompanying condensed consolidated balance sheet.

(7) Stock-Based Compensation

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

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Stock option activity for the nine-month periods ended September 30, 2005 and September 30, 2004 are as follows:

	2005		2004	
	Number of Shares	Weighted-Average Exercise Price Per Share	Number of Shares	Weighted-Average Exercise Price Per Share
Outstanding January 1	4,500,270	$ 4.23	1,862,229	$ 0.87
Granted	358,500	7.27	43,789	2.90
Exercised	(13,668)	1.50	(164,966)	0.48
Cancelled	(3,540)	5.28	(266)	0.38
Outstanding March 31	4,841,562	$ 4.46	1,740,786	$ 0.96
Granted	311,000	5.64	361,336	5.78
Exercised	(1,383)	5.86	(20,676)	3.10
Cancelled	(58,000)	6.50	(13,336)	5.63
Outstanding June 30	5,093,179	$ 4.51	2,068,110	$ 1.75
Granted	695,250	6.54	1,999,500	6.01
Exercised	(34,811)	6.16	(1,557)	0.38
Cancelled	(86,914)	3.35	(3,413)	0.88
Outstanding September 30	5,666,704	$ 4.78	4,062,640	$ 3.85
Exercisable September 30	1,388,238	$ 3.04	458,280	$ 1.10

The Company expenses deferred stock-based compensation as charges to operations over the vesting period of the options and recorded $1.0 million and $2.0 million and $32,000 and $85,000 as stock-based compensation expense during the three- and nine-month periods ended September 30, 2005 and 2004, respectively. In the nine months ended September 30, 2005 and 2004, respectively, the Company granted 226,000 and 1,333 options to purchase common stock to non-employees which resulted in additional deferred compensation of $394,000 and $4,000 for each period, respectively.

The remaining number of shares of common stock available for award under the Company s 2004 Stock Incentive Plan, as amended, totaled 959,435 at September 30, 2005.

Had employee compensation expense been determined based on the fair value at the date of grant consistent with SFAS No. 123, the Company s pro forma net loss and pro forma net loss per share would have been as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
(in thousands, except loss per share data)	2005	2004	2005	2004
Net loss available to common stockholders as reported	($13,957)	($6,584)	($32,403)	($22,124)
Add: Stock-based compensation expense included in reported net loss	439	449	1,335	1,336
Deduct: Stock-based compensation expense determined under fair value method	(982)	(761)	(2,655)	(1,811)
Net loss pro forma	($14,500)	($6,896)	($33,723)	($22,599)

Net loss per share (basic and diluted):				
As reported	($0.41)	($0.28)	($1.17)	($1.91)
Pro forma	($0.43)	($0.29)	($1.22)	($1.95)

Option valuation models require the input of highly subjective assumptions. Because changes in subjective input assumptions can materially affect the fair value estimate, in management s opinion, the calculated fair value may not necessarily be indicative of the actual fair value of the stock options. The Company has computed the pro forma disclosures required under SFAS No. 123 for options granted using the Black-Scholes option-pricing model prescribed by SFAS No. 123. The Company reduced its assumption for the three and nine months ended September 30, 2005 regarding expected volatility to 59% and 58%, respectively, from 100% for the three and nine months ended September 30, 2004. The rates used in 2005 are based on the Company s actual historical volatility since its initial public offering. The assumptions used and weighted-average information are as follows:

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	Three Months Ended September 30,		Nine Months Ended September 30,	
	2005	2004	2005	2004
Risk free interest rate	4.1%	3.2%	4.0%	3.2%
Expected dividend yield	0%	0%	0%	0%
Expected lives	4 years	4 years	4 years	4 years
Expected volatility	59%	100%	58%	100%
Weighted-average fair value of options granted equal to fair value	$ 3.20	$ 4.22	$ 3.11	$ 4.23
Weighted-average fair value of options granted below fair value				$ 5.03

In December 2004, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards No. 123R, *Share-Based Payment*, or SFAS No. 123R. This Statement is a revision of SFAS No. 123, *Accounting for Stock-Based Compensation*, amends SFAS No. 95, *Statement of Cash Flows*, and supersedes Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, and its related implementation guidance. SFAS No. 123R focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. The Statement requires entities to recognize in their income statement stock compensation expense for awards (with limited exceptions) based on their fair value. SFAS No. 123R is effective for the Company commencing January 1, 2006, at which time the Company will begin recognizing an expense for unvested share-based compensation that has been issued or will be issued after that date. SFAS No. 123R permits a prospective or two modified versions of retrospective application under which financial statements for prior periods are adjusted on a basis consistent with the pro forma disclosures required for those periods by the original SFAS No. 123. The Company currently accounts for stock options granted to employees in accordance with the intrinsic value method permitted under APB Opinion No. 25 and does not recognize compensation expense. The adoption of SFAS No. 123R is expected to have a significant impact on the Company s operating results. At this time, the Company is evaluating the impact of the adoption of SFAS 123R and has not yet determined how the financial statements will be effected.

(8) Basic and Diluted Loss per Share

Basic and diluted net loss per common share is calculated by dividing the net loss available to common stockholders by the weighted-average number of unrestricted common shares outstanding during the period. Diluted net loss per common share is the same as basic net loss per common share, since the effects of potentially dilutive securities are anti-dilutive for all periods presented. Anti-dilutive securities that are not included in the diluted net loss per share calculation aggregated 9,214,279 and 4,446,067 as of September 30, 2005 and 2004, respectively. These anti-dilutive securities consist of outstanding stock options, warrants, and unvested restricted common stock as of September 30, 2005 and 2004.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2005	2004	2005	2004
Weighted-average common shares outstanding	34,052,961	24,037,558	27,816,918	12,063,921
Less: weighted-average restricted common shares outstanding	76,935	398,706	151,965	489,427
	33,976,026	23,638,852	27,664,953	11,574,494

Basic and diluted weighted-average
common shares outstanding

(9) Commitments and Contingencies

The Company has entered into various agreements with third parties and certain related parties in connection with the research and development activities of its existing product candidates as well as discovery efforts on potential new product candidates. These agreements include costs for research and development and license agreements that represent the Company s fixed obligations payable to sponsor research and minimum royalty payments for licensed patents. These amounts do not include any additional amounts that the Company may be required to pay under its license agreements upon the achievement of scientific, regulatory and commercial milestones that may become payable depending on the progress of scientific development and regulatory approvals, including milestones such as the submission of an investigational new drug application to the U.S. Food and Drug Administration, or FDA,

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similar submissions to foreign regulatory authorities and the first commercial sale of the Company s products in various countries. These agreements include costs related to manufacturing, clinical trials and preclinical studies performed by third parties. The estimated amount that may be incurred in the future under these agreements totals approximately $23.1 million as of September 30, 2005. The amount and timing of these commitments may change, as they are largely dependent on the rate of enrollment in and timing of the development of the Company s product candidates. As of September 30, 2005, the Company has $182,000 and $660,000 included in prepaid expenses and accrued expenses, respectively, related to these agreements on the accompanying consolidated balance sheet. These agreements are accounted for under the percentage of completion method.

The Company is also party to a number of agreements that require it to make milestone payments, royalties on net sales of the Company s products and payments on sublicense income received by the Company. In addition, the Company entered into a manufacturing and supply agreement with Rhodia Pharma Solutions Ltd., or Rhodia, for commercial production of the active pharmaceutical ingredient, or API, of ZYFLO, subject to specified limitations, through December 31, 2009. Under this agreement, the Company committed to purchase a minimum amount of API by December 31, 2006. The API purchased from Rhodia currently has a shelf-life of 24 months. The Company evaluates the need to provide reserves for contractually committed future purchases of inventory that may be in excess of forecasted future demand. In making these assessments, the Company is required to make judgments as to the future demand for current or committed inventory levels and as to the expiration dates of its product.

In the three months ended September 30, 2005, the Company also entered into a capital lease arrangement primarily for computers for its sales force totaling $125,000. Assets acquired under capital lease agreements are recorded at the present value of the future minimum rental payments using interest rates appropriate at the inception of the lease. Property and equipment subject to capital lease agreements are amortized over the shorter of the life of the lease or the estimated useful life of the asset unless the lease transfers ownership or contains a bargain purchase option.

