EPIX Pharmaceuticals, Inc.
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PROSPECTUS SUPPLEMENT NO. 1 DATED DECEMBER 23, 2004 (AS AMENDED)
(TO PROSPECTUS DATED NOVEMBER 5, 2004)

EPIX PHARMACEUTICALS, INC.

$100,000,000 3.00% CONVERTIBLE SENIOR NOTES DUE 2024
3,359,086 SHARES OF COMMON STOCK ISSUABLE UPON CONVERSION OF THE NOTES

This amendment to Prospectus Supplement No. 1 filed on December 23, 2004 is being filed to correct ownership information as set forth in the selling stockholder table. Prospectus Supplement No. 1 supplements and amends the Prospectus dated November 5, 2004 (the "Prospectus"), relating to the resale from time to time by holders of our 3.00% Convertible Senior Notes Due 2024 (the "Notes") and shares of our common stock issuable upon the conversion of the Notes. Such information has been obtained from the selling holders. This prospectus supplement should be read in conjunction with the Prospectus, which is to be delivered with this prospectus supplement.

Our common stock is quoted on The Nasdaq National Market under the symbol "EPIX." The last reported sale price of our common stock on December 21, 2004 was $17.99 per share.

See "Risk Factors" beginning on page 8 of the Prospectus to read about factors you should consider before buying the Notes or our common stock.

Neither the Securities and Exchange Commission, any state securities commission nor any other regulatory authority, has approved or disapproved the securities nor have any of the foregoing authorities passed upon or endorsed the merits of this offering or the accuracy or adequacy of this Prospectus Supplement or the Prospectus or the documents incorporated by reference therein. Any representation to the contrary is a criminal offense.

The information appearing in the table below, as of the date hereof, supplements and amends the information in the table appearing under the heading "Selling Holders" in the Prospectus, and, where the name of a selling holder identified in the table below also appears in the table in the Prospectus, the information set forth in the table below regarding that selling holder supercedes the information in the Prospectus:

Name	Principal Amount of Notes Beneficially Owned That May Be Sold ($) (1)	Shares of Common Stock That May Be Sold (2)	Principal Amount of Notes Owned After Completion of Offering ($)	Shares of Common Stock Beneficially Owned After Completion of Offering
SG Americas Securities, LLC	200,000	6,718	0	0
Allstate Insurance Company	2,000,000	67,182	0	0
Fidelity Financial Trust: Fidelity Convertible Securities Fund (3)	14,000,000	470,273	0	0

(1) Amounts indicated may be in excess of the total amount registered due to sales or transfers exempt from the registration requirements of the Securities Act since the date upon which the selling holders provided to us the information regarding their notes and common stock.

(2) Unless otherwise noted, represents shares of common stock issuable upon conversion of notes.

(3) The entity is a registered investment fund (the "Fund") advised by Fidelity Management & Research Company ("FMR Co."), a registered investment adviser under the Investment Advisers Act of 1940, as amended. FMR Co., 82 Devonshire Street, Boston, Massachusetts 02109, a wholly-owned subsidiary of FMR Corp. and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of shares of the Common Stock outstanding of the Company as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Edward C. Johnson 3d, FMR Corp., through its control of FMR Co., and the funds each has sole power to dispose of the shares owned by the Funds. Neither FMR Corp. nor Edward C. Johnson 3d, Chairman of FMR Corp., has the sole power to vote or direct the voting of the shares owned directly by the Funds, which power resides with the Funds' Boards of Trustees. The Fund is an affiliate of a broker-dealer. The Fund purchased the Securities in the ordinary course of business and, at the time of the purchase of the Securities to be resold, the Fund did not have any agreements or understandings, directly or indirectly, with any person to distribute the notes or conversion shares. The holdings listed for the Fund are as of December 3, 2004.

The selling holders identified above may have sold, transferred or otherwise disposed of all or a portion of their Notes since the date on which they provided the information about their Notes in transactions exempt from the registration requirements of the Securities Act.

