EPIX Pharmaceuticals, Inc.
Form 10-Q
November 02, 2004

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

ý **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2004

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 0-21863

EPIX Pharmaceuticals, Inc.

(Exact name of Registrant as Specified in its Charter)

Delaware	**04-3030815**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
161 First Street **Cambridge, Massachusetts** (Address of principal executive offices)	**02142** (Zip Code)

Registrant s telephone number, including area code: **(617) 250-6000**

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $.01 par value per share

(Title of Class)

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 ý No o

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

As of October 29, 2004, 23,089,499 shares of the registrant s Common Stock, $.01 par value per share, were issued and outstanding.

EPIX Pharmaceuticals, Inc.

INDEX

PART I. FINANCIAL INFORMATION

ITEM 1. CONDENSED FINANCIAL STATEMENTS (unaudited)

EPIX PHARMACEUTICALS, INC.

BALANCE SHEETS

(unaudited)

		September 30, 2004		December 31, 2003
ASSETS				
Current assets:				
Cash and cash equivalents	$	70,255,485	$	36,658,557
Available-for-sale marketable securities		98,786,566		43,299,675
Accounts receivable		843,895		46,072
Prepaid expenses and other current assets		588,416		393,679
Total current assets		170,474,362		80,397,983
Property and equipment, net		2,731,755		1,413,346
Other assets		3,567,944		63,401
Total assets	$	176,774,061	$	81,874,730
LIABILITIES AND STOCKHOLDERS EQUITY				
Current liabilities:				
Accounts payable	$	1,215,329	$	1,938,365
Accrued expenses		6,671,684		7,858,859
Contract advances		3,966,580		3,172,707
Loan payable to strategic partner		15,000,000		7,500,000
Deferred revenue		3,192,270		2,917,429
Total current liabilities		30,045,863		23,387,360
Deferred revenue		1,301,112		4,330,798
Convertible Debt		100,000,000		
Commitments and contingencies				
Stockholders equity:				
Preferred Stock, $0.01 par value; 1,000,000 shares authorized; no shares issued				
Common Stock, $0.01 par value; 40,000,000 shares authorized; 23,034,735 and 22,318,642 shares issued and outstanding at September 30, 2004 and December 31, 2003, respectively		230,347		223,187
Additional paid-in-capital		195,534,257		188,851,948
Accumulated deficit		(150,191,269)		(134,952,516)
Accumulated other comprehensive income		(146,249)		33,953
Total stockholders equity		45,427,086		54,156,572
Total liabilities and stockholders equity	$	176,774,061	$	81,874,730

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS

(unaudited)

	Three months ended September 30,		Nine months ended September 30,	
	2004	**2003**	**2004**	**2003**
Revenues:				
Product development revenue	$ 2,273,957	$ 2,834,438	$ 6,887,949	$ 8,159,640
Royalty revenue	700,601	682,116	2,398,116	1,782,312
License fee revenue	263,585	401,300	822,048	1,293,768
Total revenues	3,238,143	3,917,854	10,108,113	11,235,720
Operating expenses:				
Research and development	6,508,418	5,618,628	17,094,950	18,901,011
General and administrative	2,878,916	1,677,654	8,170,522	4,842,662
Total operating expenses	9,387,334	7,296,282	25,265,472	23,743,673
Operating loss	(6,149,191)	(3,378,428)	(15,157,359)	(12,507,953)
Interest income	688,424	181,988	1,199,047	410,868
Interest expense	(935,069)	(165,150)	(1,234,099)	(266,795)
Loss before provision for income taxes	(6,395,836)	(3,361,590)	(15,192,411)	(12,363,880)
Provision for income taxes	16,676	2,973	46,342	68,985
Net loss	$ (6,412,512)	$ (3,364,563)	$ (15,238,753)	$ (12,432,865)
Weighted average shares:				
Basic and diluted	22,987,878	19,765,976	22,810,300	18,021,100
Net loss per share, basic and diluted	$ (0.28)	$ (0.17)	$ (0.67)	$ (0.69)

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

(unaudited)

	Nine months ended September 30, 2004	2003
Operating activities:		
Net loss	$ (15,238,753)	$ (12,432,865)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	701,417	468,875
Changes in operating assets and liabilities:		
Accounts receivable	(797,823)	175,132
Prepaid expenses and other current assets	(194,737)	27,574
Other assets	145,457	
Accounts payable	(723,036)	(289,757)
Accrued expenses	1,151,865	(421,152)
Contract advances	793,873	(381,006)
Deferred revenue	(2,754,845)	(2,386,235)
Net cash used in operating activities	(16,916,582)	(15,239,434)
Investing activities:		
Purchases of property and equipment	(2,019,826)	(308,370)
Purchases of marketable securities	(79,366,215)	(13,917,217)
Sale or redemption of marketable securities	23,699,122	19,308,634
Net cash (used in) provided by investing activities	(57,686,919)	5,083,047
Financing activities:		
Proceeds from loan payable to strategic partner	37,500,000	7,500,000
Repayment of loan payable to strategic partner	(30,000,000)	
Proceeds from issuance of convertible debt	96,350,000	
Proceeds from employee stock purchase plan and stock options	4,350,429	2,215,578
Proceeds from sale of common stock		65,510,325
Net cash provided by financing activities	108,200,429	75,225,903
Net increase in cash and cash equivalents	33,596,928	65,069,516
Cash and cash equivalents at beginning of period	36,658,557	4,540,444
Cash and cash equivalents at end of period	$ 70,255,485	$ 69,609,960
Supplemental cash flow information:		
Cash paid for interest	$ 123,055	$ 160,849
Cash paid for taxes	$ 34,356	$ 95,541
Supplemental disclosure of non cash financing activity:		
Issuance of common stock in connection with Intellectual Property Agreement, dated November 2003	$ 2,339,040	$

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

(unaudited)

1. Nature of Business

EPIX Pharmaceuticals, Inc. (EPIX or the Company), formerly EPIX Medical, Inc., is developing innovative pharmaceuticals both to improve the capability and expand the use of magnetic resonance imaging (MRI) as a tool for diagnosing human disease. The Company s lead product under development, MS-325, is an injectable targeted contrast agent specifically designed for vascular imaging using magnetic resonance angiography (MRA) to diagnose atherosclerotic disease, including non-coronary vascular disease and coronary artery disease. In December 2003, the Company submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for MS-325, which was accepted for filing in February 2004. In October 2004, the Company was notified by the FDA that it had extended the action date for completion of its review of MS-325 by 90 days to January 2005. In June 2004, the Company s worldwide marketing partner, Schering Aktiengesellschaft (Schering AG) submitted MS-325 for marketing approval in the European Union. MS-325 is being co-developed by EPIX and Schering AG. The Company is also collaborating with Schering AG on the development of its second drug candidate, EP-2104R, for detecting human thrombus, or blood clots, using MRI, is engaged in research activities for other pharmaceutical products and has an exclusive research collaboration agreement with Schering AG to discover additional novel compounds for diagnosing human diseases using MRI.

2. Basis of Presentation

The unaudited condensed financial statements of EPIX have been prepared in accordance with accounting principles generally accepted in the U.S. for interim financial information and the instructions to Form 10-Q and the rules of the Securities and Exchange Commission (the Commission). Accordingly, they do not include all of the information and footnotes required to be presented for complete financial statements. The accompanying unaudited condensed financial statements reflect all adjustments (consisting only of normal recurring adjustments) which are, in the opinion of management, necessary for a fair presentation of the results for the interim periods presented. The results of the interim period ended September 30, 2004 are not necessarily indicative of the results expected for the full fiscal year.

The unaudited condensed financial statements and related disclosures have been prepared with the assumption that users of the unaudited condensed financial statements have read or have access to the audited financial statements for the preceding fiscal year. Accordingly, these unaudited condensed financial statements should be read in conjunction with the audited financial statements and the related notes thereto included in the Company s Annual Report on Form 10-K for the year ended December 31, 2003.

3. Significant Accounting Policies

Revenue

Product development revenue

In June 2000, the Company entered into a strategic collaboration agreement with Schering AG, whereby each party to the agreement shares equally in MS-325 development costs and will share equally in any related U.S. operating profits, and the Company will receive royalties related to non-U.S. sales. The Company recognizes product development revenue at the time it performs research and development activities for which Schering AG and other collaborators are obligated to reimburse the Company. Product development revenues from Schering AG are recorded net of the Company s portion of Schering AG s actual or most recent estimate of their MS-325 research and development costs.

In May 2003, the Company entered into a development agreement with Schering AG for EP-2104R and a collaboration agreement with Schering AG for MRI research. Under the EP-2104R development agreement, Schering AG has made and will make fixed payments to the Company totaling approximately $9.0 million over two years beginning in the second quarter of 2003 to cover the Company s expenditures for the feasibility program for that product candidate. The Company recognizes reimbursement from Schering AG for the EP-2104R feasibility program as revenue proportionate to the Company s actual cost incurred relative to its estimate of expected total program costs. Total estimated costs of the feasibility program are based on management s assessment of costs to complete the program based upon an evaluation of the portion of the program completed, costs incurred to date and expected future costs of the program. To the extent that estimated costs to complete the feasibility program change materially from previous periods, adjustments to revenue are recorded. In June 2004, management increased its EP-2104R estimate to complete the feasibility program, resulting in a reduction of revenue of $131,000 in the second quarter of 2004. In September 2004, management again increased its EP-2104R estimate to complete the feasibility program, resulting in a reduction of revenue of $219,000 in the third quarter of 2004.

Revenue under the MRI research collaboration is recognized at the time services are provided for which Schering AG is obligated to reimburse the Company.

Payments received by the Company from Schering AG in advance of EPIX performing research and development activities are recorded as contract advances.

Royalty revenue

The Company earns royalty revenues pursuant to its sub-license on certain of its patents with Bracco Imaging S.p.A. (Bracco). Massachusetts General Hospital (MGH) owns those patents and has exclusively licensed those patents to the Company, which in turn have been non-exclusively sub-licensed to Bracco. The Company owes MGH a percentage of all royalties received from its sub-licenses, which are classified as general and administrative expenses in the Statements of Operations.

Royalty revenues are recognized based on actual revenues as reported by Bracco to the Company, as available. Otherwise, the Company estimates royalty revenues based on Bracco s estimates, historical revenues and trends. In connection with the execution of the sub-licensing arrangement in September 2001, Bracco made a $4.0 million refundable advance royalty payment to the Company, which was accounted for as deferred revenue. When royalty revenue is earned, a portion of the royalty revenue earned is offset against the $4.0 million refundable advance royalty payment. Prior to July 2003, the remaining portion of royalty revenue earned was paid to the Company in cash. Beginning in July 2003 and until the earlier of FDA approval of Bracco s principal product, MultiHance®, or December 31, 2005, a portion of royalty revenue earned that was previously paid to the Company in cash is being offset against another advance payment from Bracco related to the $3.0 million FDA approval license fee, discussed below under *License fee revenue*. At September 30, 2004, the remaining balances of the refundable advance royalty and the refundable advance license fee were $1.0 million and $1.4 million, respectively.