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

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Item 2. Management s Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion together with our financial statements and accompanying notes included in this quarterly report and our audited financial statements included in our annual report on Form 10-K for the year ended December 31, 2004 which is on file with the SEC. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results could differ materially from those anticipated by the forward-looking statements due to important factors and risks including, but not limited to, those set forth under Factors That May Affect Future Results below.

Financial Operations Overview

We are 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 only commercial product is ZYFLO®, a tablet formulation of zileuton, which the FDA approved in 1996 for the prevention and chronic treatment of asthma. We licensed from Abbott Laboratories exclusive worldwide rights to ZYFLO and other formulations of zileuton for multiple diseases and conditions. We have completed the process of changing manufacturing sites for ZYFLO, and the FDA approved our supplemental new drug application, or sNDA, on September 28, 2005. We began selling ZYFLO in the United States in October of 2005. In addition, we believe that zileuton has potential therapeutic benefits in a range of other diseases and conditions, such as acne, chronic obstructive pulmonary disease, or COPD, nasal polyposis and acute asthma exacerbations. We are currently incurring costs to expand our applications of zileuton through development of additional formulations, including controlled-release and intravenous formulations.

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

CTI-01. We are developing a small molecule product candidate, CTI-01, that we believe may be effective in regulating the inflammatory response. Results from preclinical studies suggest that CTI-01 inhibits the release of protein molecules called cytokines that are responsible for communication between cells in the body and are associated with conditions such as damage to vital organs that can occur in patients after cardiopulmonary bypass, a procedure commonly performed during heart surgery and post-operative ileus, which is the loss of normal intestine movement following surgery.

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

Alpha-7. We are developing small molecules designed to inhibit the body s inflammatory response by acting on the nicotinic alpha-7 cholinergic target, which is a cell receptor associated with the production of the cytokines that play a fundamental role in the inflammatory response. We believe that successful development of a product candidate targeting the nicotinic alpha-7 cholinergic receptor could lead to an oral anti-cytokine therapy for acute and chronic inflammatory diseases.

Since our inception, we have incurred significant losses each year. As of September 30, 2005, we had an accumulated deficit of $90.9 million. We expect to incur significant losses for the foreseeable future. The size and timing of our future operating expenses and losses are subject to significant uncertainty. We expect our operating expenses to continue to increase over the next several years, which could result in increased operating losses, as we continue to fund our development programs and prepare for the potential commercial launch of our product candidates. We do not expect to achieve profitability in the foreseeable future; and we cannot assure you that we will achieve profitability at all. Since inception, we have raised proceeds to fund our operations through our initial public

offering of common stock, private placements of equity securities, debt financings, the receipt of interest income and payments from our collaborators MedImmune and Beckman Coulter.

Revenue. We have not generated any operating revenues from product sales since our inception on July 14, 2000; however, we expect to generate operating revenues from product sales in the fourth quarter of 2005 from sales of ZYFLO. All of our revenues to date have been derived from license fees, research and development payments and milestone payments that we have received from our

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collaboration agreements with MedImmune and Beckman Coulter. In the future, we expect to generate revenues from a combination of product sales and payments under corporate collaborations.

Research and Development Expenses. Research and development expenses consist of expenses incurred in identifying, developing and testing product candidates. These expenses consist primarily of salaries and related expenses for personnel, fees paid to professional service providers for monitoring and analyzing clinical trials, costs related to the development of our new drug application, or NDA, for the controlled-release formulation of zileuton**,** costs of contract research and manufacturing and the cost of facilities. After FDA approval of a product candidate, manufacturing expenses associated with a product will be recorded as cost of sales rather than research and development expenses. We expense research and development costs and patent related costs as incurred. Because of our ability to utilize resources across several projects, many of our research and development costs are not tied to any particular project and are allocated among multiple projects. We record direct costs on a project-by-project basis. We record indirect costs in the aggregate in support of all research and development. Development costs for later stage programs such as zileuton and CTI-01 tend to be higher than earlier stage programs such as our HMGB1 and alpha-7 programs due to the costs associated with conducting clinical trials and scaling-up manufacturing processes for commercial scale.

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

Sales and Marketing. Sales and marketing expenses consist primarily of salaries and other related costs for personnel in sales and marketing functions as well as cost related to our recent product launch of ZYFLO. We expect to continue to incur significant sales and marketing costs associated with our recent hiring of our sales force and the continued enhancement of the sales and marketing infrastructure to support the commercialization of ZYFLO. We expect to incur additional expenses related to our product introduction of ZYFLO.

General and Administrative Expenses. General and administrative expenses consist primarily of salaries and other related costs for personnel in executive, finance, accounting, legal, business development, information technology and human resource functions. Other costs reflected in general and administrative expenses include facility costs not otherwise included in research and development expenses and professional fees for legal and accounting services. We anticipate that our general and administrative expenses will also increase as we expand our operations, facilities and other activities related to operating as a publicly traded company. In addition, we expect to incur additional general and administrative expenses related to our recent product launch of ZYFLO.

Deferred Stock-Based Compensation Expense. As discussed more fully in Note 7 to our condensed consolidated financial statements included herein and in Notes 7 and 8 to our consolidated financial statements in our annual report on Form 10-K for the year ended December 31, 2004, in lieu of cash payments, we granted 226,000 and 67,999 shares of common stock and options to purchase common stock to non-employees during the nine months ended September 30, 2005 and 2004, respectively. We recorded these grants at fair value when granted. We periodically remeasure the fair value of the unvested portion of these grants, resulting in charges or credits to operations in periods when such remeasurement results in differences between the fair value of the underlying common stock and the exercise price of the options that is greater than or less than the differences, if any, between the fair value of the underlying common stock and the exercise price of the options at their respective previous measurement dates.

As discussed more fully in Note 7 to our condensed consolidated financial statements included herein and Notes 7 and 8 to our consolidated financial statements in our annual report on Form 10-K for the year ended December 31, 2004, we granted 1,138,750 and 2,403,288 stock options to employees during the nine months ended September 30, 2005 and 2004, respectively. Certain of the employee options granted during 2004 and prior years were deemed for accounting purposes to have been granted with exercise prices below their then-current market value. We recorded the value of these differences as deferred stock-based compensation. We amortize the deferred amounts as charges to operations over the vesting periods of the grants, resulting in stock-based compensation expense. We anticipate

recording stock-based compensation expense of $422,000 in the fourth quarter of 2005, $1.7 million in 2006, $1.5 million in 2007 and $18,000 in 2008, less adjustment for forfeitures, relating to the amortization of employee deferred stock-based compensation recorded as of September 30, 2005.

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Critical Accounting Policies

The discussion and analysis of our financial condition and results of operations is based on our unaudited consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires us to make estimates and judgments that affect our reported assets and liabilities, revenues and expenses, and other financial information. Actual results may differ significantly from these estimates under different assumptions and conditions. In addition, our reported financial condition and results of operations could vary due to a change in the application of a particular accounting standard.

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

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

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

Our significant accounting policies are more fully described in the Notes to Consolidated Financial Statements and Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies in our annual report on Form 10-K for the year ended December 31, 2004. Not all of these significant accounting policies, however, fit the definition of critical accounting estimates. We have discussed our accounting policies with the audit committee of our board of directors, and we believe that our estimates relating to revenue recognition, accrued expenses, stock-based compensation and income taxes described under the caption Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies in our annual report on Form 10-K for the year ended December 31, 2004, fit the definition of critical accounting estimates.