PROSPECTUS

$100,000,000 PRINCIPAL AMOUNT OF 3.00% CONVERTIBLE SENIOR NOTES DUE 2024

3,359,086 SHARES OF COMMON STOCK
ISSUABLE UPON CONVERSION OF THE NOTES

EPIX PHARMACEUTICALS, INC.

We issued $100,000,000 aggregate principal amount of our 3.00% Convertible Senior Notes due 2024 in a private placement on June 7, 2004. The initial purchasers resold the notes to qualified institutional buyers in accordance with Rule 144A under the Securities Act of 1933, as amended. This prospectus will be used by the selling security holders from time to time to resell their notes and the common stock issuable upon the conversion of the notes. We will not receive any proceeds from the sale of the notes or the shares of common stock issuable upon the conversion of the notes.

The notes bear interest at the rate of 3.00% per annum, from December 15, 2004, payable semi-annually in arrears on June 15 and December 15 of each year, beginning December 15, 2004.

The notes will mature on June 15, 2024. We may redeem some or all of the notes at any time after June 15, 2009 at the redemption prices specified in this prospectus plus accrued and unpaid interest and additional interest, if any, to, but excluding, the date of redemption.

Holders of the notes have the right to require us to repurchase the notes at a purchase price equal to 100% of the principal amount of the notes plus accrued and unpaid interest, if any, on June 15, 2011, 2014 and 2019 or upon a termination of trading or a change of control event, each as described in this prospectus.

Holders of the notes may convert the notes into shares of our common stock only in the following circumstances:

- if the price of our common stock reaches a specified threshold over a specified period as described in this prospectus;
- if the notes are called for redemption;
- if we make specified distributions on our common stock or engage in specified corporate transactions; and
- at any time before June 15, 2019 if the trading price of the notes falls below certain thresholds.

The initial conversion price is $29.77 per share (equivalent to an initial conversion rate of approximately 33.5909 shares per $1,000 principal amount of the notes), subject to adjustment in certain circumstances. Our common stock is traded on the Nasdaq National Market under the symbol "EPIX." The last reported closing price of our common stock on November 4, 2004 was $16.03 per share.

The notes are unsecured and will rank equally with all existing and future unsecured senior indebtedness except that the notes are subordinated to certain senior indebtedness described in this prospectus. The notes will rank senior in right of payment to all existing and future unsecured subordinated debt.

For a more detailed description of the notes, see the "Description of Notes" beginning on page 24.

Our address is EPIX Pharmaceuticals, Inc., 161 First Street, Cambridge, Massachusetts, and our telephone number is (617) 250-6000.

INVESTING IN THE NOTES OR OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 8.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES, OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is November 5, 2004

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You should rely only on the information provided or incorporated by reference in this prospectus or any prospectus supplement. Neither we nor the selling holders have authorized anyone to provide you with additional or different information. The selling holders are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should assume that the information in this prospectus and any prospectus supplement is accurate only as of the date on the front of the document and that information incorporated by reference in this prospectus or any prospectus supplement is accurate only as of the date of the document incorporated by reference. In this prospectus and any prospectus supplement, unless otherwise indicated, "we," "us" and "our" refer to EPIX Pharmaceuticals, Inc., and do not refer to the selling holders.

 In September 2004, we changed our name from EPIX Medical, Inc. to EPIX Pharmaceuticals, Inc.

PROSPECTUS SUMMARY

This summary highlights information about EPIX Pharmaceuticals, Inc. Because this is a summary, it may not contain all the information you should consider before investing in the notes or the common stock issuable upon their conversion. you should read this entire prospectus carefully.

EPIX PHARMACEUTICALS, INC.