License fee revenue

The Company records license fee revenue in accordance with SEC Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104). Pursuant to SAB 104, the Company recognizes revenues from non-refundable license fees and milestone payments, not specifically tied to a separate earnings process, ratably over the period during which the Company has a substantial continuing obligation to perform services under contract. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed.

In September 2001, the Company sub-licensed certain patents to Bracco and received a non-refundable $2.0 million license fee from Bracco. This license fee is included in deferred revenue and is being recorded as revenue ratably from the time of the payment until the expiration of MGH s patent in 2006. The balance of the original $2.0 million non-refundable license fee at September 30, 2004 was $737,000.

The Company also received a refundable $3.0 million license fee from Bracco, which is contingent upon MultiHance® gaining FDA approval in the U.S. This license fee, which is included in deferred revenue in the accompanying balance sheet, will be recorded as revenue when the FDA grants approval for MultiHance®. Beginning in July 2003, a portion of royalty revenue earned is being offset against the FDA approval license fee. If MultiHance® is approved prior to December 31, 2005, Bracco will be obligated to pay the Company the amount of royalties previously

offset against the license fee beginning in July 2003. If MultiHance® does not gain FDA approval by December 31, 2005, the Company is obligated to repay the remaining balance of the $3.0 million to the extent such royalties are insufficient to meet the entire obligation. The balance of the original $3.0 million license fee at September 30, 2004 was $1.4 million.

In March 2004, the Company increased its estimate of the time period over which it believes it will provide services under the agreement with Mallinckrodt, Inc., a subsidiary of Tyco/Mallinckrodt, from 99 months to 101 months because the FDA notified the Company that its NDA for MS-325 had been accepted for filing under a standard review cycle, instead of an accelerated review cycle. In September 2004, the Company again increased its estimated time period for providing services under the agreement with Tyco/Mallinckrodt to103 months because of the FDA s notice to extend its review by an additional 90 days. The impact of the increase in these estimates resulted in a reduction of revenue of $76,000 for the first nine months of 2004.

In March 2004, the Company received a milestone payment related to its filing of the NDA with the FDA of $2.5 million pursuant to the collaboration agreement with Schering AG for MS-325. During the same period, the Company paid Tyco/Mallinckrodt $2.5 million for the NDA milestone. These payments were offset in the Company s Statements of Operations, resulting in no impact on revenues, expenses or net loss.

Research and Development Expenses

Research and development costs, including those associated with technology, licenses and patents, are expensed as incurred. Research and development costs primarily include employee salaries and related costs, third party service costs, the cost of preclinical and clinical trial supplies and consulting expenses.

In order to conduct research and development activities and compile regulatory submissions, the Company enters into contracts with vendors who render services over an extended period of time, generally one to three years. The Company typically enters into three types of vendor contracts; time-based, patient-based or a combination thereof. Under a time-based contract, using critical factors contained within the contract, such as the stated duration of the contract and the timing of services provided, the Company records the contractual expense for each service provided ratably over the period during which the Company estimates the service will be performed. Under a patient based contract, the Company first determines an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. The Company then records expenses based upon the total number of patients enrolled during the period.

On a quarterly basis, the Company reviews both the timetable of services to be rendered and the timing of services actually rendered. Based upon this review, revisions may be made to the forecasted timetable or the extent of services performed, or both, in order to reflect the Company s most current estimate of the contract.

In January 2004, the Company issued 132,000 shares of common stock to Dr. Martin Prince in connection with the Intellectual Property Agreement entered into in November of 2003. The estimated value of these shares was recognized as a research and development expense in the fourth quarter of 2003 when the Company entered into the Intellectual Property Agreement.

Loss per Share

Basic and diluted net loss per share are computed using the weighted-average number of common shares outstanding during the period. For the three and nine months ended September 30, 2004 and 2003, the Company was in a net loss position and, therefore, the basic and diluted net loss per share are the same. Basic net loss per share excludes any dilutive effect from outstanding stock options and awards and from the conversion of convertible senior notes.

Common stock potentially issuable but excluded from the calculation of dilutive net loss per share for the three and nine months ended September 30, 2004 and 2003 because their inclusion would have been antidilutive consisted of the following:

	2004	2003
Stock options and awards (exercise price ranging from $0.45 to $25.37, with a weighted average exercise price of $12.09)	3,687,615	3,792,954
Shares issuable on conversion of 3% Convertible Senior Notes	3,359,090	
	7,046,705	3,792,954

Comprehensive Loss

Comprehensive loss is comprised of net loss and unrealized gains or losses on the Company s available-for-sale marketable securities. The Company s comprehensive loss for the three months ended September 30, 2004 and 2003 amounted to $6.3 million and $3.4 million, respectively, and for the nine months ended September 30, 2004 and 2003 amounted to $15.4 million and $12.6 million, respectively.

Employee Stock Compensation

The Company has elected to follow Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), in accounting for its stock-based compensation plans under the intrinsic value method, rather than the alternative fair value accounting method provided for under SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123). Under APB 25, because the exercise price of the Company s employee stock options is equal to the market price of the underlying stock on the date of grant, no compensation expense is recognized.

The following table illustrates the effect on net loss and net loss per share if the Company had applied the fair value recognition provisions of SFAS 123 to stock-based employee compensation.

	Three months ended September 30,		Nine months ended September 30,	
	2004	2003	2004	2003
Net loss - as reported	$ (6,412,512)	$ (3,364,563)	$ (15,238,753)	$ (12,432,865)
Add: employee stock-based compensation included in net loss as reported				
Less: pro forma adjustment for stock-based compensation	(1,670,110)	(1,070,073)	(4,387,454)	(2,955,786)
Net loss - pro forma	$ (8,082,622)	$ (4,434,636)	$ (19,626,207)	$ (15,388,651)
Net loss per share, basic and diluted				
As reported	$ (0.28)	$ (0.17)	$ (0.67)	$ (0.69)
Pro forma	(0.35)	(0.22)	(0.86)	(0.85)
Effect of pro forma adjustment	$ (0.07)	$ (0.05)	$ (0.19)	$ (0.16)

The weighted-average fair value of stock options granted during the three months ended September 30, 2004 and 2003 was $15.52 and $14.40, respectively, and for the nine months ended September 30, 2004 and 2003 was $15.89 and $5.72 per share, respectively, on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Options		ESPP	
	Three Months Ended September 30,			
	2004	2003	2004	2003
Expected option term (years)	7.2	7.2	0.5	0.5
Expected stock price volatility	0.83	0.87	0.86	0.86
Risk-free interest rate	3.52%	3.30%	1.01%	1.17%

	Nine Months Ended September 30,			
	2004	2003	2004	2003
Expected option term (years)	7.3	6.5	0.5	0.5
Expected stock price volatility	0.85	0.87	0.86	0.86
Risk-free interest rate	3.24%	3.26%	1.01%	1.17%

Because options vest over several years and the Company expects to grant options in future years, the above pro forma results of applying the provisions of FAS 123 are not necessarily indicative of the pro forma results in future years.

4. Loan Payable to Strategic Partner

In May 2003, the Company entered into a Non-Negotiable Note and Security Agreement (the Loan Agreement) with Schering AG under which the Company is eligible to borrow up to a total of $15.0 million. The Loan Agreement carries a variable, market-based interest rate, which was 8.75% at September 30, 2004 and 8.0% at December 31, 2003. The entire $15 million amount under the Loan Agreement was available and

drawn as of September 30, 2004. The entire outstanding balance of $15.0 million, plus accrued interest, was repaid to Schering AG in October 2004. Of the $15 million available under the Loan Agreement with Schering AG, $7.5 million is available to be redrawn by EPIX until May of 2007 and the remaining $7.5 million is available to be redrawn until May 2008, subject to specified conditions and covenants contained in the Loan Agreement, including a commitment to maintain cash and cash equivalents of at least $2.0 million. The Company was in compliance with such covenants at September 30, 2004 and December 31, 2003. Any outstanding balance of the Loan Agreement is repayable beginning in May 2007 and there is no penalty for prepayment. The Loan Agreement is secured by a first priority security interest in certain of the Company s intellectual property. The carrying value of the loan balance approximated fair value due to its variable interest rate.

5. Convertible Debt

In June 2004, the Company completed a sale, pursuant to Rule 144A of the Securities Act of 1933, of $100 million of 3% convertible senior notes due 2024 for net proceeds of approximately $96.4 million. Each $1,000 of senior notes is convertible into 33.5909 shares of the Company s common stock at a conversion rate of approximately $29.77 per share if (1) the price of the Company s common stock trades above 120% of the conversion price for a specified time period, (2) the trading price of the senior notes is below a certain threshold, (3) the senior notes have been called for redemption, or (4) specified corporate transactions have occurred. Each of the senior notes is also convertible into the Company s common stock in certain other circumstances. The senior notes bear an interest rate of 3%, payable semiannually on June 15 and December 15, beginning on December 15, 2004. The senior notes are unsecured and are subordinated to secured debt, including the loan payable to Schering AG.

The Company has the right to redeem the notes on or after June 15, 2009 at an initial redemption price of 100.85%, plus accrued and unpaid interest. Noteholders may require the Company to repurchase the notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other events, including change of control and termination of trading.

In connection with the issuance of the senior notes, we incurred $3.65 million of issuance costs, which primarily consisted of investment banker fees and legal and other professional fees. The costs are being amortized as interest expense using the effective interest method over the term from issuance through the first date that the holders are entitled to require repurchase of the senior notes (June 2009). Amortization of the issuance costs was $113,000 and $141,000 for the three and nine months, respectively, ended September 30, 2004.

ITEM 2. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

OVERVIEW

We develop innovative pharmaceuticals designed to improve the diagnostic quality of images produced by MRI. Since commencing operations in 1992, we have been principally engaged in research and development activities related to our product candidates, as well as seeking various regulatory clearances and patent protection. We have had no revenues from sales of our products and have incurred cumulative losses since inception through September 30, 2004 aggregating to approximately $150.2 million. Most of our revenues to date have come from license fees and product development revenues from collaboration agreements for our product candidates.

Our primary activities relate to three projects: MS-325, for which we have completed Phase III clinical trials and submitted a New Drug Application, or NDA, to the Food and Drug Administration, or FDA; our feasibility program for EP-2104R, which is in late preclinical development; and our joint MRI research program with Schering Aktiengesellschaft, or Schering AG.