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

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

Stock-Based Compensation. To date, we have elected to follow Accounting Principles Board Opinion, or APB, No. 25, *Accounting for Stock Issued to Employees,* or APB 25, and related interpretations, in accounting for our stock-based compensation plans, rather than the alternative fair value accounting method provided for under Statement of Financial Accounting Standards, or SFAS, No. 123, *Accounting for Stock-Based Compensation Accounting Principles Board Opinion,* or SFAS 123. Accordingly, we have not recorded stock-based compensation expense for stock options issued to employees in fixed amounts with exercise prices at least equal to the

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fair value of the underlying common stock on the date of grant. In the notes to our consolidated financial statements included herein, we provide pro forma disclosures in accordance with SFAS 123 and related pronouncements. We account for transactions in which services are received in exchange for equity instruments based on the fair value of such services received from non-employees or of the equity instruments issued, whichever is more reliably measured, in accordance with SFAS 123 and Emerging Issues Task Force Issue No. 96-18, or EITF 96-18, *Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*. The two factors which most affect charges or credits to operations related to stock-based compensation are the fair value of the common stock underlying stock options for which stock-based compensation is recorded and the volatility of such fair value. Accounting for equity instruments granted or sold by us under APB 25, SFAS 123 and EITF 96-18 requires fair value estimates of the equity instrument granted or sold. If our estimates of the fair value of these equity instruments are too high or too low, it would have the effect of overstating or understating expenses. When equity instruments are granted or sold in exchange for the receipt of goods or services and the value of those goods or services can be readily estimated, we use the value of such goods or services to determine the fair value of the equity instruments. When equity instruments are granted or sold in exchange for the receipt of goods or services and the value of those goods or services cannot be readily estimated, as is true in connection with most stock options and warrants granted to employees or non-employees, we estimate the fair value of the equity instruments based upon the consideration of factors which we deem to be relevant at the time using cost, market or income approaches to such valuations.

In December 2004, the FASB issued SFAS No. 123R, which focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. SFAS No. 123R requires entities to recognize stock compensation expense for awards, with limited exceptions. SFAS No. 123R is effective for the Company commencing January 1, 2006, at which time the Company will begin recognizing an expense for unvested share-based compensation that has been issued or will be issued after that date. The adoption of SFAS No. 123R is expected to have a significant impact on our results of operations. Currently, the Company is evaluating the impact of the adoption of SFAS 123R and has not yet determined how the financial statements will be effected.

Income Taxes. As part of the process of preparing our consolidated financial statements, we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves us estimating our actual current tax exposure together with assessing temporary differences resulting from differing treatments of items for tax and accounting purposes. These differences result in deferred tax assets and liabilities. In addition, as of September 30, 2005, we had federal and state tax net operating loss carryforwards of approximately $71.8 million, which expire beginning in 2021 and 2006, respectively. We also have research and experimentation credit carryforwards of approximately $888,000 which expire beginning in 2021. We have recorded a full valuation allowance as an offset against these otherwise recognizable net deferred tax assets due to the uncertainty surrounding the timing of the realization of the tax benefit. In the event that we determine in the future that we will be able to realize all or a portion of its net deferred tax benefit, an adjustment to deferred tax valuation allowance would increase net income in the period in which such a determination is made. The Tax Reform Act of 1986 contains provisions that may limit the utilization of net operating loss carryforwards and credits available to be used in any given year in the event of significant changes in ownership interest, as defined.

Results of Operations

Three Months Ended September 30, 2005 and 2004

Revenue Under Collaboration Agreements. We recognized revenues of $1.3 million for the three months ended September 30, 2005 compared to $1.9 million for the three months ended September 30, 2004. These revenues were primarily due to the portion of the $12.5 million of initial fees MedImmune paid us that we recognized in each period and a portion of the $1.5 million and $1.3 million billed to MedImmune in 2004 and for the nine months ended September 30, 2005, respectively, for development support. We have reported the balance of the payments as deferred revenue and will recognize such amount over the estimated 41-month research term of our agreement with MedImmune based on the proportion of cumulative costs incurred as a percentage of the total costs estimated for the performance period. As of September 30, 2005, we had $6.0 million in deferred revenue remaining to be recognized under our collaboration agreements with MedImmune and Beckman Coulter.

Research and Development Expenses. Research and development expenses for the three months ended September 30, 2005 were $8.9 million compared to $6.0 million for the three months ended September 30, 2004. The increase of approximately $2.9 million was primarily due to the achievement of several milestones in the third quarter of 2005, higher expenses associated with the growth in the number of employees performing research and development functions and their related stock-based compensation expense and increased facilities, equipment and laboratory charges associated with our increased research and development activities.

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The following table summarizes the primary components of our direct research and development expenses for the three months ended September 30, 2005 and 2004:

	Three Months Ended September 30,	
	2005	2004
	(in thousands)	
Zileuton	$ 4,502	$ 3,562
CTI-01	664	875
HMGB1	423	430
Alpha-7	833	365
General research and development expenses	1,743	928
Stock-based compensation expense	708	(123)
Total research and development expenses	$ 8,873	$ 6,037

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

Zileuton. During the three months ended September 30, 2005, we incurred $4.5 million in expenses related to our zileuton program compared to $3.6 million during the three months ended September 30, 2004. This increase was primarily due to a $750,000 milestone payment to Abbott related to FDA approval of ZYFLO, a $750,000 milestone payment to SkyePharma related to the commencement of the manufacturing of our NDA registration batches for our controlled-release formulation of zileuton, and increased preclinical costs related to our intravenous formulation of zileuton, which were offset in part by a decrease in manufacturing costs related to the product registration of ZYFLO and product development of our controlled-release formulation of zileuton. In the fourth quarter of 2005, we expect our research and development expenses for zileuton will relate principally to the transfer of Abbott s manufacturing technology relating to the controlled-release formulation of zileuton and the anticipated clinical trials of the controlled-release and intravenous formulations of zileuton. We also expect to incur expenses related to additional clinical studies of zileuton in certain patient populations after we commercialize ZYFLO. The actual costs and timing for the development and commercialization of our zileuton product candidates are highly uncertain, subject to risk and will change depending upon the clinical indication developed and the development strategy adopted. As a result, we are unable to estimate the costs or the timing of advancing our zileuton product candidates through clinical development and commercialization.

CTI-01. Expenses for CTI-01 decreased in the three months ended September 30, 2005 primarily due to lower preclinical costs, offset by higher clinical and manufacturing costs compared to the three months ended September 30, 2004. We expect to continue to incur additional costs for this program for the remainder of 2005 as we continue a Phase II clinical trial of CTI-01 in patients undergoing major cardiac surgery including the use of a cardiopulmonary bypass machine. This trial and the other development work required for this program will require significant expenditures before we can seek regulatory approval. We estimate that the total direct costs that we will need to incur to advance CTI-01 through clinical development will be at least $30.0 million. However, the actual costs and timing of clinical trials and associated activities to enable a regulatory submission are highly uncertain, subject to risk and will change depending upon the clinical indication developed and the development strategy adopted. As a result, we believe that these estimated direct costs may change significantly as the product advances through clinical development.

HMGB1. Expenses for HMGB1 remained consistent in the three months ended September 30, 2005. Expenses related to HMGB1 are related to laboratory supplies for our continued testing obligations under our collaboration agreement with MedImmune. Our expenses for this program may vary from period to period depending on the

resources required for activities being performed by us and those performed by MedImmune. We currently anticipate that most research and development costs relating to HMGB1 in 2005 will be covered by funding from MedImmune under our collaboration agreement. However, we expect to undertake some internal research and preclinical testing of HMGB1, and we cannot be certain that the research payments received from MedImmune will fully cover the costs associated with these activities. The funding from MedImmune beyond 2005 will be based only on milestones achieved under the collaboration agreement. Because our HMGB1 program is still in preclinical development, the actual costs and timing of preclinical development, clinical trials and associated activities are highly uncertain, subject to risk and will change depending upon the clinical indication developed and the development strategy adopted. As a result, we are not able to estimate the costs or the timing of advancing any HMGB1-inhibiting product candidate or candidates through clinical development. A significant amount of these clinical costs will be incurred by MedImmune. The expenses for HMGB1 are reflected in the accompanying statement of operations as part of research and development expenses, while the funding received from MedImmune to fund our research efforts is included in revenue under collaboration agreement.

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Alpha-7. During the three months ended September 30, 2005, we incurred $833,000 of expenses in connection with our alpha-7 program compared to $365,000 during the three months ended September 30, 2004. This increase is primarily due to personnel costs and contract research associated with our efforts to discover and develop small molecule product candidates. We anticipate that significant additional expenditures will be required to advance any product candidate or device through preclinical and clinical development, and we expect to incur additional expenses to in-license or discover additional molecules under this program. However, because this project is at a very early stage, the actual costs and timing of research, preclinical development, clinical trials and associated activities are highly uncertain, subject to risk and will change depending upon the project we choose to develop, the clinical indication developed and the development strategy adopted. As a result, we are unable to estimate the costs or the timing of advancing a small molecule or medical device to stimulate the vagus nerve from our alpha-7 program through clinical development.