We are a leading developer of targeted contrast agents, designed to improve the diagnostic quality of images produced by magnetic resonance imaging, or MRI. MRI has been established as the imaging technology of choice for a broad range of applications, including the identification and diagnosis of a variety of medical disorders. MRI is safe, relatively cost-effective and provides three-dimensional images that enable physicians to diagnose and manage disease in a minimally invasive manner. We are currently developing two products for use in MRI to improve the diagnosis of multiple cardiovascular diseases affecting the body's arteries and veins, collectively known as the vascular system. In December 2003, we submitted a New Drug Application, or NDA, for MS-325, our principal product under development, to the U. S. Food and Drug Administration, or FDA. 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. 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 and we are in discussions with the FDA about open review issues. 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. In June 2004, Schering AG submitted MS-325 for marketing approval in the European Union.

OUR PRODUCT CANDIDATES

Ms-325. Our principal product under development, MS-325, is designed to provide visual imaging of the vascular system, through a type of MRI known as magnetic resonance angiography, or MRA. We believe that MS-325-enhanced MRA has the potential to improve the diagnosis of multiple diseases of the vascular system, including vascular disease outside the heart, known as peripheral vascular disease, and diseases that affect the coronary arteries and reduce blood flow to the heart. Our initial target indication for MS-325 is for use in MRA imaging of peripheral vascular disease. We are also developing MS-325 for imaging the coronary arteries and the heart and initiated Phase II cardiac studies in July 2004.

We believe that MS-325 will significantly enhance the quality of MRI and provide physicians with a minimally-invasive and cost-effective method for diagnosing vascular disease. We also believe that MS-325-enhanced MRA has the potential to simplify the diagnosis of vascular disease and to replace a significant portion of X-ray angiographic procedures, a highly invasive and expensive catheter-based method most frequently used for the detection of vascular disease. In 2003, approximately 8.5 million angiographic procedures were performed in the U.S. for the diagnosis of diseases of the vascular system, of which 4.6 million procedures were by way of X-ray angiography. We believe that MS-325-enhanced MRA will be a less invasive method of imaging a patient's vascular anatomy for the evaluation of disease.

Clinical Trial Results and Nda. We have submitted an NDA for MS-325 based on a 780-patient Phase III clinical trial program designed to test the safety and efficacy of MS-325 for the imaging of peripheral vascular disease. We conducted four Phase III trials to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the lower abdomen and pelvic regions, in the renal arteries of the kidneys and in the pedal arteries of the feet. All four trials in the Phase III program for MS-325 met their primary endpoints. 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.

Mri in The Diagnosis of Vascular Disease. The use of MRI has grown steadily over the past 10 years due to reduced cost and improved imaging capabilities. MRI provides an effective method for diagnosing a broad range of diseases. MRI manufacturers have improved both the hardware and software used in their systems, reducing the procedure time and significantly enhancing image resolution. While MRI is currently used extensively to image many organs and tissues in the body, its use in imaging the vascular system has been limited. Currently available MRI contrast agents for MRA are not optimal for the diagnosis of vascular disease in many vascular beds due to the rapid leakage of the injectable contrast agent from the vascular system into the surrounding tissue, usually within 30 to 60 seconds. As a result of this leakage, the time available to image blood vessels with these contrast agents is too short to obtain the high resolution images necessary for broad clinical application. In addition, performance of MRA using currently approved contrast agents generally requires specialized equipment and specially trained staff. None of the currently available MRI contrast agents is approved by the FDA for use in MRA. In 2003, approximately 2.7 million MRAs were performed in the U.S., an increase of 22% over 2002.

Ms-325-enhanced Mra. MS-325 is specifically designed to enhance the quality of magnetic resonance images of the arteries and veins and to provide physicians with a superior method for diagnosing vascular disease. MS-325 is a small molecule, which produces an MRI signal because of the presence of gadolinium, a magnetically active element favored by clinicians for enhancing magnetic resonance images. MS-325 is designed with our proprietary technology to bind reversibly to albumin, the most common protein in the blood. Using standard MRI techniques, MS-325-enhanced MRA produces a strong magnetic signal, resulting in bright images of the blood against the dark background of surrounding tissue. Because of its affinity for albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam, providing the extended, approximately 60-minute image time and signal strength required to obtain a high resolution image of multiple regions of the vascular system. Like most currently available general use MRI contrast agents, MS-325 is designed to be safely eliminated from the body through the kidneys over time. In addition, in clinical studies of renally-compromised patients, MS-325 appeared safe and well tolerated, a potentially important feature given the renal risks of X-ray angiography.