MS-325 is an injectable intravascular contrast agent intended to enhance the quality of MR images and provide physicians with an improved method for diagnosing diseases affecting the vasculature. We have completed our Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MR angiography, or MRA, for the evaluation of non-coronary vascular disease and submitted our NDA for MS-325 to the FDA in December 2003. In February 2004, we were notified by the FDA that the NDA for MS-325 had been accepted for filing and had been designated for a standard review cycle. The target date for the first official FDA action in the standard review cycle is ten months from the date of submission. In October 2004, we were notified by the FDA that it had extended the action date for completion of its review of MS-325 by 90 days to January 2005. In communications with the FDA in October 2004, the FDA indicated that its principal open review questions relate to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. We have subsequently provided detailed responses to the FDA s questions. Although we remain confident in the safety and efficacy profile of MS-325, the FDA s review of the additional analyses and interpretations we have provided could adversely affect the approval, timeliness of approval or labeling of MS-325. If our NDA for MS-325 is approved by the FDA, our partner, Schering AG, will have primary responsibility for the product launch and marketing of MS-325. Late in the second quarter and early in the third quarter of 2004, we initiated further Phase II clinical studies of MS-325 for use in cardiac imaging and a Phase IIIb/IV clinical program of MS-325 for high resolution imaging of patients as a first step in the characterization of vascular wall structures and vulnerable plaque. In June 2004, Schering AG submitted MS-325 to the European Agency for the Evaluation of Medicinal Product (EMEA) for marketing approval in the European Union. In September 2004, Schering AG initiated Phase I trials in Japanese subjects in support of the Japanese development program for MS-325.

If our MS-325 NDA is approved by the FDA and if MS-325 receives marketing approval from EMEA, in each case, in a timely manner, we believe that we will have a significant opportunity related to revenues generated from sales of MS-325. Our ability to generate revenues from sales of MS-325 and other products will depend on the success of commercialization efforts by us and our collaborators and on the success and timing of clinical trials and regulatory approvals for our products. The successful commercialization of MS-325 and other products will also depend on the development, regulatory approval and commercialization of competing products and on the intellectual property claims in the field of diagnostic imaging. More broadly, the markets for our products will be subject to the effects of a number of additional factors, including developments in reimbursement policies in the U. S. and other countries and changes in the cost of and demand for diagnostic procedures for cardiovascular disease.

EP-2104R is an injectable MRI contrast agent that is specifically targeted to fibrin, the dominant protein in blood clots, or thrombi. It is designed to provide a bright MR image of blood clots anywhere in the body and may allow clinicians to identify potential problems early. Finding blood clots is of critical medical significance in the evaluation and diagnosis of patients with stroke, chest pain, heart attack, irregular

heartbeat and clots in the lungs and legs. We designed EP-2104R to bind reversibly to fibrin, the dominant protein found in clots. In May 2003, we entered into a collaboration agreement with Schering AG for the development and commercialization of EP-2104R. Under terms of the agreement, we are responsible for the execution of a clinical feasibility program for EP-2104R in humans for which Schering AG is obligated to make fixed payments to us of approximately $9.0 million over a two year period. At the end of the feasibility program, Schering AG may exercise an option to develop EP-2104R through which Schering AG will receive an exclusive, worldwide license for EP-2104R and become responsible for all further development, manufacturing, marketing and sales. We announced the initiation of human clinical studies for EP-2104R in August 2004.

We are engaged in research activities to discover other pharmaceutical product candidates. In May 2003, we entered into an agreement with Schering AG covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. Under the terms of the three-year joint research agreement, we and Schering AG are exclusively combining our existing

research programs in the field of MRI to discover novel MRI product candidates for clinical development. Under the agreement, Schering AG has agreed to fund a portion of our related personnel costs and third party research costs of up to $2.0 million per year and has made available to us a loan facility of up to $15 million, with principal repayment beginning in 2007.

We expect continued operating losses through 2005 and possibly thereafter as we incur expenses to support research and development efforts and to support commercialization of our initial product candidate, MS-325.

Our financial results have been affected significantly by the scope and speed of our clinical trial program and by our interaction with the FDA related to an appropriate clinical trial program for regulatory approval. We filed an investigational new drug, or IND, application and initiated a Phase I clinical trial for MS-325 in 1996. We completed a Phase II clinical trial in 1998 to test the safety and preliminary efficacy of MS-325-enhanced MRA, for the evaluation of non-coronary vascular disease and also completed a Phase II trial in 2001 that was designed to compare the diagnostic accuracy of five different doses of MS-325-enhanced MRA with that of X-ray angiography in the aortoiliac arteries. We completed two Phase III studies, with results announced in 2002 and 2003, to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease. In 2001 after discussions with the FDA, we expanded our initial target indication for MS-325 beyond aortoiliac occlusive disease to a broad peripheral vascular disease indication, which we expect will include the entire vasculature, except for the heart. As a result of this expansion, we added two new trials to our Phase III MRA clinical trial program; one in the renal arteries and the other in the pedal arteries. These two trials were completed and results announced in 2003. We submitted our NDA to the FDA in December 2003 and our NDA was accepted as fileable by the FDA in February 2004. In October 2004, the Company was notified by the FDA that it had extended the action date for completion of its review of MS-325 by 90 days to January 2005. We also completed Phase II feasibility trials to test MS-325 in detecting coronary artery disease, in detecting breast cancer and in diagnosing female sexual arousal dysfunction. We are co-developing MS-325 with Schering AG.

We anticipate fluctuations in our results of operations due to several factors, including: the timing of fees and milestone payments received from strategic partners; the formation of new strategic alliances between us and third parties; the timing and magnitude of expenditures in connection with research and development activities; the timing of product introductions and expense of associated launches, marketing and sales activities; and the timing and extent of product acceptance for different indications and geographical areas of the world.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. 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 the estimates under different assumptions and conditions.

Our significant accounting policies are more fully described in Note 2 of the Company s Annual Report on Form 10-K for the year ended December 31, 2003 and in Note 3 to the financial statements set forth in Item 1 above. Not all significant accounting policies, however, require management to make difficult, subjective or complex judgments or estimates. We believe that our accounting policies related to revenue recognition, research and development and employee stock compensation, as described below, require critical accounting estimates and judgments.

Revenue Recognition

We recognize revenues from non-refundable license fees and milestone payments not specifically tied to a separate earnings process ratably over the period during which we have substantial continuing obligations to perform services under the contract. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed. When the period of deferral cannot be specifically identified from the contract, we estimate the period of deferral based upon our obligations under the contract. We continually review these estimates and, if any of these estimates change, an adjustment is recorded in the period in which they become reasonably estimable. These adjustments could have a material effect on our results of operations. In March 2004, we increased the estimated time period over which we will provide services under our agreement with Mallinckrodt, Inc., a subsidiary of Tyco/Mallinckrodt, from 99 months to 101 months because the FDA notified the Company that its NDA for MS-325 had been accepted for filing under a standard review cycle, instead of an accelerated review cycle. In September 2004, we again increased our estimated time period for providing services under the agreement with Tyco/Mallinckrodt to 103 months because of the FDA s notice to extend its review by an additional 90 days. The impact of the increase of these estimates resulted in a reduction in revenue of $76,000 for the first nine months of 2004. We will continue to review these estimates and make appropriate adjustments as information becomes available.

Under the MS-325 program, we recognize product development revenue at the time we perform research and development

activities for which Schering AG and other collaborators are obligated to reimburse us. Product development revenues from Schering AG are recorded net of the Company s portion of Schering AG s actual or most recent estimate of their MS-325 research and development costs.

We recognize product development revenue from Schering AG for the EP-2104R feasibility program as revenue proportionate to our actual cost incurred relative to our estimate of the total cost of the feasibility program. Total estimated costs of the feasibility program are based on an evaluation of the portion of the program completed, costs incurred to date, planned program activities, anticipated program timelines and the expected future costs of the program. Adjustments to revenue are recorded if estimated costs to complete change materially from previous periods. To the extent that our estimated costs change materially, our revenues recorded under this activity could materially be affected and such change could have a material adverse effect on our operations in future periods. In June 2004, management increased its EP-2104R estimate to complete the feasibility program, resulting in a reduction of revenue of $131,000 in the second quarter of 2004. In September, management again increased its EP-2104R estimate to complete the feasibility program resulting in a reduction of revenue of $219,000 in the third quarter of 2004.

Revenue under our research collaboration with Schering AG in MRI is recognized as services are provided for which Schering AG is obligated to reimburse us.

Royalty revenues are recognized based on actual revenues as reported to us by Bracco Imaging S.p.A, or Bracco. When actual results are not available, we estimate royalty revenues based on Bracco s estimates, historical revenues and trends. We continually review these estimates and record adjustments to the estimates when we receive actual information from Bracco. These adjustments have not been significant to date, but could have a material effect on our future results of operations.

Research and Development

Research and development costs, including those associated with technology, licenses and patents, are expensed as incurred. Research and development costs include employee salaries and related costs, third party service costs, the costs of preclinical and clinical trial supplies and consulting expenses.

In order to conduct research and development activities and compile regulatory submissions, we enter into contracts with vendors who render services over an extended period of time, generally one to three years. Typically, we enter into three types of vendor contracts; time based, patient based or a combination thereof. Under a time based contract, using critical factors contained within the contract, usually the stated duration of the contract and the timing of services provided, we record the contractual expense for each service provided under the contract ratably over the period during which we estimate the service will be performed. Under a patient based contract, we first determine an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. We then record expense based upon the total number of patients enrolled during the period. On a quarterly basis, we review both the timetable of services to be rendered and the timing of services actually rendered. Based upon this review, revisions may be made to the forecasted timetable or to the extent of services performed, or both, in order to reflect our most current estimate of the contract. Adjustments are recorded in the period in which the revisions are estimable. These adjustments could have a material effect on our results of operations.

Employee Stock Compensation

We have elected to follow Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees,* or APB 25, and related interpretations in accounting for our employee stock options under the intrinsic value method, rather than the alternative fair value accounting provided for under Statement of Financial Accounting Standards (SFAS) No. 123, *Accounting for Stock-Based Compensation,* as amended by SFAS No. 148. Under APB 25, because the exercise price is equal to the market price of the underlying stock on the date of the grant, no compensation expense is recognized.

If we are unable to or decide not to continue to account for stock options under APB 25, our financial results could be materially adversely affected to the extent of the additional compensation expense that we would have to recognize, which could change significantly from period to period based on several factors, including the number of stock options granted and fluctuations in our stock price and/or interest rates. See Note 3 to the Notes to Condensed Financial Statements (unaudited).

RESULTS OF OPERATIONS

Comparison of Three Months Ended September 30, 2004 and 2003

Revenues

Our revenues arise principally from our collaboration agreements with Schering AG for MS-325, EP-2104R and MRI discovery research; from license fee revenues relating to our agreements with Schering AG, Tyco/Mallinckrodt and Bracco; and from royalties related to our agreement with Bracco. Revenues for the three months ended September, 30 2004 and 2003 were $3.2 million and $3.9 million, respectively. Revenues for the three-month period ended September 30, 2004 consisted of $2.3 million of product development revenue from Schering AG, $806,000 of royalty and license fee revenue related to the Bracco agreement, and $158,000 of license fee revenue related to the Schering AG and Tyco/Mallinckrodt strategic collaboration agreements for the development and marketing of MS-325. The decrease in revenues of $827,000 for the three months ended September 30, 2004 compared to the same period last year was due to the combined impact of our lower development costs combined with Schering AG s higher development costs on MS-325 product development revenues, lower EP-2104R product development revenues and lower license fee revenue. The lower license fees related to the Schering AG and Tyco/Mallinckrodt agreements resulted from the changes in our estimate of the time period for obtaining approvals of MS-325 in the U.S. and Japan.