Our general research and development expenses, which are not allocated to any specific program, increased by $815,000 in the three months ended September 30, 2005 compared to the three months ended September 30, 2004 primarily due to higher expenses associated with the growth in the number of employees performing research and development functions and increased facility costs. Facility and related costs for the three months ended September 30, 2005 were $417,000 compared to $177,000 for the three months ended September 30, 2004.

In addition, our stock-based compensation expense increased $831,000 from the third quarter of 2005 compared to the third quarter of 2004, primarily due to the effects of the change in the market price of our common stock on unvested non-employee options. The adjustment to stock-based compensation expense is calculated based on the change in fair value of our common stock during the period. The fair value of our common stock decreased during the three months ended September 30, 2004, which resulted in a $172,000 adjustment to our stock-based compensation expense to non-employees, while the fair value of our common stock increased during the three months ended September 30, 2005, which resulted in $585,000 of stock-based compensation expense to non-employees.

Sales and Marketing. Sales and marketing expenses for the three months ended September 30, 2005 were $4.0 million compared to $288,000 for the three months ended September 30, 2004. The $3.7 million increase in the three months ended September 30, 2005 was primarily attributable to the hiring of our sales management, the hiring and training of our 80-person specialty sales force and marketing and other costs associated with our recent launch of ZYFLO. The number of employees performing sales and marketing functions increased from six employees at September 30, 2004 to 93 employees at September 30, 2005.

General and Administrative Expenses. General and administrative expenses for the three months ended September 30, 2005 were $3.1 million compared to $2.4 million for the three months ended September 30, 2004. The $0.7 million increase in the three months ended September 30, 2005 was primarily attributable to the increase in personnel costs as a result of the increase in the number of employees performing general and administrative functions and the increase in consulting and audit fees related to Sarbanes-Oxley compliance. The number of employees performing general and administrative functions increased from 22 employees at September 30, 2004 to 35 employees at September 30, 2005.

Other Income. Interest income for the three months ended September 30, 2005 was $794,000 compared to $327,000 for the three months ended September 30, 2004. The increase in the three months ended September 30, 2005 was primarily attributable to higher interest rates and higher cash and investment balances from our recently completed financings. Interest expense amounted to $61,000 and $29,000 for the three months ended September 30, 2005 and September 30, 2004, respectively.

Nine Months Ended September 30, 2005 and 2004

Revenue Under Collaboration Agreements. We recognized revenues of $4.1 million for the nine months ended September 30, 2005 compared to $3.5 million for the nine months ended September 30, 2004. These revenues were primarily due to the portion of the $12.5 million of initial fees MedImmune paid us that we recognized in each period and a portion of the $1.5 million and $1.3 million billed to MedImmune in 2004 and for the nine months ended September 30, 2005, respectively, for development support. We have reported the balance of the payments as deferred revenue and will recognize such amount over the estimated 41-month research term of our agreement with MedImmune based on the proportion of cumulative costs incurred as a percentage of the total costs estimated for the

performance period. As of September 30, 2005, we had $6.0 million in deferred revenue remaining to be recognized under our collaboration agreements with MedImmune and Beckman Coulter.

Research and Development Expenses. Research and development expenses for the nine months ended September 30, 2005 were $22.2 million compared to $16.7 million for the nine months ended September 30, 2004, an increase of approximately $5.5 million. This increase was primarily due to higher expenses associated with the growth in the number of employees performing research and

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development functions and increased facilities, equipment and laboratory charges associated with our increased research and development activities during the nine months ended September 30, 2005.

The following table summarizes the primary components of our direct research and development expenses for the nine months ended September 30, 2005 and 2004:

	Nine Months Ended September 30,	
	2005	2004
	(in thousands)	
Zileuton	$ 11,311	$ 7,612
CTI-01	1,896	2,333
HMGB1	1,411	1,294
Alpha-7	1,907	1,053
General research and development expenses	4,638	3,460
Stock-based compensation expense	1,025	925
Total research and development expenses	$ 22,188	$ 16,667

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

Zileuton. During the nine months ended September 30, 2005, we incurred $11.3 million in expenses related to our zileuton program compared to $7.6 million during the nine months ended September 30, 2004. This increase was primarily due to our manufacturing costs related to the product registration of ZYFLO, our recently completed Phase II clinical trial of ZYFLO for moderate to severe inflammatory acne, the initiation of the ZYFLO open-label study in patients with asthma or mastocytosis, our development and manufacturing cost related to our intravenous and controlled-release formulations and the achievement of several milestones during the nine months ended September 30, 2005.

CTI-01. Expenses for CTI-01 decreased by $437,000 in the nine months ended September 30, 2005 compared to the nine months ended September 30, 2004. This decrease was primarily due to lower preclinical costs offset by higher clinical and manufacturing costs in the nine months ended September 30, 2005. We expect to incur additional costs for this program for the remainder of 2005 as we continue a Phase II clinical trial of CTI-01 in patients undergoing major cardiac surgery including the use of a cardiopulmonary bypass machine.

HMGB1. Expenses for HMGB1 remained consistent in the nine months ended September 30, 2005 compared to the nine months ended September 30, 2004. Expenses related to HMGB1 are related to our continued testing under our collaboration agreement with MedImmune. We currently anticipate that most research and development costs relating to HMGB1 in 2005 will be covered by funding from MedImmune under our collaboration agreement.

Alpha-7. During the nine months ended September 30, 2005, we incurred $1.9 million of expenses in connection with our alpha-7 program compared to $1.1 million during the nine months ended September 30, 2004. As discussed earlier this increase is primarily due to personnel costs and contract research associated with our efforts to discover and develop small molecule product candidates.

Our general research and development expenses, which are not allocated to any specific program, increased by $1.2 million in the nine months ended September 30, 2005, compared to the corresponding period in 2004 primarily due to a $1.1 million increase in personnel costs and a $574,000 increase in facility and related costs, offset by a $619,000 decrease in leasehold amortization expense primarily attributable to non-recurring charges resulting from our move into a larger research facility.

Stock-based compensation expense from the nine months ended September 30, 2005 compared to the nine months ended September 30, 2004 remained relatively consistent. The adjustment to stock-based compensation expense is calculated based on the change in fair value of our common stock during the period. The fair value of our common

stock remained relatively constant during the nine months ended September 30, 2005 and decreased slightly during the nine months ended September 30, 2004.

Sales and Marketing. Sales and marketing expenses for the nine months ended September 30, 2005 were $7.0 million compared to $599,000 for the nine months ended September 30, 2004. The $6.4 million increase in the nine months ended September 30, 2005 was primarily attributable to the hiring of our sales management, the hiring and training of our 80-person specialty sales force and

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marketing and other costs associated with our recent launch of ZYFLO. The number of employees performing sales and marketing functions increased from six employees at September 30, 2004 to 93 employees at September 30, 2005.

General and Administrative Expenses. General and administrative expenses for the nine months ended September 30, 2005 were $8.8 million compared to $6.7 for the nine months ended September 30, 2004. The $2.1 million increase in the nine months ended September 30, 2005 was primarily attributable to the following:

Personnel costs increased $1.6 million as a result of the increase in the number of employees performing general and administrative functions from 22 employees at September 30, 2004 to 35 employees at September 30, 2005.

Directors and officers insurance and general business insurance costs increased $367,000 due to an increase in premiums following our initial public offering.

Other Income. Interest income for the nine months ended September 30, 2005 was $1.6 million compared to $690,000 for the nine months ended September 30, 2004. The increase in the nine months ended September 30, 2005 was primarily attributable to higher interest rates and higher cash and investment balances from our recently completed financings. Interest expense amounted to $140,000 and $84,000 for the nine months ended September 30, 2005 and September 30, 2004, respectively.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception on July 14, 2000, we have financed our operations through the sale of common and preferred stock, debt financings, the receipt of interest income and payments from our collaborators MedImmune and Beckman Coulter. As of September 30, 2005, we had $97.3 million in cash, cash equivalents and short-term investments. We have invested the net proceeds from our financings in highly liquid, interest-bearing, investment grade securities in accordance with our established corporate investment policy.