Ep-2104r. We are developing a second targeted contrast agent, EP-2104R, which is designed to illuminate and identify blood clots using MRI. 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 pre-clinical studies, EP-2104R has been shown to enhance the ability of MRI to image clots. We announced the initiation of human clinical studies for EP-2104R in August 2004.

OUR STRATEGIC COLLABORATIONS

We have established collaborations with large pharmaceutical companies to enhance our internal development capabilities and to offset a substantial portion of the financial risk of developing our product candidates. At the same time, we maintain substantial rights to product candidates covered by these collaborations, which provide us the opportunity to participate in a significant portion of the potential economic benefit from their successful development and commercialization. Our most significant collaborations involve Schering AG for the development and commercialization of MS-325, EP-2104R and for the discovery of other MRI contrast agents. We have also formed collaborations with the three leading MRI scanner manufacturers, GE Medical Systems (now GE Healthcare), Philips

Medical Systems and Siemens Medical Systems, to develop advanced imaging techniques and tools designed to facilitate the use of MS-325-enhanced MRA.

OUR STRATEGY

Our objective is to become a worldwide leader in MRI contrast agents by developing and commercializing products using our proprietary technology platform. We intend to pursue this strategy through internal product development efforts, collaborations with strategic partners and by acquiring the rights to complementary technologies. We also intend to expand the potential applications for our current product candidates. We believe we can build on our leadership in developing targeted contrast agents for MRI through further research and development programs in cardiovascular imaging and therapeutics. In addition, we intend to consider other opportunities to expand beyond MRI.

CORPORATE INFORMATION

We incorporated in Delaware in 1988 and commenced operations in 1992. Our principal executive offices are located at 161 First Street, Cambridge, Massachusetts 02142-1118 and our telephone number is (617) 250-6000. Our website is located at http://www.epixpharma.com. Our Corporate Code of Conduct and Ethics as well as our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and all amendments to these reports, which have been filed with the SEC, are available to you free of charge through the Investor Relations section on our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC. We do not intend for the other information contained in our website to be considered a part of this prospectus.

THE OFFERING

Issuer	EPIX Pharmaceuticals, Inc.
Notes Offered	$100,000,000 aggregate principal amount of 3.00% Convertible Senior Notes due 2024.
Issue Price	The notes have been issued at a price of 100% of their principal amount, which is $1,000 per note, plus accrued interest, if any, from December 15, 2004.
Maturity Date	June 15, 2024
Ranking	The notes will: -
	be our senior unsecured obligations; -
	be subordinated in right of payment to up to $15,000,000 plus accrued and unpaid interest on existing and future indebtedness under our Loan Agreement, dated May 26, 2003, as amended, with Schering AG, referred to as our Schering AG loan facility;
	rank on parity in right of payment with all of our existing and future senior debt other than our Schering AG loan facility; and
	rank senior in right of payment to all of our future debt that is subordinated to the notes.
	The notes also are effectively subordinated in right of payment to our existing and future secured debt, to the extent of such security, and will be effectively subordinated in right of payment to any liabilities of any subsidiary that we may create in the future.
Interest	The notes will bear interest at 3.00% per annum on the principal amount of the notes, payable semi-annually in arrears on June 15 and December 15 of each year, beginning December 15, 2004.
Conversion Rights	You may convert the notes into shares of our common stock at a conversion rate of 33.5909 shares per $1,000 principal amount of notes (which represents an initial conversion price of $29.77 per share), subject to adjustment, prior to the close of business on the final maturity date under any of the following circumstances:
	during any fiscal quarter prior to June 15, 2019, if the closing sale price of our common stock for at least 20 trading days in the period of 30 consecutive trading days ending on the eleventh trading day of any fiscal quarter is more than 120% of the conversion price in effect on such eleventh trading day (initially 120% of $29.77, or $35.72);
	if the notes are called for redemption;