Research and Development Expenses

Our research and development expenses arise from our development activities for MS-325 and EP-2104R and from our discovery research programs. Research and development expenses for the three months ended September 30, 2004 were $6.5 million as compared to $5.6 million for the same period in 2003. The increase of $890,000 was primarily attributable to higher spending for EP-2104R and other research programs, partly offset by lower costs related to the completion of the Phase III clinical trial program for MS-325.

Both the time-frame and costs involved in developing MS-325 and EP-2104R, gaining regulatory approval and commercializing the products may vary greatly for several reasons, including the following:

We conduct our clinical trials in accordance with specific protocols, which we have filed with the FDA or other relevant authorities. If the FDA requires us to perform additional studies or to increase patient numbers, we could incur significant additional costs and additional time to complete our clinical trials. This could result in a delay in our ability to make regulatory submissions and a delay in the commercialization, increased competition or slower sales growth of our product.

We rely on third party clinical trial centers to find suitable patients for our clinical trial program. If these third parties do not find suitable patients in the timeframe for which we have planned, we will not be able to complete our clinical trials according to our expected schedule. Such a delay could result in an increase in development costs for MS-325 or EP-2104R, a delay in making regulatory submissions and a delay in the

commercialization, increased competition or slower sales growth of our product.

We rely on third party contract research organizations for a variety of activities in our development program, including conducting blinded reading activities, lab testing and analysis of clinical samples, data collection, cleanup and analysis and drafting study reports and regulatory submissions. A delay in these activities could result in an increase in costs, a delay in making regulatory submissions and a delay in the commercialization, increased competition or slower sales growth of our product.

The length of time that the FDA or other regulatory authorities take to review our regulatory submissions and the length of time it takes us to respond to the FDA or other regulatory authorities questions can also vary widely. Recently we were notified by the FDA that the agency had extended the action date for the completion of their review of our NDA for MS-325 by 90 days. This extension and any other delays in that process could result in an increase in costs and a delay in the commercialization or slower sales growth of our product.

Our partner, Schering AG, is responsible for the commercial launch and marketing of MS-325. If Schering AG does not launch the product in a timely manner or market the product effectively, we may incur a delay in receiving revenues after the launch of MS-325 or may not receive enough revenue to enable us to become profitable.

Our current plans for developing and commercializing MS-325 and EP-2104R reflect our best estimate of the time involved in the development program based on factors currently known to us. The third parties described above have the ability to greatly impact this timetable and we may not have control over or be able to respond within our current plan to changes they cause. Any such delays could result in a significant increase in costs to develop MS-325 or EP-2104R as well as a delay in product launch, which could enable competition to intensify.

Under our EP-2104R agreement, Schering AG has made and will continue to make fixed payments to us totaling approximately $9.0 million over a two year period intended to cover our costs of the feasibility program. The amount of expenditure necessary to execute the feasibility program, currently estimated to be $11.8 million, is subject to numerous uncertainties, which may adversely affect our cash outlay, net of Schering s reimbursement to us. In addition, we cannot predict whether Schering AG will exercise its option to develop EP-2104R or, if Schering AG does exercise its option, whether we will exercise our option to bear a portion of the development costs in return for an increase in our royalty rate. If Schering AG does not exercise its option, then we would have to bear the additional cost of a clinical program to develop EP-2104R, which may adversely affect our liquidity and capital resources. Consequently, at this time, we cannot predict the amount of additional research and development costs that we will incur with regard to the development and commercialization of EP-2104R.

The cost to execute our joint research plan with Schering AG is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources.

The duration and cost of bringing a product to market may vary significantly over the life of a project as a result of various matters arising during and after clinical trials, including among others, the following:

Time needed for regulatory approval;

Number of patients, costs per patient and the rate of patient recruitment in the clinical trial program;

Complexity and cost of project management, data collection and data management services provided by outside vendors; and

Unanticipated adverse safety and efficacy results from the pre-clinical or clinical trials.

We test our potential product candidates in numerous pre-clinical studies to identify disease indications for which they may be product candidates. We may conduct multiple clinical trials to cover a variety of indications for each product candidate. As we obtain results from trials, we may elect to discontinue clinical trials for certain product candidates or for certain indications in order to focus on more promising product candidates or indications. In addition, the FDA may require us to modify our future clinical trial plans or to conduct additional clinical trials in ways that we cannot currently anticipate. Such modifications or additional clinical trials could result in an increase in costs of our product development and a delay in the commercialization or slower sales growth of our product.

General and Administrative Expenses

General and administrative expenses, which consist primarily of salaries, benefits, outside professional services and related costs associated with our executive, finance and accounting, business development, marketing, human resources, legal and corporate communications activities, were $2.9 million for the three months ended September 30, 2004 as compared to $1.7 million for the three months ended September 30, 2003. The increase of $1.2 million was primarily attributable to higher spending both by EPIX and by Schering AG for MS-325 marketing activities, higher business development expenses, higher legal expenses related to patent and intellectual property filings, compliance costs due to the internal control review required by the Sarbanes-Oxley Act and higher liability insurance premiums. General and administrative expenses also include royalties payable to Massachusetts General Hospital, or MGH, based on sales by Bracco of MultiHance®. Royalty expenses totaled $31,000 and $32,000 for the three months ended September 30, 2004 and 2003, respectively.

Interest Income and Interest Expense

Interest income for the three months ended September 30, 2004 was $688,000 as compared to $182,000 for the three months ended September 30, 2003. The increase of approximately $506,000 was primarily due to higher average levels of invested cash, cash equivalents and marketable securities during the three months ended September 30, 2004 related to net proceeds from the issuance of $100 million convertible senior notes in June 2004. We also classify net realized gains and losses as interest income. During the three months ended September 30, 2004 and 2003, there were no realized gains or losses on marketable securities. Interest expense for the three months ended September 30, 2004 and 2003 was $935,000 and $165,000, respectively. The increase in interest expense of $770,000 during the three months ended September 30, 2004 also resulted from the issuance of convertible senior notes in June 2004 and to the draw down of the entire $15.0 million loan facility made available to us by Schering AG as part of the joint MRI research collaboration entered into in May 2003, partly offset by the reduction in the outstanding balance of interest-bearing prepaid royalties from Bracco. The entire principal balance of the Schering loan facility, which was $15.0 million as of September 30, 2004, plus accrued interest were repaid in October 2004.

Provision for Income Taxes

The provision for income taxes, which represents Italian income taxes related to the Bracco agreement, was $17,000 for the three months ended September 30, 2004 as compared to $3,000 for the three months ended September 30, 2003. Beginning in July 2003, and until the earlier of FDA approval of Bracco s principal product, MultiHance®, or December 31, 2005, a portion of Bracco royalty revenue earned that was previously paid to us in cash is primarily being offset against the prepaid FDA approval license fee. As a result, there will not be a requirement to withhold foreign income tax expense to the same level as was required prior to July 2003 until full royalty payments are reinstated upon FDA approval of MultiHance®, or until the end of the royalty obligation period on December 31, 2005.

Comparison of Nine Months Ended September 30, 2004 and 2003

Revenues

Revenues for the nine months ended September 30, 2004 and 2003 were $10.1 million and $11.2 million, respectively. Revenues for the nine-month period ended September 30, 2004 consisted of $6.9 million of product development revenue from Schering AG, $2.7 million of royalty and license fee revenue related to the Bracco agreement and $506,000 of license fee revenue related to the Schering AG and Tyco /Mallinckrodt strategic collaboration agreements for the development and marketing of MS-325. The decrease in revenues of $1.1 million for the nine months ended September 30, 2004 compared to the same period last year related to the combined impact of our lower development costs incurred by EPIX combined with Schering AG s higher development expense on MS-325 product development revenues and to lower license fee revenue, partly offset by higher product development revenues from EP-2104R and from our Schering AG MRI research collaboration and higher royalties from Bracco. The decrease in license fee revenues was directly attributable to the changes in our estimate of the time period for obtaining approvals for MS-325 in the U.S. and Japan.

Research and Development Expenses

Research and development expenses for the nine months ended September 30, 2004 were $17.1 million as compared to $18.9 million for the same period in 2003. The decrease of $1.8 million was primarily attributable to decreased costs related to the completion of the Phase III clinical trial program for MS-325, partly offset by higher spending for EP-2104R and other research programs.

General and Administrative Expenses

General and administrative expenses were $8.2 million for the nine months ended September 30, 2004 as compared to $4.8 million for the nine months ended September 30, 2003. The increase of $3.4 million was primarily attributable to higher spending both by EPIX and by Schering AG for MS-325 marketing, higher business development, and higher legal expenses related to patent and intellectual property filings, compliance costs due to the internal control review required by the Sarbanes-Oxley Act and to higher liability insurance premiums. General and administrative expenses also include royalties payable to Massachusetts General Hospital, or MGH, based on sales by Bracco of MultiHance®. Royalty expenses totaled $108,000 and 78,000 for the nine months ended September 30, 2004 and 2003.

Interest Income and Interest Expense

Interest income for the nine months ended September 30, 2004 was $1.2 million as compared to $411,000 for the nine months ended September 30, 2003. The increase of approximately $788,000 was primarily due to higher average levels of invested cash, cash equivalents and marketable securities during the nine months ended September 30, 2004 related to net proceeds from the issuance of $100 million convertible senior notes in June 2004. We also classify net realized gains and losses as interest income. During the nine months ended September 30, 2004 and 2003, there were no realized gains or losses on marketable securities. Interest expense for the nine months ended September 30, 2004 and 2003 was $1.2 million and $267,000, respectively. The increase in interest expense of $967,000 during the nine months ended September 30, 2004 resulted from the issuance of convertible senior notes in June 2004 and the drawdown of the entire $15.0 million loan facility made available to us by Schering AG as part of the joint MRI research collaboration entered into in May 2003, partly offset by the reduction in the outstanding balance of interest-bearing prepaid royalties from Bracco. The entire principal balance of the loan facility, which was $15.0 million as of September 30, 2004, plus accrued interest were repaid in October 2004.

Provision for Income Taxes

The provision for income taxes was $46,000 for the nine months ended September 30, 2004 as compared to $69,000 for the nine months ended September 30, 2003. Beginning in July 2003, and until the earlier of FDA approval of Bracco s principal product, MultiHance®, or December 31, 2005, the portion of Bracco royalty revenue earned that was previously paid to us in cash is primarily

being offset against the prepaid FDA approval license fee. As a result, there will not be a requirement to withhold foreign income tax expense to the same level as was required prior to July 2003 until full royalty payments are reinstated upon FDA approval of MultiHance®, or until the end of the royalty obligation period on December 31, 2005.

LIQUIDITY AND CAPITAL RESOURCES

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities of $169.0 million at September 30, 2004 as compared to $80.0 million at December 31, 2003. The increase in cash, cash equivalents and available-for-sale marketable securities was primarily attributable to the net proceeds of approximately $96.4 million resulting from the issuance of convertible senior notes in June 2004.