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

In July 2003, we entered into an exclusive license and collaboration agreement with MedImmune for the discovery and development of novel drugs for the treatment of acute and chronic inflammatory diseases associated with HMGB1, a newly discovered cytokine. Under this collaboration, MedImmune paid us initial fees of $12.5 million and an additional $2.8 million through September 30, 2005 to fund certain research expenses incurred by us for the HMGB1 program.

Under our collaboration with MedImmune, we may receive additional payments upon the achievement of research, development and commercialization milestones up to a maximum of $124.0 million, after taking into account payments we are obligated to make to North Shore-Long Island Jewish Research Institute on milestone payments we receive from MedImmune. We anticipate that by the end of 2005, in addition to payments already received, we will receive $1.0 million in aggregate milestone payments from MedImmune, after taking into account payments we are obligated to make to North Shore. In addition, we expect to receive $205,000 in the fourth quarter of 2005 for additional development support under the MedImmune agreement.

We finance the purchase of general purpose computer equipment, office equipment, fixtures and furnishings, test and laboratory equipment and software licenses and the completion of leasehold improvements through advances under our credit agreement with Silicon Valley Bank which was most recently modified as of June 30, 2004. We have granted Silicon Valley Bank a first priority security interest in substantially all of our assets, excluding intellectual property, to secure our obligations under the credit agreement. As of September 30, 2005, there was $1.9 million in debt outstanding under our credit agreement due to our outstanding debt under equipment advances.

The equipment advances made prior to the modification of our credit agreement on June 30, 2004 accrue interest at an effective interest rate up to 9.1% per year. We are required to make equal monthly payments of principal and interest with respect to each advance made prior to June 30, 2004. The total repayment term for equipment advances made prior to June 30, 2004 is 48 months. Upon the maturity of any advance made prior to June 30, 2004, we are

required to make a final payment in addition to the repayment

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of principal and interest. The final payment will be in an amount equal to a specified percentage of the original advance amount up to 8.5% of the original principal. As of September 30, 2005, we had $403,000 in outstanding equipment advances made prior to June 30, 2004.

Advances made under the modified credit agreement accrue interest at a rate equal to the prime rate plus 2% per year. Advances made under the modified credit agreement are required to be repaid in equal monthly installments of principal plus interest accrued through the repayment term, which range from 36 to 42 months. Repayment begins the first day of the month following the advance. As of September 30, 2005, we had $1.5 million in outstanding equipment advances under the modified credit agreement. During the nine months ended September 30, 2005, $418,000 in advances were made under the modified credit agreement, and we have approximately $882,000 of borrowing capacity under the modified credit agreement available until December 31, 2005.

Cash Flows

Operating Activities. Net cash used in operating activities was $30.4 million in the nine months ended September 30, 2005 compared to $18.2 million for the nine months ended September 30, 2004. Net cash used in operations for the nine months ended September 30, 2005 consisted of a net loss of $32.4 million, depreciation, amortization and the amortization of premiums on short-term investments of $1.4 million, stock-based compensation expense of $2.0 and cash used to fund working capital of $1.3 million.

Investing Activities. Investing activities provided $22.5 million of cash in the nine months ended September 30, 2005 compared to $71.9 million of cash used in investing activities in the nine months ended September 30, 2004. In the nine months ended September 30, 2005, we made capital expenditures of $1.7 million, primarily for laboratory equipment associated with our increased research and development activities and upgrades to our financial and accounting software. In addition, we sold $55.4 million of our short-term investments, which was offset by purchases of $31.3 million of short-term investments.

Financing Activities. Financing activities provided $51.1 million of cash in the nine months ended September 30, 2005 compared to $67.0 million in the nine months ended September 30, 2004. Net cash provided by financing activities for the nine months ended September 30, 2005 related to our private placement of common stock and warrants in June 2005 to certain institutional and other accredited investors. We sold 9,945,261 shares of our common stock at a price of $5.48 per share, together with warrants to purchase an additional 3,480,842 shares of our common stock, resulting in gross proceeds of $54.5 million. In connection with the private placement, we paid approximately $3.1 million in offering expenses and placement agent fees.

Funding Requirements

We expect to devote substantial resources to continue our research and development efforts, including preclinical testing and clinical trials, expand our sales and marketing infrastructure, achieve regulatory approvals, commercialize ZYFLO and, subject to regulatory approval, commercially launch the controlled-release formulation of zileuton and any future product candidates. We also expect to spend approximately $0.9 million in capital expenditures in the remainder of 2005 for the purchase of software, computer equipment, manufacturing equipment and equipment for our laboratories which will be purchased, in part, with funds available under our credit agreement with Silicon Valley Bank. Our funding requirements will depend on numerous factors, including:

- the costs to commercialize ZYFLO
- the costs and timing of the development, regulatory submission and approval and the commercial launch of the controlled-release formulation of zileuton, if and when it is approved by regulatory authorities;
- the scope and results of our clinical trials;
- advancements of other product candidates into development;
- potential acquisition or in-licensing of other products or technologies;
- the time and costs involved in preparing, submitting 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;

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

the cost of manufacturing, marketing and sales activities;

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

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

our ability to establish and maintain additional collaborative arrangements; and

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

Other than payments that we receive from our collaborations with MedImmune and Beckman Coulter, we expect that sales of ZYFLO will represent our only source of operating income until we commercially launch the controlled-release formulation of zileuton, if it is approved. In addition to the foregoing factors, we believe that our ability to access external funds will depend upon the 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. We believe that the key factors that will affect our internal and external sources of cash are:

our ability to successfully commercialize ZYFLO;

our ability to develop, achieve regulatory approval for and successfully commercialize the controlled-release formulation of zileuton;

the success of our other preclinical and clinical development programs;

the receptivity of the capital markets to financings by biopharmaceutical companies; and

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

Based on our operating plans, we believe that our available cash and cash equivalents 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.

If our existing resources are insufficient to satisfy our liquidity requirements, if our assumptions underlying our beliefs regarding future revenues and expenses change, if unexpected opportunities or needs arise or if we acquire or license rights to additional product candidates, we may need to raise additional external funds through collaborative arrangements and public or private financings. Additional financing may not be available to us on acceptable terms or at all. In addition, the terms of the financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, 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 commercial programs, which could harm our financial condition and operating results. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products which we would otherwise pursue on our own.

Contractual Obligations

We have summarized in the table below our fixed contractual obligations as of September 30, 2005.

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	Payments Due by Period				
Contractual Obligations	Total	Less than One Year	One to Three Years	Three to Five Years	After Five Years
			(in thousands)		
Short- and long-term debt	$ 2,114	$ 984	$ 1,130	$	$
Research and license agreements	7,639	451	201	234	6,753
Consulting agreements	427	320	107		
Manufacturing and clinical trial agreements	15,078	6,597	8,434	47	
Lease obligations	6,573	2,037	4,536		
Total contractual cash obligations	$ 31,831	$ 10,389	$ 14,408	$ 281	$ 6,753

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

The amounts listed for research and license agreements represent our fixed obligations payable to sponsor research and minimum royalty payments for licensed patents. These amounts do not include any additional amounts that we may be required to pay under our license agreements upon the achievement of scientific, regulatory and commercial milestones that may become payable depending on the progress of scientific development and regulatory approvals, including milestones such as the submission of an investigational new drug application to the FDA, similar submissions to foreign regulatory authorities and the first commercial sale of our products in various countries.