	if we make specified distributions on our common stock or engage in specified corporate transactions; or during the five trading day period immediately following any five consecutive trading day period in which the average trading price per $1,000 principal amount of the notes for such five day period is less than 98% of the product of the closing sale price of our common stock on a given day multiplied by the number of shares of common stock into which each $1,000 principal amount of the notes is convertible. See "Description of Notes Conversion of Notes."
Redemption	On or after June 15, 2009, we may redeem the notes, in whole or in part, at the following percentages of the principal amount of the notes, plus accrued and unpaid interest and additional interest, if any, to, but excluding, the redemption date:

Date	Redemption Price
June 15, 2009 to June 14, 2010	100.857%
June 15, 2010 to June 14, 2011	100.429%
June 15, 2011 and thereafter	100.000%

	We will give you at least 20 days' notice of any such redemption. If we redeem the notes in whole or in part, other than a redemption of less than $7.5 million in cumulative principal amount of the notes, then we will be required to repay the then outstanding principal amount, together with accrued and unpaid interest, under our Schering AG loan facility.
Repurchase at the Option of the Holder	You may require us to repurchase the notes, in whole or in part, on June 15, 2011, 2014 and 2019 for a repurchase price equal to 100% of the principal amount of the notes plus accrued and unpaid interest and additional interest, if any, to, but excluding, the date of redemption. Before we repurchase the notes in whole or in part, we will be required to repay the then outstanding principal amount, together with accrued and unpaid interest, under our Schering AG loan facility.
Sinking Fund	None.

Repurchase at the Option of the Holder Upon a Designated Event	Upon a change in control or a termination of trading (each as defined under "Description of Notes Repurchase at the Option of the Holder Upon a Designated Event"), each holder of the notes may require us to repurchase some or all of its notes at 100% of the principal amount of the note, plus accrued and unpaid interest and additional interest, if any, to, but excluding, the date of redemption. Upon a change in control we may, at our option, elect to pay the repurchase price in cash, shares of our common stock valued at a discount of 5% from the market price of our common stock, or any combination thereof, subject to our satisfaction of the conditions set forth in "Description of Notes Repurchase at the Option of the Holder Upon a Designated Event." Upon a termination of trading we will pay the repurchase price in cash. Before we repurchase the notes in whole or in part for cash, we will be required to repay the then outstanding principal amount, together with accrued and unpaid interest, under our Schering AG loan facility.
Registration Rights	We have agreed to use our reasonable best efforts to keep a shelf registration statement with respect to the resale of the notes and shares of common stock issuable upon conversion of the notes effective during the periods specified in "Description of Notes - Registration Rights."
Additional Interest	If the prospectus included in the shelf registration statement is suspended for more than 30 days in any three-month period or more than 90 days in any 12-month period, additional interest will accrue equal to 0.25% per annum for the first 90 days from and including the date on which the registration default has occurred, and 0.50% per annum as additional interest on the notes from and including the 91st day after the registration default, to, but excluding, the date on which the registration default is cured. Additional interest will be paid semi-annually in arrears.
DTC Eligibility	The notes have been issued in book-entry form and will be represented by one or more permanent global certificates deposited with a custodian for and registered in the name of a nominee of the Depository Trust Company, or DTC, in New York, New York. Beneficial interests in the notes will be shown on, and transfers will be effected only through, records maintained by DTC and its direct and indirect participants. Any such interest may not be exchanged for certificated securities, except in limited circumstances. See "Description of Notes - Global Note, Book-Entry Form."
Trading	The notes are not listed on any national securities exchange. The notes are eligible for trading on The PORTAL(SM) Market; however, we provide no assurance as to the liquidity of, or trading markets for, the notes.