We used approximately $16.9 million of net cash to fund operations for the nine months ended September 30, 2004, which compares to $15.2 million for the same period last year. A net loss of $15.2 million, combined with a reduction in deferred revenue of $2.8 million and an increase in accounts receivable of $797,000, partly offset by increases in accrued expenses of $1.2 million and contract advances of $794,000 accounted for the net cash used in operations during the nine months ended September 30, 2004. The reduction in deferred revenue resulted from royalty revenues from sales by Bracco of MultiHance®, which were offset against advanced payments. The increase in accounts receivable resulted from an increase in the billings to Schering AG related to MS-325 pre-launch activities and some product development activities. The increase in accrued expenses is due to higher accrued clinical costs associated with recently initiated trials and higher accrued interest related to the convertible senior notes, partly offset by the issuance of common stock to Dr. Martin Prince in early January 2004 to offset a yearend 2003 accrual in connection with the Intellectual Property Agreement entered into in November of 2003. The increase in contract advances primarily relates to Schering AG s funding of both EPIX s and Schering AG s MS-325 pre-launch activities. Also during the first nine months of 2004, we received a $2.5 million milestone payment from Schering AG related to the acceptance of the filing of the NDA with the FDA for MS-325. Immediately following this receipt, we paid Tyco/Mallinckrodt $2.5 million in recognition of the same milestone. These payments were offset in the Company s Statements of Operations, resulting in no impact on revenues, expenses or net loss. For the nine months ended September 30, 2003, net cash used for operating activities of $15.2 million was primarily attributable to our net loss of $12.4 million, combined with a reduction in deferred revenue of $2.4 million resulting from royalty revenues from sales by Bracco of MultiHance ®, contract advances of $381,000 due to the annual adjustment of contract advances under the MS-325 collaboration agreement and to lower funding of research and development in subsequent quarters pursuant to the same agreement with Schering AG.

Our investing activities resulted in net cash used of $57.7 million for the nine months ended September 30, 2004 as compared to net cash provided of $5.1 million for the same period last year. During the nine months ended September 30, 2004, we purchased available-for-sale marketable securities of $79.4 million, which was primarily funded from the convertible debt issuance and partly offset by the cash generated from the redemption or sale of $23.7 million of available-for-sale marketable securities. During the same period in 2003, we redeemed approximately $19.3 million of available-for-sale marketable securities, which was partly offset by the purchase of available-for-sale marketable securities of $13.9 million. Other investing activities included capital expenditures of $2.0 million for the nine months ended September 30, 2004 as compared to $308,000 for the same period last year. The increase in our capital expenditures was primarily attributable to leasehold improvements and to the acquisition of equipment, including lab equipment, computer equipment and software related to the refurbishment of our laboratory space.

Cash provided by financing activities was $108.2 million for the nine months ended September 30, 2004. The primary sources of financing during the nine months ended September 30, 2004 came from net proceeds of $96.4 million attributable to the issuance of convertible senior notes, the cumulative drawdown of the loan facility of $37.5 million with Schering, of which $15 million was outstanding at September 30, 2004, and all proceeds of stock option exercises of $4.4 million. Also during this period, we repaid $30.0 million on a cumulative basis against the loan facility with Schering AG, which was outstanding at September 30, 2004. During the nine months ended September 30, 2003, we received net proceeds of $65.5 million from the sale and issuance of 4.645 million shares of common stock, pursuant to our effective shelf

registration statement, previously filed with the Securities and Exchange Commission, and another $2.2 million from stock option exercises. In addition, we borrowed $7.5 million during the nine months ended September 30, 2003 against our loan facility with Schering AG.

We currently receive quarterly cash payments from Schering AG for their share of development costs of MS-325 and EP-2104R and for their share of research costs in our joint MRI research collaboration. We also receive monthly interest income on our cash, cash equivalents and available-for-sale marketable securities. Prior to July 2003, we received quarterly royalty payments from Bracco for a portion of the royalty revenue actually earned from the sales of MultiHance®. Beginning in July 2003, and until the earlier of FDA approval of MultiHance®, or December 31, 2005, a portion of royalty revenue earned that was previously paid to us in cash is primarily being offset against the prepaid FDA approval license fee. If MultiHance® is approved in the U.S. by the FDA prior to December 31, 2005, Bracco will be obligated to pay us the amount of royalties previously offset against prepaid FDA approval license fee and resume quarterly royalty payments. Other potential cash inflows include: a milestone payment of $1.3 million from Schering AG, which is

dependent on the FDA s approval of MS-325, and up to $22.0 million in additional milestone payments from Schering AG as well as our share of the profits earned on sales of MS-325 worldwide. Additional future cash flows from our EP-2104R collaboration with Schering AG depend on the successful completion of the EP-2104R feasibility program, on Schering AG s decision to exercise its development option and on the success of further development, regulatory and commercialization work by Schering AG. Additional future cash flows from our MRI research collaboration with Schering AG depend on the success of the research program and the success of further development, regulatory and commercialization activities with respect to any products generated. We may also receive royalties on sales of Schering AG s Primovist product, if it is approved for sale by the FDA or international regulatory authorities pursuant to a license agreement with Schering AG. In October 2004, Schering AG announced that Primovist had been approved in 25 countries of the European Union and that Schering AG expects to begin marketing the product in those countries in the first quarter of 2005.

Known outflows, in addition to our ongoing research and development and general and administrative expenses, include: the semi-annual royalties that we owe to MGH on sales by Bracco of MultiHance®, a milestone payment of $2.5 million owed to Tyco/Mallinckrodt, which is dependent on the FDA s approval of MS-325, a share of profits due Tyco/Mallinckrodt on sales of MS-325 worldwide, a royalty to Daiichi on sales of MS-325 in Japan and a royalty due MGH on our share of the profits of MS-325 worldwide. We will also be required to repay Bracco any unearned prepaid royalties, equaling $1.0 million at September 30, 2004, upon termination of our license agreement with Bracco, plus an additional $1.4 million if MultiHance® does not receive FDA approval in the U.S by December 2005. In November 2002, Bracco announced that it had received an approvable letter from the FDA for MultiHance®.

Based on our current plans, expense rates, targeted timelines and our view regarding acceptance of MS-325 in the marketplace, we estimate that cash, cash equivalents and marketable securities on hand as of September 30, 2004 will be sufficient to fund our operations until we turn cash flow positive. If we consider other opportunities or change our planned activities, we may require additional funding. As of September 30, 2004, we had outstanding the entire balance of our $15.0 million loan facility available from Schering AG as part of our MRI research collaboration. We repaid the entire $15.0 million loan, plus accrued interest, in October 2004, but expect to redraw the $15.0 million loan as needed. We expect to be able to redraw the $15.0 million from the Schering AG loan facility, of which $7.5 million can be redrawn until May 2007 and the remaining $7.5 million until May 2008, but could be unable to draw under the terms of the loan if we fail to meet certain covenants or conditions precedent in the loan. As of September 30, 2004, we were in compliance with the covenants of the loan facility. If holders of our convertible senior notes require redemption of the notes, we may be required to repay $100 million in June 2011. Our future liquidity and capital requirements will depend on numerous factors, including the following: the progress and scope of clinical trials; the timing and costs of filing future regulatory submissions; the timing and costs required to receive both U.S. and foreign governmental approvals; the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; the extent to which our products, if any, gain market acceptance; the timing and costs of product introductions; the extent of our ongoing and new research and development programs; the costs of training physicians to become proficient with the use of our potential products; and, if necessary, once regulatory approvals are received, the costs of developing marketing and distribution capabilities.

Because of anticipated spending to support new research programs as well as the continued development of MS-325 and EP-2104R, we do not expect positive cash flow from operating activities for any future quarterly or annual period prior to commercialization of MS-325. Our ability to reach positive cash flow subsequent to the commercialization of MS-325 will depend on its market acceptance and successful launch by our partner Schering AG as well as the ability of our partner Tyco/Mallinckrodt to manufacture sufficient quantities of MS-325 to support Schering AG s sales and marketing activities. We anticipate continued investments in fixed assets, including equipment and facilities expansion to support new and continuing research and development programs.

We have entered into the following material contractual obligations since the presentation of our table of Contractual Obligations as set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2003:

the drawdown of an additional $7.5 million on our Non-Negotiable Note and Security Agreement with Schering AG, in September 2004, which amount was subsequently repaid in full in October 2004; and

the issuance in June 2004 of $100 million in principal amount of our 3.00% convertible senior notes due 2024.

We have incurred tax losses to date and therefore have not paid significant federal or state income taxes since inception. As of December 31, 2003, we had net operating loss carryforwards of approximately $127.9 million available to offset future taxable income. These amounts expire at various times through 2023. As a result of ownership changes resulting from sales of equity securities, our ability to use the net operating loss carryforwards is subject to limitations as defined in Sections 382 and 383 of the Internal Revenue Code of 1986, or the Code, as amended. We currently estimate that the annual limitation on our use of net operating losses through May 31, 1996 to be approximately $900,000. Pursuant to Sections 382 and 383 of the Code, the change in ownership resulting from public equity offerings in 1997 and any other future ownership changes may further limit utilization of losses and credits in any one year. We also are eligible for research and development tax credits that can be carried forward to offset federal taxable income. The annual limitation and the timing of

attaining profitability may result in the expiration of net operating loss and tax credit carryforwards before utilization.

Certain Factors That May Affect Future Results of Operations

This report contains certain forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. Such statements are based on management s current expectations and are subject to a number of factors and uncertainties, which could cause actual results to differ materially from those described in the forward-looking statements. We caution investors that there can be no assurance that actual results or business conditions will not differ materially from those projected or suggested in such forward-looking statements as a result of various factors, including, but not limited to, the following: the uncertainties associated with pre-clinical studies and clinical trials; the early stage of our product development and lack of product revenues; our history of operating losses and accumulated deficit; our lack of commercial manufacturing experience and commercial sales, distribution and marketing capabilities; reliance on suppliers of key materials necessary for production of our products and technologies; the potential development by competitors of competing products and technologies; our dependence on existing and potential collaborative partners, and the lack of assurance that we will receive any funding under such relationships to develop and maintain strategic alliances; the lack of assurance regarding patent and other protection for our proprietary technology; governmental regulation of our activities, facilities, products and personnel; our dependence on key personnel; uncertainties as to the extent of reimbursement for the costs of our potential products and related treatments by government and private health insurers and other organizations; the potential adverse impact of government-directed health care reform; the risk of product liability claims; and economic conditions, both generally and those specifically related to the biotechnology industry. As a result, our future development efforts involve a high degree of risk. For further information, refer to the more specific risks and uncertainties discussed below or throughout the Company s Annual Report on Form 10-K for the year ended December 31, 2003.

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the following risk factors, and other information in our periodic reports filed with the SEC. If any of the following risks actually occur, our business, financial condition or results of operations could be materially and adversely affected.

We have never generated revenues from commercial sales of our products and, if MS-325 does not receive approval from the Food and Drug Administration (FDA), we will have no products to market in the foreseeable future.