We are party to a number of agreements that require us to make milestone payments. In particular, under our license agreement with Abbott Laboratories for zileuton, we agreed to make aggregate milestone payments of up to $13.0 million to Abbott upon the achievement of various development and commercialization milestones relating to zileuton, including the completion of the technology transfer from Abbott to us, filing and approval of a product in the United States and specified minimum net sales of licensed products. Through September 30, 2005, we have paid and accrued an aggregate of $4.3 to Abbott under our agreement. In addition, under our manufacturing agreement with SkyePharma, through its subsidiary Jagotec, for the controlled-release version of zileuton, we agreed to make aggregate milestone payments of up to $6.6 million upon the achievement of various development and commercialization milestones. Through September 30, 2005, we have paid and accrued an aggregate of $2.0 million to SkyePharma under our agreement. In the third quarter of 2005, we accrued for a $750,000 milestone payment to Abbott related to our FDA approval of ZYFLO and a $750,000 milestone payment to SkyePharma related to the commencement of the manufacturing of our NDA registration batches for our controlled-release formulation.

The amounts shown in the table do not include royalties on net sales of our products and payments on sublicense income that we may owe as a result of receiving payments under our collaboration agreement with MedImmune. Our license agreements are described more fully in Note 11 of the Notes to Consolidated Financial Statements in our annual report on Form 10-K for the year ended December 31, 2004.

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

The amounts listed for manufacturing and clinical trial agreements represent amounts due to third parties for manufacturing, clinical trials and preclinical studies. As discussed in Note 9 to our condensed consolidated financial statements included herein, we entered into a manufacturing and supply agreement with Rhodia for commercial production of the API of ZYFLO, subject to specified limitations, through December 31, 2009. Under this agreement, we committed to purchase a minimum amount of API by December 31, 2006. The API purchased from Rhodia currently has a shelf-life of 24 months. We evaluate the need to provide reserves for contractually committed future purchases of inventory that may be in excess of forecasted future demand. In making these assessments, we are required to make judgments as to the future demand for current or committed inventory levels and as to the expiration

dates of its product.

Significant differences between our current estimates and judgments and future estimated demand for our product and the useful life of our inventory may result in significant charges for excess inventory or purchase commitments in the future. These differences could have a material adverse effect on our financial condition and results of operations during the period in which we recognize an inventory reserve. To date, we have not had any charges to cost of goods sold for excess inventory and contractual purchase commitments for inventory in excess of forecasted needs.

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

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

Forward-Looking Statements

This quarterly report on Form 10-Q includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For this purpose, any statements contained herein regarding possible therapeutic benefits and market acceptance of ZYFLO, the progress and timing of our drug development program and related trials and the efficacy of our drug candidates, our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management, other than statements of historical facts, are forward-looking statements made under the provisions of The Private Securities Litigation Reform Act of 1995. We may, in some cases, use words such as anticipate, believe, could, estimate, expect, intend, may, plan, project, should, will, would or other words that convey uncertain events or outcomes to identify these forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including our critical accounting estimates and risks relating to: the extent of market acceptance of ZYFLO; our ability to maintain regulatory approval to market and sell ZYFLO; our ability to develop and maintain the necessary sales, marketing, distribution and manufacturing capabilities to commercialize ZYFLO; patient, physician and third-party payor acceptance of ZYFLO as a safe and effective therapeutic product; adverse side effects experienced by patients taking ZYFLO; the results of preclinical studies and clinical trials with respect to our products under development and whether such results will be indicative of results obtained in later clinical trials; the timing and success of submission, acceptance and approval of regulatory filings; our heavy dependence on the commercial success of ZYFLO and the controlled-release formulation of zileuton; our ability to obtain the substantial additional funding required to conduct our research, development and commercialization activities; our dependence on our strategic collaboration with MedImmune, Inc.; and our ability to obtain, maintain and enforce patent and other intellectual property protection for ZYFLO, our discoveries and drug candidates. These and other risks are described in greater detail below under the caption Factors That May Affect Future Results . If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. In addition, any forward-looking statements in this quarterly report represent our views only as of the date of this quarterly report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, whether as a result of new information, future events or otherwise. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

Factors That May Affect Future Results

Risks Relating to Our Business

If the market is not receptive to ZYFLO or, if approved for sale, the controlled-release formulation of zileuton, we will be unable to generate significant revenues.

The FDA approved our sNDA to manufacture and market ZYFLO for commercial sale on September 28, 2005. In October 2005, we commercially launched ZYFLO. The commercial success of ZYFLO and, if approved for sale, the controlled-release formulation of zileuton will depend upon their acceptance by the medical community, third-party payors and patients. Physicians will prescribe ZYFLO and the controlled-release formulation of zileuton only if they determine, based on experience, clinical data, side effect profiles or other factors, that these products either alone or in combination with other products are 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 or view its clinical data as

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outdated. In addition, ZYFLO requires dosing four times per day, which some physicians and patients may find inconvenient compared to other available asthma therapies that require dosing only once or twice daily.

Moreover, perceptions about the safety of ZYFLO could limit the market acceptance of ZYFLO and the controlled-release formulation of zileuton. In the placebo-controlled clinical trials that formed the basis for FDA approval of the NDA for ZYFLO, 1.9% of patients taking ZYFLO experienced increased levels of a liver enzyme called alanine transaminase, or ALT, of over three times the levels normally seen in the bloodstream, compared to 0.2% of patients receiving placebo. In addition, prior to FDA approval, a long-term trial was conducted in 2,947 patients to evaluate the safety of ZYFLO, particularly in relation to liver enzyme effects. In this safety trial, 4.6% of the patients taking ZYFLO experienced increased levels of ALT of over three times the levels normally seen in the bloodstream, compared to 1.1% of patients receiving placebo. The overall percentage of patients that experienced increases in ALT of over three times the levels normally seen in the bloodstream was 3.2% in approximately 5,000 asthma patients who received ZYFLO in the clinical trials that were reviewed by the FDA prior to its approval of ZYFLO. In these trials, one patient developed symptomatic hepatitis with jaundice, which resolved upon discontinuation of therapy, and three patients developed mild elevations in bilirubin, a protein. Furthermore, because ZYFLO can elevate liver enzyme levels, periodic liver function tests are recommended for patients taking ZYFLO and may be advisable for patients taking our other zileuton product candidates. Some physicians and patients may perceive liver function tests as inconvenient or indicative of safety issues, which could make them reluctant to prescribe or accept ZYFLO and other zileuton product candidates. As a result, many physicians may have negative perceptions about the safety of ZYFLO and other zileuton product candidates, which could limit their commercial acceptance. The absence of ZYFLO from the market prior to our commercial launch in October 2005 may have exacerbated any negative perceptions about ZYFLO if physicians believe the absence of ZYFLO from the market was related to safety or efficacy issues.

The position of ZYFLO in managed care formularies, which are lists of products approved by managed care organizations, may also make it difficult to expand the current market for this product. As a result of a lack of a sustained sales and marketing effort prior to our commercial launch in October 2005, ZYFLO had been removed from some formularies or relegated to third-tier status, which requires the highest co-pay for patients. In addition, ZYFLO may have been removed from some managed care formularies as a result of the absence of ZYFLO from the market prior to our commercial launch.

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

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

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

If we do not successfully recruit, train and retain qualified sales and marketing personnel and build and maintain an adequate marketing and sales infrastructure, our ability to independently launch and market our product

candidates, including ZYFLO, will be impaired. We are incurring significant costs and devoting significant efforts to establish a direct sales force.

We are independently launching and marketing ZYFLO. If approved for sale, we intend to independently launch and market the controlled-release formulation of zileuton and other product candidates for which we believe the target physician market can be effectively reached by our sales and marketing force. As of October 24, 2005, the commercial launch date for ZYFLO, we had a sales force of approximately 80 sales representatives. All of these sales representatives joined us in 2005. For the nine months ended September 30, 2005, we had incurred sales and marketing costs of approximately $7.0 million, which included costs related to our

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launch of ZYFLO. We expect to incur additional costs as we further expand our sales force and sales and marketing efforts. We may not be able to attract, hire, train and retain qualified sales and marketing personnel to build and maintain a significant or effective sales force. If we are not successful in our efforts to develop and maintain an effective internal sales force, our ability to independently launch and market our product candidates, including ZYFLO and the controlled-release formulation of zileuton, will be impaired.