Absence of a Public Market	There is currently no public market for the notes. An active or liquid market may not develop for the notes.
Nasdaq National Market Symbol Of our Common Stock	"EPIX."

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.

RISKS RELATED TO OUR BUSINESS

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(R) and Gadovist(R) by Schering AG, Dotarem(R) by Guerbet, S.A., Omniscan(R) by Amersham Health, ProHance(R) and MultiHance(R) by Bracco and OptiMark(R) 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(R), 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	Requires high level of training
	Minimally-invasive	Inadvisable for patients with cardiac pacemakers
	Favorable safety profile	Less widely available
	High quality images	
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	Invasive
	Opportunity to treat in same procedure	Radiation
	Highest resolution	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.

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.

RISKS RELATED TO THE SECURITIES

We have significantly increased our leverage as a result of the sale of the notes.

In connection with the sale of the notes, 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.

Your right to receive payment on the notes is junior to the rights of the holders of the SCHERING AG Loan Facility and will be effectively subordinated to certain other debt.

The payment of principal and interest on the notes is contractually subordinated in right of payment to up to $15.0 million aggregate principal amount of indebtedness under the Schering AG loan facility plus accrued and unpaid interest. The entire $15 million amount under the loan agreement was available and drawn as of September 30, 2004. The entire outstanding balance of $15 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 us 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. No payment will be able to be made in respect of the notes if the indebtedness under the Schering AG loan facility is not paid when due or any other default under the Schering AG loan facility occurs and the maturity of such indebtedness is accelerated in accordance with its terms. Furthermore, if certain other defaults exist with respect to the Schering AG loan facility, the holders of such indebtedness will be able to prevent payments on the notes for specified periods of time. The Schering AG loan facility is secured by certain of our assets. Upon the occurrence of an event of default under the Schering AG loan facility, Schering AG will have the ability to foreclose on its security, and as a result there may be insufficient assets remaining to pay the amounts due on the notes.

The notes will also be structurally subordinated to the indebtedness and other liabilities of any subsidiaries that we may create in the future. In addition, the notes are not secured by any of our assets. As a result, the notes will be effectively subordinated to any secured debt that we or any future subsidiaries may incur to the extent of such security. As a result of the effective subordination of the notes to such debt, we may not have sufficient assets remaining to pay amounts due on any or all of the notes then outstanding in the event of our bankruptcy, liquidation or reorganization or upon acceleration of the notes.

In addition, before we redeem or repurchase for cash the notes in whole or in part, we will be required to repay the then outstanding principal amount, together with accrued and unpaid interest, under our Schering AG loan facility, other than a redemption by us of less than $7.5 million cumulative principal amount of the notes. Upon the occurrence of a repayment of the Schering AG loan facility there may be insufficient funds available to pay the amounts due on the notes.

The notes are not protected by restrictive covenants, including financial covenants.

We are not restricted under the indenture from incurring additional debt, including senior debt, or other liabilities. In addition, the indenture does not restrict us or any subsidiaries we may create in the future from paying dividends or issuing or repurchasing securities. If we or any future subsidiaries were to incur additional debt or liabilities, our ability to pay our obligations on the notes could be adversely affected. We are not required under the indenture to meet any financial tests, such as those that measure our working capital, interest coverage, fixed charge coverage or net worth, in order to maintain compliance with the terms of the indenture covering the notes.

We may be unable to repay, repurchase or redeem the notes.

At maturity, the entire outstanding principal amount of the notes will become due and payable by us. Upon a designated event, as defined in the indenture, or upon certain specified dates, you may require us to repurchase all or a portion of your notes. We may not have enough funds or be able to arrange for additional financing to pay the principal at maturity or to repurchase the notes tendered by the holders upon a designated event or upon such specified dates. Upon a designated event that is a change in control you may not necessarily receive cash as we may elect to pay you the purchase price in cash, shares of common stock that are publicly listed on a national securities exchange or on Nasdaq, or a combination of both.