We currently have no products for sale and we cannot guarantee that we will ever have marketable products. MS-325 and EP2104R are currently our only product candidates that have undergone human clinical trials and we cannot be certain that any of our other development projects will yield a product candidate suitable for substantial human clinical testing. As a result, our initial revenues and profits from commercial sales of our products, if any, will be derived from sales of MS-325. In October 2004, we were notified by the FDA that it had extended the action date for completion of its review of the MS-325 NDA by 90 days, to January 2005. In communications with the FDA in October 2004, the FDA indicated that its principal open review questions relate to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. We have subsequently provided detailed responses to the FDA s questions. Although we remain confident in the safety and efficacy profile of MS-325, the FDA s review of the additional analyses and interpretations we have provided could adversely affect the approval, timeliness of approval or labeling of MS-325. If MS-325 fails to achieve regulatory approval and market acceptance, and if we do not succeed in bringing any of our other product candidates to human clinical trials and achieve regulatory approval and market acceptance for them, our business will fail, and as a result, you may lose all or part of your investment.

To date, we have received revenues from payments made under licensing, royalty arrangements, and product development and marketing agreements with strategic collaborators. In particular, our revenue for the nine months ended September 30, 2004 was $10.1 million and consisted of $6.9 million from the product development portion of our collaboration agreements with Schering AG for MS-325, EP-2104R and MRI research, $2.7 million from a patent licensing and royalty agreement with Bracco and $506,000 of license fee revenue related to the strategic collaboration agreements for the development, manufacturing and marketing of MS-325 with Schering AG and Tyco/Mallinckrodt. In addition to these sources of revenue, we have financed our operations to date through public stock offerings, private sales of equity securities, debt financing and equipment lease financings.

Although we are currently in compliance with the terms of our collaboration agreements, the revenues derived from them are subject to fluctuation in timing and amount. We may not receive anticipated revenue under our existing collaboration or licensing agreements and, additionally, these agreements may be terminated upon certain circumstances. Therefore, to achieve profitable and sustainable operations, we, alone or with others, must successfully develop, obtain regulatory approval for, introduce, market and sell products. We may not receive revenue from the sale of any of our product candidates for the next several years because we may not:

successfully complete our product development efforts;

obtain required regulatory approvals in a timely manner, if at all;

manufacture our product candidates at an acceptable cost and with acceptable quality; or

successfully market any approved products.

As a result, we may never generate revenues from sales of our product candidates and our failure to generate positive cash flow could cause our business to fail.

We anticipate future losses and may never become profitable.

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of September 30, 2004 were approximately $150.2 million. These losses have primarily resulted from expenses associated with our research and development activities, including pre-clinical and clinical trials, and general and administrative expenses. We anticipate that our research and development expenses will remain significant in the future and we expect to incur losses over at least the next two years as we continue our research and development efforts, pre-clinical testing and clinical trials and as we implement manufacturing, marketing and sales programs. As a result, we cannot predict when we will become profitable, if at all, and if we do, we may not remain profitable for any substantial period of time. If we fail to achieve profitability within the timeframe expected by investors, the market price of our common stock may decline and consequently our business may not be sustainable.

If the market does not accept our technology and products, we may not generate sufficient revenues to achieve or maintain profitability.

The commercial success of MS-325 and our other product candidates, when and if approved for marketing by the FDA and corresponding foreign agencies, depends on their acceptance by the medical community and third party payors as clinically useful, cost-effective and safe. While contrast agents are currently used in an estimated 25% to 35% of all MRI exams, there are no MRI agents approved by the FDA for vascular imaging. Furthermore, clinical use of MRA has been limited and use of MRA for some vascular disease imaging has occurred mainly in research and academic centers. Market acceptance, and thus sales of our products, will depend on several factors, including:

safety;

cost-effectiveness relative to alternative vascular imaging methods;

availability of third party reimbursement;

ease of administration;

clinical efficacy; and

availability of competitive products.

Market acceptance will also depend on our ability and that of our strategic partners to educate the medical community and third party payors about the benefits of diagnostic imaging with MRA enhanced with MS-325 compared to imaging with other technologies. MS-325 represents a new approach to imaging the non-coronary vascular system, and market acceptance both of MRA as an appropriate imaging technique for the non-coronary vascular system, and of MS-325, is critical to our success. If MS-325 or any of our other product candidates, when and if commercialized, do not achieve market acceptance, we may not generate sufficient revenues to achieve or maintain profitability.

We may need to raise additional funds necessary to fund our operations, and if we do not do so, we may not be able to implement our business plan.

Since inception, we have funded our operations primarily through our public offerings of common stock, private sales of equity securities, debt financing, equipment lease financings and product development revenue, royalty and license payments from our strategic partners. Although we believe that we have adequate funding for the foreseeable future, we may need to raise substantial additional funds for research, development and other expenses, through equity or debt financings, strategic alliances or otherwise. Our future liquidity and

capital requirements will depend upon numerous factors, including the following:

- the progress and scope of clinical trials;
- the timing and costs of filing future regulatory submissions;
- the timing and costs required to receive both U.S. and foreign governmental approvals;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the extent to which our products gain market acceptance;
- the timing and costs of product introductions;
- the extent of our ongoing and any new research and development programs;
- the costs of training physicians to become proficient with the use of our products; and
- the costs of developing marketing and distribution capabilities.

Based on our current plans, expense rates, targeted timelines and our view regarding acceptance of MS-325 in the marketplace, we estimate that cash, cash equivalents and marketable securities on hand as of September 30, 2004 will be sufficient to fund our operations until we turn cash flow positive. If we consider other opportunities or change our planned activities, we may require additional funding. As of September 30, 2004, we had outstanding the entire $15.0 million loan facility available from Schering AG as part of our MRI research collaboration. We repaid the $15.0 million loan, plus accrued interest, in October 2004. We expect to redraw the $15.0 million loan as needed, but could be unable to draw under the terms of the loan if we fail to meet certain covenants or conditions precedent in the loan.

We have a limited manufacturing capability and we intend to rely on outsourced manufacturing to produce MS-325.

We do not have, nor do we currently have plans to develop, full-scale manufacturing capability for MS-325. While we have manufactured small amounts of MS-325 for research and development efforts, we rely on, and we intend to continue to rely on, Tyco/Mallinckrodt as the primary manufacturer of MS-325 for any future human clinical trials and commercial use. In the event that Tyco/Mallinckrodt fails to fulfill its manufacturing responsibilities satisfactorily, Schering AG has the right to purchase MS-325 from a third party or to manufacture the compound itself. However, either course of action could materially delay the manufacture and development of MS-325. Schering AG may not be able to find an alternative manufacturer. In addition, Schering AG may not be able to manufacture MS-325 itself in a timely manner. If we experience a delay in manufacturing, it could result in a delay in the approval or commercialization of MS-325 and have a material adverse effect on our business, financial condition and results of operations.

If MRI manufacturers are not able to enhance their hardware and software sufficiently, we will not be able to complete development of our contrast agent for the evaluation of cardiac indications.

Although MRI hardware and software is sufficient for the evaluation of non-coronary vascular disease, which is our primary target indication, we believe that the technology is not as advanced for cardiac applications, which will be our next clinical development target. Our initial NDA filing for MS-325 is related to non-coronary vascular disease. Imaging sequences on scanners currently allow for the use of MS-325-enhanced MRA for diagnosing non-coronary vascular disease, our lead indication. Based on feasibility studies we completed in 2001, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, was not developed to the point where there was clear visualization of the cardiac region, due to the effects of motion from breathing and from the beating of the heart. We recently initiated feasibility studies for cardiac indications using available software and hardware that can be adapted for coronary and cardiac perfusion data acquisition. We have entered into research collaborations with GE Healthcare, Siemens Medical Systems and Philips Medical Systems that include development and optimization of cardiac imaging sequences with contrast agents like MS-325. We have also collaborated with a number of leading academic institutions to help optimize cardiac imaging with MS-325. While significant progress has been made in developing these clinical applications for cardiac imaging, we do not know when, or if, these techniques will enable MS-325 to provide clinically relevant images in cardiac indications. If MRI device manufacturers are not able to enhance their scanners to perform clinically useful cardiac imaging, we will not be able to complete our development activities of MS-325 for that application, thereby reducing the potential market for a product in this area.

Our competitors may have greater financial resources, superior products or product candidates, manufacturing capabilities and/or marketing expertise, and we may not be able to compete with them successfully.

Medical technology is subject to intense competition and rapid technological change. We have many competitors, including pharmaceutical, biotechnology and chemical companies, a number of which, including our strategic partners, are actively developing and marketing products that could compete with our product candidates. Specifically, although there are no MRI contrast agents that are FDA-approved for vascular imaging, there are a number of general use MRI agents approved for other clinical applications in the U.S. and certain foreign markets that are likely to compete with MS-325, if MS-325 is approved for MRA. Collectively, these general use agents are referred to as extracellular agents, and include: Magnevist® and Gadovist® by Schering AG, Dotarem® by Guerbet, S.A., Omniscan® by Amersham Health, ProHance® and MultiHance® by Bracco and OptiMark® by Tyco/Mallinckrodt. Extracellular agents are broadly accepted in the market as general use MRI agents. None of these agents is currently approved by the FDA for MRA, but their use in applications outside of the primary indication described in the product labeling is increasing and could present significant adoption hurdles for MS-325 if such uses become entrenched in the marketplace. Additionally, we believe that some of these general use agents are in clinical trials for an MRA indication. However, these general use agents are not specifically designed for vascular imaging, and because they leak out of the blood vessels into the extracellular space, they do not provide the extended imaging window associated with MS-325. In addition, we are aware of five agents that are under clinical development for use with MRA: Schering AG s Gadomer-17 and SHU555C, Guerbet s Vistarem®, Bracco s B-22956/1 and Advanced Magnetics Code 7228. Public information on the status of clinical development and performance characteristics for these agents is limited. However, many of these competitors have substantially greater capital and other resources than we do and may represent significant competition for us. These companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. In addition, these companies may be more successful than we are in developing, manufacturing and marketing products.

Moreover, there are several well-established medical imaging methods that currently compete and will continue to compete with MRI, including Digital Subtraction Angiography, or DSA, which is an improved form of X-ray angiography, computed tomography angiography, or CTA, nuclear medicine and ultrasound, and there are companies that are actively developing the capabilities of these competing methods to enhance their effectiveness in cardiovascular system imaging. DSA is currently considered the clinical gold standard for cardiovascular angiography, but all methods offer advantages and disadvantages, which are described in the following table:

	Advantages	Disadvantages
MRI	Three-dimensional images Minimally-invasive Favorable safety profile High quality images	Requires high level of training Inadvisable for patients with cardiac pacemakers Less widely available
CT Angiography	Rapid and easy data acquisition	Radiation Varying levels of toxicity Calcium and bone artifacts Time consuming post-processing
DSA (X-ray angiography)	Significant clinical experience Opportunity to treat in same procedure Highest resolution	Invasive Radiation Varying levels of toxicity Significant safety risks Two-dimensional images Expensive Patient recuperation time

Ultrasound	Low cost	Operator dependent
	Fast	Lack of anatomic detail
	Widely available	Bone precludes use in many vascular beds
	Non-invasive	Inability to visualize small vessels

We cannot guarantee that we will be able to compete successfully in the future, or that developments by others will not render MS-325 or our future product candidates obsolete or non-competitive, or that our collaborators or customers will not choose to use

competing technologies or products. Any inability to compete successfully on our part will have a materially adverse impact on our operating results.