We are investing significant amounts of money and management resources to develop internal sales and marketing capabilities. We are using a third party for distribution of ZYFLO. Because we minimized sales and marketing expenditures and activities, including the hiring and training of sales personnel, prior to obtaining regulatory approval to market and sell ZYFLO, our ability to successfully commercialize ZYFLO may be impaired. If we are unable to successfully commercialize ZYFLO, we will have incurred significant unrecoverable expenses. Likewise, if we further expand our sales force in anticipation of approval of the controlled-release formulation of zileuton or our other product candidates, we will incur significant costs.

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

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

We have no prior experience managing commercial supplies of ZYFLO. Our current forecasting of inventory levels is based on our estimate of expected customer orders rather than actual sales. If we fail to maintain an adequate inventory or if our inventory were to be destroyed or damaged or reached its expiration date, patients might not have access to ZYFLO, our reputation could be harmed and physicians may be less likely to prescribe ZYFLO in the future. Conversely, if we are unable to sell our inventory in a timely manner, we could experience cash flow difficulties and financial losses.

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

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

- the timing of our receipt of any marketing approvals, the terms of any approval and the countries in which approvals are obtained;
- the safety, efficacy and ease of administration;
- the therapeutic benefit or other improvement over existing comparable products;
- 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 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

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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.

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

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

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

Zileuton will also face intense competition if we are able to develop it as a treatment for COPD or acne. COPD is currently treated predominantly with drugs that are indicated for use in asthma only or asthma and COPD 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 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®, Johnson &

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

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

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

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

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

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

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

We depend on the principal members of our scientific and management staff, including Paul D. Rubin, M.D., our president and chief executive officer, 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.

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.

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

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

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

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

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

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

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

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

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

state and foreign law equivalents of the foregoing;

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

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

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

to a variety of interpretations, and additional legal or regulatory change.

If our promotional activities fail to comply with the FDA s regulations or guidelines, we may be subject to enforcement action by the FDA. For example, we received a warning letter from the FDA on November 8, 2005 relating to certain promotional material that included an illustration of the mechanism of action for ZYFLO. The FDA asserted that the promotional material incorporating the illustration was false or misleading because it presented efficacy claims for ZYFLO, but failed to contain fair balance by not communicating the risks associated with its use and failing to present the approved indication for ZYFLO. In response to the warning letter, and as requested by the FDA, we stopped disseminating the promotional material containing the mechanism of action and we will provide a written response to the FDA by November 23, 2005. As part of our response, we will provide a description of our plan to disseminate corrective messages about the promotional material to those who received this material. We plan to revise the promotional material containing the mechanism of action to address the FDA s concerns regarding fair balance. If we were to receive any additional warning letters, we could be subject to additional regulatory actions by the FDA, including product seizure, injunctions, and other penalties and our reputation in the market could be harmed.

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

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

In recent years, several states, including California, Maine, Minnesota, New Mexico, Vermont and West Virginia, and the District of Columbia have enacted legislation requiring pharmaceutical companies to establish marketing and promotional compliance

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

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

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

The development, manufacturing, pricing, marketing, sales and reimbursement of ZYFLO and our product candidates, together with our general operations, are subject to extensive regulation by federal, state and other authorities within the United States and numerous entities outside of the United States. We are a relatively small company, with 170 employees as of September 30, 2005, the majority of whom joined us in 2004 and 2005. We rely heavily on third parties to conduct many important functions. While we have developed and instituted a corporate compliance program based on what we believe are the current best practices and continue to update the program in response to newly implemented and changing regulatory requirements, it is possible that we may not be in compliance with all potentially applicable regulations. If we fail to comply with any of these regulations, we could be subject to a range of regulatory actions, including significant fines, litigation or other sanctions. Any action against us for a violation of these regulations, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management s attention and harm our reputation.

As a publicly traded company, we are subject to significant legal and regulatory requirements, including the Sarbanes-Oxley Act of 2002 and related regulations, some of which have either only recently been adopted or are subject to change. For example, we are currently evaluating our internal control systems in order to allow our management to report on, and our independent accounting firm to attest to, our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. We are incurring additional expenses and devoting significant management time and attention to this evaluation. If we are not able to implement the requirements of Section 404 in a timely manner or with adequate compliance, we may be subject to sanctions or investigation by regulatory authorities, including the Securities and Exchange Commission or the Nasdaq National Market. This type of action could adversely affect our financial results or investors confidence in our company and our ability to access the capital markets. In addition, the controls and procedures that we implement may not comply with all of the relevant rules and regulations of the Securities and Exchange Commission and the Nasdaq National Market. If we fail to develop and maintain adequate controls and procedures, we may be unable to provide the required financial information in a timely and reliable manner, which could cause a decline in our stock price.

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

Our sales of ZYFLO are dependent, in part, on the availability of reimbursement from third-party payors such as state and Federal governments, under programs such as Medicare and Medicaid, and private insurance plans. There have been, there are and we expect there will continue to be, state and Federal legislative and administrative proposals that could limit the amount that state or Federal governments will pay to reimburse the cost of pharmaceutical and biologic products. The Medicare Prescription Drug Improvement and Modernization Act of 2003, or the MMA, was

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

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ZYFLO or our product candidates, including those at a late stage of development, and current reimbursement policies for marketed products may change at any time.

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

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

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

If our Medicaid rebate program practices are investigated, the costs could be substantial and could divert the attention of management.

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

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

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and marketing and sale of drugs. If the use of ZYFLO or one or more of our product candidates harms people, we may be subject to costly and damaging product liability claims. We currently have a $20.0 million annual aggregate limit for insurance covering both product liability claims for ZYFLO and clinical trial liability claims for our product candidates. We expect to seek additional product liability insurance prior to marketing the controlled-release formulation of zileuton or any of our other product candidates. However, our insurance may not provide adequate coverage against potential liabilities. Furthermore, product liability and clinical trial insurance is

becoming increasingly expensive. As a result, we may be unable to maintain current amounts of insurance coverage, obtain additional insurance or obtain sufficient insurance at a reasonable cost to protect against losses that we have not anticipated in our business plans. Any product liability claim against us, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management s attention and harm our reputation.

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

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

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

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

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

If we do not obtain the regulatory approvals or clearances required to market and sell the controlled-release formation of zileuton or our other product candidates under development, our business 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. ZYFLO is our only commercial product and can only be marketed in the United States. We expect to submit a NDA to the FDA for the controlled-release formulation of zileuton in mid- 2006. At present, we are completing production of registration batches for stability testing and 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. 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 mid-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. If the FDA does not permit us to rely on the prior clinical data or if the data at the clinical sites do not pass FDA audits, we could be required to repeat some or all of the clinical trials, which would lead to unanticipated costs and delays. Problems with the previous trials, such as incomplete or otherwise unacceptable data, could cause our NDA to be delayed or rejected.

The regulatory process to obtain market approval or clearance for a new drug, 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 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.

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

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

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

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

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

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

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays or the inability to obtain required approvals from institutional review boards or other governing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling patients and volunteers into clinical trials;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- the need to repeat clinical trials as a result of inconclusive or negative results or poorly executed testing;
- insufficient supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials;
- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;

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

the placement of a clinical hold on a trial.

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Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis will be subject to a number of factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, competing trials with other product candidates and the eligibility criteria for the clinical trial. Delays in patient enrollment can result in increased costs and longer development times. In addition, subjects may drop out of our clinical trials and thereby impair the validity or statistical significance of the trials.

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

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

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

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

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

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

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

- product seizures;
- voluntary or mandatory recalls;
- suspension of review or refusal to approve pending applications;
- voluntary or mandatory patient or physician notification;
- 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;

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injunctions; and

civil and criminal penalties.

Risks Relating to Our Dependence on Third Parties

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

We are relying on MedImmune to fund the development of and to commercialize product candidates in our HMGB1 program. We are relying on Beckman Coulter to fund the development and to commercialize diagnostics in our HMGB1 program. All of our revenues for the years ended December 31, 2003 and 2004 were derived from fees paid to us by MedImmune, and all of our revenues for the nine months ended September 30, 2005 were derived from fees paid to us by MedImmune and Beckman Coulter, under collaboration agreements. We expect that we will generate revenue from the sale of ZYFLO beginning in the fourth quarter of 2005; however, a significant portion 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.