In addition, before we redeem or repurchase for cash the notes in whole or in part, we will be required to repay the then outstanding principal amount, together with accrued and unpaid interest, under our Schering AG loan facility, other than a redemption by us of less than $7.5 million cumulative principal amount of the notes. In addition, future credit agreements or other agreements relating to our indebtedness may restrict the redemption or repurchase of the notes and provide that a change in control constitutes an event of default. If the maturity date or a designated event occurs at a time when we are prohibited from repaying or repurchasing the notes, we could seek the consent of our lenders to purchase the notes or could attempt to refinance this debt. If we do not obtain the necessary consents or cannot refinance the debt on favorable terms, if at all, we will be unable to repay or repurchase the notes. Our failure to repay the notes at maturity or repurchase tendered notes would constitute an event of default under the indenture, which might constitute a default under the terms of our other debt.

You may not have the right to require us to repurchase the notes in the event of certain mergers and similar transactions.

The definition of change in control set forth in the indenture governing the notes is limited and certain mergers and similar transactions are not deemed a change in control. In such instance, you would not be able to require us to repurchase the notes. As a result, our obligation to offer to repurchase the notes upon a change in control will not necessarily afford you protection in the event of certain highly leveraged transactions, mergers or similar transactions in which we are involved.

The contingent conversion feature of the notes could result in you receiving less than the value of the common stock into which a note would otherwise be convertible.

The notes are convertible into shares of our common stock only if specified conditions are met. If the specific conditions for conversion are not met, you will not be able to convert your notes, and you may not be able to receive the value of the common stock into which the notes would otherwise be convertible.

Conversion of the notes will dilute the ownership interest of existing stockholders.

The conversion of notes into shares of our common stock will dilute the ownership interests of existing stockholders. Any sales in the public market of the common stock issuable upon conversion of the notes could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short selling by market participants due to this dilution or facilitate trading strategies involving the notes and our common stock.

There may not be an active, liquid market for our common stock.

There is no guarantee that an active trading market for our common stock will be maintained on the Nasdaq Stock Market's National Market. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active.

The value of the conversion right associated with the notes may be substantially lessened or eliminated if we are party to a merger, consolidation or other similar transaction.

If we are party to a consolidation, merger or binding share exchange or transfer or lease of all or substantially all of our assets pursuant to which our common stock is converted into cash, securities or other property, at the effective time of the transaction, the right to convert a note into our common stock will be changed into a right to convert it into the kind and amount of cash, securities or other property which the holder would have received if the holder had converted its note immediately prior to the transaction. Accordingly, upon the consummation of any such transaction, the notes may not be convertible into shares of our common stock but rather convertible into securities of another entity. This change could substantially lessen or eliminate the value of the conversion privilege associated with the notes in the future. For example, if we were acquired in a cash merger, each note would become convertible solely into cash and would no longer be convertible into securities whose value would vary depending on our future prospects and other factors.

The price at which our common stock may be purchased on NASDAQ is currently lower than the conversion price of the notes and may remain lower in the future.

Prior to electing to convert the notes, the noteholder should compare the price at which our common stock is trading in the market to the conversion price of the notes. Our common stock trades on the Nasdaq under the symbol "EPIX." On November 4, 2004, the last reported closing price of our common stock was $16.03 per share. The initial conversion price of the notes is approximately $29.77 per share. The market prices of our securities are subject to significant fluctuations. Such fluctuations, as well as economic conditions generally, may adversely affect the market price of our securities, including our common stock and the notes.

Our stock price has been volatile, and an investment in our stock could suffer a decline in value, adversely affecting the value of the notes or the shares into which those notes may be converted.

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 November 4, 2004 was $16.03. If our stock price declines significantly, we may be unable to raise additional capital. Significant decli