We currently depend on our strategic collaborators for support in product development and the regulatory approval process, and, in the future, will depend on them for product marketing support as well. These efforts may suffer if we experience problems with our collaborators.

We depend on strategic collaborators for support in product development and the regulatory approval process as well as a variety of other activities including manufacturing, marketing and distribution of our products in the U.S. and abroad, when, and if, the FDA and corresponding foreign agencies approve our product candidates for marketing. To date, we have entered into strategic alliances and collaborations with Schering AG, Tyco/Mallinckrodt, GE Healthcare, Philips Medical Systems and Siemens Medical Systems. Four of our key agreements include three collaboration agreements with Schering AG, to perform joint research and to develop and commercialize MS-325, EP-2104R and other MRI vascular agents worldwide, and an agreement with Tyco/Mallinckrodt, granting Tyco/Mallinckrodt rights to enter into an agreement with Schering AG to manufacture MS-325 for clinical development and commercial use. We may not receive milestone payments from these alliances should MS-325 or EP-2104R fail to meet certain performance targets in development and commercialization. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development, and commence marketing of MS-325, EP-2104R or other products in their respective territories, or they may not successfully market MS-325, EP-2104R or other products. In addition, Schering AG and Tyco/Mallinckrodt currently manufacture imaging agents for other technologies that will compete against MS-325 and Schering AG will be responsible for setting the price of the product worldwide. However, Schering AG may not set prices in a manner that maximizes revenues for us. We are currently in compliance with the terms of these agreements, and although we have filed an NDA, our failure to receive future milestone payments, or a reduction or discontinuance of efforts by our partners would have a material adverse effect on our business, financial condition and results of operations.

Furthermore, our collaboration agreement with Schering AG may be terminated early under certain circumstances, including if there is a material breach of the agreement by either of us. In addition, we intend to seek additional collaborations with third parties, who may negotiate provisions that allow them to terminate their agreements with us prior to the expiration of the negotiated term under certain circumstances. If Schering AG or any other third party collaborator were to terminate its agreement with us or otherwise fail to perform its obligations under our collaboration or to complete them in a timely manner, we could lose significant revenue. If we are unable to enter into future strategic alliances with capable partners on commercially reasonable terms, we may delay the development and commercialization of future product candidates and could possibly postpone them indefinitely.

In addition, we rely on certain of our collaborators, such as GE Healthcare, Siemens Medical Systems and Philips Medical Systems, to develop software that can be used to enhance or suppress veins or arteries from MS-325-enhanced MRA images. Although not required for clinical use of MS-325, the ability to separate veins from arteries using MS-325-enhanced MRA may be useful to clinicians in reading MS-325-enhanced images for the evaluation of vascular disease. Therefore, if our collaborators do not develop or implement the required software successfully, some clinicians may not be able to easily interpret the information provided from MS-325-enhanced images and therefore may not be inclined to use the product. Our inability to market MS-325 successfully to some clinicians may have a material adverse effect on our business.

We depend on exclusively licensed technology from the Massachusetts General Hospital and if we lose this license, it is unlikely we could obtain this technology elsewhere, which would have a material adverse effect on our business.

Under the terms of a license agreement that we have with Massachusetts General Hospital, or MGH, we are the exclusive licensee to certain technology, including patents, which relate to our product candidates, including MS-325. The license agreement imposes various commercialization, sublicensing, royalty and other obligations on us. If we fail to comply with these and other requirements, our license could

convert from exclusive to nonexclusive or terminate entirely. It is unlikely that we would be able to obtain this technology elsewhere. Any such event would mean that we would be unlikely to produce our product candidates, including MS-325, and would therefore have a material adverse effect on our business, financial condition and results of operations. Currently, we are in compliance with the terms of the license agreement, and we do not have any reason to believe that this license may be terminated.

We depend on patents and other proprietary rights, and if they fail to protect our business, we may not be able to compete effectively.

The protection of our proprietary technologies is material to our business prospects. We pursue patents for our product candidates in the U.S. and in other countries where we believe that significant market opportunities exist. We own or have an exclusive license to patents and patent applications on aspects of our core technology as well as many specific applications of this technology. Specifically, patents and patent applications related to our core technology consist of two U.S. patents that are exclusively licensed to us from MGH, as

well as their counterpart patents and applications in foreign countries; seven U.S. patents and their counterpart patents and applications in certain foreign countries that we own; 19 U.S. patent applications as well as their counterpart patents and applications in certain foreign countries and three U.S. provisional patent applications. One of our issued patents covers aspects of the process by which MS-325 is manufactured. Another issued patent covers the MS-325 composition of matter. Two of our patents cover certain methods of imaging with MS-325. We have eight patent applications relating to EP-2104R, fibrin binding peptides and methods of imaging. Even though we hold these patents and have made these patent applications, because the patent positions of pharmaceutical and biopharmaceutical firms, including ours, generally include complex legal and factual questions, our patent position remains uncertain. For example, because most patent applications are maintained in secrecy for a period after filing, we cannot be certain that the named applicants or inventors of the subject matter covered by our patent applications or patents, whether directly owned or licensed to us, were the first to invent or the first to file patent applications for such inventions. Third parties may oppose, challenge, infringe upon, circumvent or seek to invalidate existing or future patents owned by or licensed to us. A court or other agency with jurisdiction may find our patents invalid, not infringed or unenforceable and we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future. Even if we have valid patents, these patents still may not provide sufficient protection against competing products or processes. If we are unable to successfully protect our proprietary methods and technologies, or, if our patent applications do not result in issued patents, we may not be able to prevent other companies from practicing our technology and, as a result, our competitive position may be harmed.

We may need to initiate lawsuits to protect or enforce our patents and other intellectual property rights, which could incur substantial costs, and which could result in the forfeiture of these rights.

We may need to bring costly and time-consuming litigation against third parties in order to enforce our issued patents, protect our trade secrets and know how, or to determine the enforceability, scope and validity of proprietary rights of others. In addition to being costly and time-consuming, such lawsuits could divert management s attention from other business concerns. These lawsuits could also result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. We may not prevail and a court may find damages or award other remedies in favor of an opposing party in any such lawsuits. During the course of these suits, there may be public announcements of the results of hearings, motions and other interim proceedings or developments in the litigation. Securities analysts or investors may perceive these announcements to be negative, which could cause the market price of our stock to decline. In addition, the cost of such litigation could have a material adverse effect on our business and financial condition.

Other rights and measures that we rely upon to protect our intellectual property may not be adequate to protect our products and services and could reduce our ability to compete in the market.

In addition to patents, we rely on a combination of trade secrets, copyright and trademark laws, nondisclosure agreements and other contractual provisions and technical measures to protect our intellectual property rights. While we require employees, collaborators, consultants and other third parties to enter into confidentiality and/or non-disclosure agreements where appropriate, any of the following could still occur:

- the agreements may be breached;
- we may have inadequate remedies for any breach;
- proprietary information could be disclosed to our competitors; or

others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technologies.

If for any of the above reasons our intellectual property is disclosed or misappropriated, it would harm our ability to protect our rights and our competitive position. Moreover, several of our management and scientific personnel were formerly associated with other pharmaceutical and biotechnology companies and academic institutions. In some cases, these individuals are conducting research in similar areas with which they were involved prior to joining us. As a result, we, as well as these individuals, could be subject to claims of violation of trade secrets and similar claims.

Our success will depend partly on our ability to operate without infringing the intellectual property rights of others, and if we are unable to do so, we may not be able to sell our products.

Our commercial success will depend, to a significant degree, on our ability to operate without infringing upon the patents of others in the U.S. and abroad. There may be pending or issued patents, held by parties not affiliated with us, relating to technologies we use

in the development or use of certain of our contrast agents. For example, in November 2003, we entered into an Intellectual Property Agreement with Dr. Martin R. Prince, an early innovator in the field of MRA relating to dynamic MRA, which involves capturing MRA images during the limited time, typically 30 to 60 seconds, available for imaging with extracellular agents. In this Agreement, Dr. Prince made certain covenants and agreements and granted us certain discharges and releases in connection with the use of any magnetic resonance imaging drug product containing MS-325. Dr. Prince also granted to us a non-exclusive license to make, use, sell or otherwise transfer MS-325. Although we are not aware of any other similar patent claims in the field of MRA, they may exist.

If any judicial or administrative proceeding upholds these or any third party patents as valid and enforceable, we could be prevented from practicing the subject matter claimed in such patents, or would be required to obtain licenses from the owners of each such patent, or to redesign our products or processes to avoid infringement. If we are unable to obtain a required license on acceptable terms, or are unable to design around these or any third party patents, we may be unable to sell our products, which would have a material adverse effect on our business.

Extensive government regulation may delay or prevent us from marketing MS-325 or our other products under development.

We are subject to extensive U.S. and foreign governmental regulatory requirements and lengthy approval processes for our product candidates. The development and commercial use of our product candidates will be regulated by numerous federal, state, local and foreign governmental authorities in the U.S., including the FDA and foreign regulatory agencies. The nature of our research and development and manufacturing processes requires the use of hazardous substances and testing on certain laboratory animals. Accordingly, we are subject to extensive federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials and wastes, as well as the use of and care for laboratory animals. Although we believe we are in compliance with all such laws and maintain policies and procedures to ensure that we remain in compliance, if we fail to comply or if an accident occurs, we may be exposed to legal risk and be required to pay significant penalties or be held liable for any damages that result. Such liability could exceed our financial resources. Furthermore, current laws could change and new laws could be passed that may force us to change our policies and procedures, an event which could impose significant costs on us.

Specifically, MS-325 is regulated by the FDA as a pharmaceutical product. The FDA has established substantial requirements for the research, development, manufacture and marketing of pharmaceutical products. The process required by the FDA before MS-325 and our other product candidates may be marketed in the U.S. typically involves the performance of pre-clinical laboratory and animal tests; submission of an investigational new drug application, or IND; completion of human clinical trials; submission of a NDA to the FDA; and FDA approval of the NDA.

This regulatory approval process is lengthy and expensive. Although some of our employees have experience in obtaining regulatory approvals, we have only limited experience in filing or pursuing applications necessary to gain regulatory approvals. Pre-clinical testing of our product development candidates is subject to Good Laboratory Practices as prescribed by the FDA and the manufacture of any products developed by us will be subject to Good Manufacturing Practices as prescribed by the FDA. We may not obtain the necessary FDA clearances and subsequent approvals in a timely manner, if at all. We cannot be sure as to the length of the clinical trial period or the number of patients that will be required to be tested in the clinical trials in order to establish the safety and efficacy of MS-325 or any of our future product candidates. Our clinical trials may not be successful, and we may not complete them in a timely manner. We could report serious side effects as the clinical trials proceed. Our results from early clinical trials may not predict results that we obtain in later clinical trials, even after promising results in earlier trials. The rate of completion of our clinical trials depends upon, among other things, the rate of patient enrollment and subsequent blinded reading of images and data analysis.