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;

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

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

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

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

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

We have contracted with Rhodia Pharma Solutions Ltd. for commercial production of the zileuton API, subject to specified limitations, through December 31, 2009. We have contracted with Patheon Pharmaceuticals Inc. for the manufacture of commercial supplies of ZYFLO tablets. We have contracted with SkyePharma PLC, through its subsidiary Jagotec AG, for the manufacture of tablets of the controlled-release formulation of zileuton for clinical trials, regulatory review and, subject to negotiation of a commercial manufacturing agreement, commercial supplies. Rhodia SA, the parent company of Rhodia Pharma Solutions, has experienced significant operating losses since 2001. In 2003, Rhodia SA initiated a corporate reorganization plan to refocus its business portfolio, and has divested a number of its operating units since that time. In addition, Rhodia SA has publicly announced that it incurred a 101 million charge in the second quarter of 2005 to fully write off the value of Rhodia Pharma Solutions. We have contracted with Patheon for a technology transfer program to enable Patheon to coat and package the core tablets of the controlled-release formulation of zileuton for clinical trials and regulatory review, and, subject to negotiation of a commercial manufacturing agreement, commercial supplies. If we were required to change manufacturers for the zileuton API, ZYFLO or the controlled-release formulation of zileuton, we would be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and all applicable regulations and guidelines, including FDA requirements. Any delays associated with the verification of a new manufacturer could adversely affect our production schedule or increase our production costs.

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

We are dependent upon Rhodia Pharma Solutions, Patheon and SkyePharma as sole providers, and will be dependent on any other third parties who manufacture our product candidates, to perform their obligations in a timely manner and in accordance with applicable government regulations. If third-party manufacturers with whom we contract fail to perform their obligations, we may be adversely affected in a number of ways, including the following:

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

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

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

we may not be able to meet commercial demands.

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

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

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

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

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

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

Our drug development programs and potential commercialization of our product candidates will require substantial additional cash to fund expenses to be incurred in connection with these activities. We may seek to enter into additional collaboration agreements with pharmaceutical companies to fund all or part of the costs of drug development and commercialization of product candidates. 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.

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

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

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; or

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

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

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

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

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

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

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

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

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

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

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

In order to protect our proprietary technology and processes, it is our general practice to enter into confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These

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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 $32.4 million in the nine months ended September 30, 2005. As of September 30, 2005, we had an accumulated deficit of approximately $90.9 million. As of September 30, 2005, we have not recorded any revenue from the sale of ZYFLO or any other product. We expect that we will continue to incur substantial losses for at least the next several years as we spend significant amounts to fund our research, development and commercialization efforts and to enhance our core technologies. We expect that the losses that we incur will fluctuate from quarter to quarter and that these fluctuations may 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, expand our sales and marketing infrastructure, achieve regulatory approvals, commercialize ZYFLO and, subject to regulatory approval, commercially launch the controlled-release formulation of zileuton and any future product candidates. Our funding requirements will depend on numerous factors, including:

- the costs to commercialize ZYFLO;
- the costs and timing of the development, regulatory submission and approval and the commercial launch of the controlled-release formulation of zileuton, if and when it is approved by regulatory authorities;
- the scope and results of our clinical trials;
- advancements of other product candidates into development;
- potential acquisition or in-licensing of other products or technologies;
- the time and costs involved in preparing, submitting 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;
- the cost of manufacturing, marketing and sales activities;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- the cost of obtaining and maintaining licenses to use patented technologies;

our ability to establish and maintain additional collaborative arrangements; and

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

Other than payments that we receive from our collaborations with MedImmune and Beckman Coulter, we expect that sales of ZYFLO will represent our only source of operating income until we commercially launch the controlled-release formulation of zileuton if it is approved. In addition to the foregoing factors, we believe that our ability to access external funds will depend upon the success of our other preclinical and clinical development programs, the receptivity of the capital markets to financings by biopharmaceutical companies, our ability to enter into additional strategic collaborations with corporate and academic collaborators and the success of such collaborations.

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

For the nine months ended September 30, 2005, our net cash used for operating activities was $30.4 million and we had capital expenditures of $1.7 million. If our existing resources are insufficient to satisfy our liquidity requirements or if we acquire or license rights to additional product candidates, we will need to raise additional external funds through collaborative arrangements and public or private financings. Additional financing may not be available to us on acceptable terms or at all. In addition, the terms of the financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our then-existing stockholders will result. If we are unable to obtain funding on a timely basis, we may be required to significantly delay, limit or eliminate one or more of our research, development or commercialization programs, which could harm our financial condition and operating results. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products which we would otherwise pursue on our own.

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

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

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

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

Risks Relating to Our Common Stock

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

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

prices of securities of pharmaceutical

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

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

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

- the amount and timing of sales of ZYFLO;
- the timing of operating expenses, including selling and marketing expenses and the costs of expanding and maintaining a direct sales force;
- the availability and timely delivery of a sufficient supply of ZYFLO;
- the amount of rebates, discounts and chargebacks to be wholesalers, Medicaid and managed care organizations related to ZYFLO;
- the amount and timing of product returns for ZYFLO;
- achievement of, or the failure to achieve, milestones under our development agreement with MedImmune, our license agreement with Beckman Coulter and, to the extent applicable, other licensing and collaboration agreements;
- the results of ongoing and planned clinical trials of our product candidates;
- production problems occurring at our third party manufacturers;
- the results of regulatory reviews relating to the 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 operating results, including the amount and timing of sales of ZYFLO;
- our licensing and collaboration agreements and the products or product candidates that are the subject of those agreements;
- the results of discovery, preclinical studies and clinical trials by us or our competitors;
- the acquisition of technologies, product candidates or products by us or our competitors;

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

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

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

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

As of September 30, 2005, our directors, executive officers and 5% or greater stockholders, together with their affiliates, to our knowledge, beneficially owned, in the aggregate, approximately 64.8% of our outstanding common stock. As a result, our directors, executive officers and 5% or greater stockholders, together with their affiliates, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

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

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

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

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

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

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

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

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our current investment policy is to maintain an investment portfolio consisting mainly of U.S. money market and corporate notes, directly or through managed funds, with maturities of two years or less. Our cash is deposited in and invested through highly-rated financial institutions in North America. Our short-term investments are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 10% from levels at September 30, 2005, we estimate that the fair value of our investment portfolio would decline by approximately $42,000. In addition, we could be exposed to losses related to these securities should one of our counterparties default. We attempt to mitigate this risk through credit monitoring procedures. Although we consider our investments to be available-for-sale securities in order to fund operations, if necessary, we have the ability to hold our fixed income investments until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Item 4. Controls and Procedures

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2005. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other

procedures of a company that are designed to ensure that information required to be disclosed by the company in the reports that it files or submits under the Exchange Act is recorded,

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processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2005, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended September 30, 2005 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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PART II. OTHER INFORMATION

Item 1. Legal Proceedings.

Not applicable.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Recent Sales of Unregistered Securities

Not applicable.

Uses of Proceeds from Registered Securities

In June 2004, we sold 6,110,000 shares of our common stock in our initial public offering, including 110,000 shares upon the exercise of an over-allotment option by the underwriters, pursuant to a registration statement on Form S-1 (File No. 333-113727), which was declared effective by the SEC on May 26, 2004. Our net proceeds from the offering equaled approximately $37.8 million. Through September 30, 2005, we have not used any of the net proceeds from the offering. The net proceeds of the offering are invested in short-term investment grade corporate and U.S. government securities. There has been no material change in our planned use of the net proceeds of the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act of 1933, as amended.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Submission of Matters to a Vote of Security Holders.

Not applicable.

Item 5. Other Information.

Not applicable.

Item 6. Exhibits.

The exhibits listed in the accompanying exhibit index are filed as part of this Quarterly Report on Form 10-Q.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

CRITICAL THERAPEUTICS, INC.

Date: November 10, 2005

/s/ Paul D. Rubin

Paul D. Rubin, M.D.
President and Chief Executive Officer
(*Principal Executive Officer*)

Date: November 10, 2005

/s/ Frank E. Thomas

Frank E. Thomas
Senior Vice President of Finance, Chief Financial Officer and Treasurer
(*Principal Financial and Accounting Officer*)

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EXHIBIT INDEX

Exhibit Number	Description
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.