Furthermore, we, the FDA or other regulatory authorities may alter, suspend or terminate clinical trials at any time. For example, in September 2001, after discussions with the FDA, we expanded our initial target indication for MS-325 from one specific body region, the aortoiliac region, to a broader indication that includes the entire body s vascular system, except for the heart. This expansion required us to add two new clinical trials to our then existing Phase III clinical trial program, one to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the renal arteries, and another to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the pedal arteries. Although providing us with greater market potential for the sale of MS-325 upon approval, this change to our Phase III clinical trial program, and the associated delay in the start up of new clinical centers, resulted in an approximate fifteen month delay in our NDA submission and an increase in costs associated with the program. If we do not successfully complete clinical trials for our product candidates, we will not be able to market these product candidates.

In addition, we may encounter unanticipated delays or significant costs in our efforts to secure necessary approvals. In October 2004, we were notified by the FDA that it had extended the action date for completion of its review of the MS-325 NDA by 90 days, to January 2005. In communications with the FDA in October 2004, the FDA indicated that its principal open review questions relate to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. We have subsequently provided detailed responses to the FDA s questions. Although we remain confident in the safety and efficacy profile of MS-325,

the FDA s review of the additional analyses and interpretations we have provided could adversely affect the approval, timeliness of approval or labeling of MS-325. We may not obtain regulatory approval, even after the performance of clinical trials and the passage of time and the expenditure of such resources, for MS-325 or any other product candidates that we develop. Our analysis of data obtained from pre-clinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent FDA regulatory approval. In addition, the FDA may require us to modify our future clinical trial plans or to conduct additional clinical trials in ways that we cannot currently anticipate, resulting in delays in our obtaining regulatory approval. Delays in obtaining government regulatory approval could adversely affect our marketing as well as our ability to generate significant revenues from commercial sales.

Future U.S. legislative or administrative actions also could prevent or delay regulatory approval of our product candidates. Even if we obtain regulatory approvals, they may include significant limitations on the indicated uses for which we may market a product. A marketed product also is subject to continual FDA and other regulatory agency review and regulation. Later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market, as well as possible civil or criminal sanctions. Further, many academic institutions and companies conducting research and clinical trials in the MRI contrast agent field are using a variety of approaches and technologies. If researchers obtain any adverse results in pre-clinical studies or clinical trials, it could adversely affect the regulatory environment for MRI contrast agents generally. In addition, if we obtain marketing approval, the FDA may require post marketing testing and surveillance programs to monitor the product s efficacy and side effects. Results of these post-marketing programs may prevent or limit the further marketing of the monitored product. If we cannot successfully market our products, we will not generate sufficient revenues to achieve or maintain profitability.

Our strategic partners and we are also subject to numerous and varying foreign regulatory requirements governing the design and conduct of clinical trials and the manufacturing and marketing of our products. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval set forth above, and we may not obtain foreign regulatory approvals on a timely basis, if at all, thereby compromising our ability to market our products abroad.

Product liability claims could increase our costs and adversely affect our results of operations.

The clinical testing of our approved products, and the manufacturing and marketing of any approved products may expose us to product liability claims, and we may experience material product liability losses in the future. We currently have limited product liability insurance for the use of our product candidates in clinical research, but our coverage may not continue to be available on terms acceptable to us or adequate for liabilities we actually incur. We do not have product liability insurance coverage for the commercial sale of our products but intend to obtain such coverage when and if we commercialize our product candidates. However, we may not be able to obtain adequate additional product liability insurance coverage on acceptable terms, if at all. A successful claim brought against us in excess of available insurance coverage, or any claim or product recall that results in significant adverse publicity against us, may have a material adverse effect on our business and results of operations.

If we fail to get adequate levels of reimbursement from third party payors for our product candidates after they are approved in the U.S. and abroad, we may have difficulty commercializing our product candidates.

We could be adversely affected by changes in reimbursement policies of governmental or private healthcare payors, particularly to the extent any such changes affect reimbursement for procedures in which our product candidates would be used. Failure by physicians, hospitals and other

users of our products to obtain sufficient reimbursement from third party payors for the procedures in which our products would be used or adverse changes in governmental and private third party payors policies toward reimbursement for such procedures may have a material adverse effect on our ability to market our products and consequently it could have an adverse effect on our business, financial condition and results of operations. If we obtain the necessary foreign regulatory approvals, market acceptance of our product candidates in international markets would be dependent, in part, upon the availability of reimbursement within prevailing healthcare payment systems. Reimbursement and healthcare payment systems in international markets vary significantly by country, and include both government sponsored health care and private insurance. We and our strategic partners intend to seek international reimbursement approvals, although we cannot assure you that any such approvals will be obtained in a timely manner, if at all, and failure to receive international reimbursement approvals could have an adverse effect on market acceptance of our products in the international markets in which such approvals are sought.

We depend on our key personnel, the loss of whom would hurt our ability to compete.

Our future business and operating results depend in significant part upon the continued contributions of our senior management and key technical personnel. If any such personnel were to be hired away from us by a competitor, or if for any reason, they could not continue to work for us, we could have difficulty hiring officers with equivalent skills in general, financial and research management and

our ability to achieve our business objectives or to operate or compete in our industry may be seriously impaired. Although we maintain key life insurance on our Chief Executive Officer, the loss of any key employee, the failure of any key employee to perform in his or her current position, or our inability to attract and retain skilled employees, as needed, could have a material adverse effect on our business, financial condition and results of operations. Our future business and operating results also depend in significant part upon our ability to attract and retain qualified management, operational and technical personnel. Competition for personnel is intense, and we may not be successful in attracting or retaining such personnel. If we were to lose these employees to our competitors, we could spend a significant amount of time and resources to replace them, which would impair our research and development or commercialization efforts.

Our stock price is volatile. It is possible that you may lose all or part of your investment.

The market prices of the capital stock of medical technology companies have historically been very volatile, and the market price of the shares of our common stock fluctuates. The market price of our common stock is affected by numerous factors, including:

- actual or anticipated fluctuations in our operating results;
- announcements of technological innovation or new commercial products by us or our competitors;
- new collaborations entered into by us or our competitors;
- developments with respect to proprietary rights, including patent and litigation matters;
- results of pre-clinical and clinical trials;
- conditions and trends in the pharmaceutical and other technology industries;
- adoption of new accounting standards affecting such industries;
- changes in financial estimates by securities analysts; and
- degree of trading liquidity in our common stock and general market conditions.

During the nine months ended September 30, 2004, the closing price of our common stock ranged from $25.99 to $15.86. The last reported closing price for our common stock on September 30, 2004 was $19.31. If our stock price declines significantly, we may be unable to raise additional capital. Significant declines in the price of our common stock could also impede our ability to attract and retain qualified employees and reduce the liquidity of our common stock.

In addition, the stock market has from time to time experienced significant price and volume fluctuations that have particularly affected the market prices for the common stock of similarly staged companies. These broad market fluctuations may adversely affect the market price of our common stock. In the past, following periods of volatility in the market price of a particular company s securities, shareholders have often

brought class action securities litigation against that company. Such litigation, if brought against us, could result in substantial costs and a diversion of management s attention and resources.

We have significantly increased our leverage as a result of the sale of our 3.00% Convertible Senior Notes due 2024.

In connection with the sale of our 3.00% Convertible Senior Notes due 2024, we have incurred new indebtedness of $100 million. The amount of our indebtedness could, among other things:

make it difficult for us to make payments on the notes;

make it difficult for us to obtain financing for working capital, acquisitions or other purposes on favorable terms, if at all;

make us more vulnerable to industry downturns and competitive pressures; and

limit our flexibility in planning for, or reacting to changes in, our business.

Our ability to meet our debt service obligations will depend upon our future performance, which will be subject to financial, business and other factors affecting our operations, many of which are beyond our control.

Certain anti-takeover clauses in our charter and by-law provisions and in Delaware law may make an acquisition of us more difficult.

Our Restated Certificate of Incorporation authorizes the Board of Directors to issue, without stockholder approval, up to 1,000,000 shares of preferred stock with voting, conversion and other rights and preferences that could adversely affect the voting power or other rights of the holders of Common Stock. The issuance of Preferred Stock or of rights to purchase Preferred Stock could be used to

discourage an unsolicited acquisition proposal. In addition, the possible issuance of Preferred Stock could discourage a proxy contest, make more difficult the acquisition of a substantial block of our Common Stock or limit the price that investors might be willing to pay for shares of our Common Stock. The Restated Certificate provides for staggered terms for the members of the Board of Directors. A staggered Board of Directors and certain provisions of our By-laws and of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us. We, for example, are subject to Section 203 of the General Corporate Law of Delaware, which, subject to certain exceptions, restricts certain transactions and business combinations between a corporation and a stockholder owning 15% or more of the corporation s outstanding voting stock for a period of three years from the date the stockholder becomes an interested stockholder. These provisions may have the effect of delaying or preventing a change in control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The objective of our investment activities is to preserve principal, while at the same time maximizing yields without significantly increasing risk. To achieve this objective, in accordance with our investment policy, we invest our cash in a variety of financial instruments, principally restricted to U.S. government issues, high-grade bank obligations, high-grade corporate bonds and certain money market funds. These investments are denominated in U.S. dollars.

Investments in both fixed rate and floating rate interest earning instruments carry a degree of interest rate risk. Fixed rate securities may have their fair market value adversely impacted due to a rise in interest rates, while floating rate securities may produce less income than expected if interest rates fall. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates or we may suffer losses in principal if forced to sell securities that have seen a decline in market value due to changes in interest rates. A hypothetical 10% increase or decrease in interest rates would result in a decrease in the fair market value of our total portfolio of approximately $128,000, and an increase of approximately $128,000, respectively, at September 30, 2004.

ITEM 4. CONTROLS AND PROCEDURES

(a) *Evaluation of Disclosure Controls and Procedures*. Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Quarterly Report on Form 10-Q, have concluded that, based on such evaluation, our disclosure controls and procedures were adequate and effective to ensure that material information relating to us, including our consolidated subsidiaries, was made known to them by others within those entities, particularly during the period in which this Quarterly Report on Form 10-Q was being prepared.

(b) *Changes in Internal Controls*. There were no significant changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control that occurred during our last fiscal quarter that have materially affected, or are likely to materially affect our internal control over financial reporting.

PAT II. OTHER INFORMATION

ITEM 6. EXHIBITS

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the Company, as amended. Filed as Exhibit 3.1 to the Company s Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.
3.2	Amendment to Certificate of Incorporation of the Company.
3.3	Amended and Restated By-Laws of the Company. Filed as Exhibit 3.2 to the Company s Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.
4.1	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company s Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.1	Fourth Amendment, dated September 27, 2004, to the Short Form Lease dated as July 7, 1998 with a commencement date as of January 1, 1998 between the Company and the Trustees of the Cambridge East Trust.

31.1	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Michael D. Webb.
31.2	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Peyton J. Marshall.
32	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)

SIGNATURES

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

EPIX Pharmaceuticals, Inc.

Date: November 2, 2004 By: /s/ PEYTON J. MARSHALL, Ph.D.

Peyton J. Marshall, Ph.D.
Sr. Vice President and Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)