EPIX MEDICAL INC
Form 424B5
July 28, 2003

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Filed pursuant to Rule 424(b)5
Registration: 333-84566

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

SUBJECT TO COMPLETION, DATED JULY 28, 2003

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated January 15, 2003)

4,300,000 Shares

Common Stock

We are selling 4,300,000 shares of our common stock.

Our common stock is quoted on the Nasdaq National Market under the symbol "EPIX." On July 24, 2003, the last reported sale price of our common stock was $17.16 per share. As of July 24, 2003, we had 17,305,907 shares of common stock issued and outstanding.

Our business and an investment in our common stock involves significant risks. These risks are described under the caption "Risk Factors" beginning on page S-5 of this prospectus supplement.

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

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

The underwriters may also purchase up to an additional 645,000 shares of our common stock from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments.

The underwriters expect to deliver the shares in New York, New York on August , 2003.

SG COWEN

WELLS FARGO SECURITIES, LLC

NEEDHAM & COMPANY, INC.

WR HAMBRECHT+CO

, 2003

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This prospectus supplement is part of a registration statement that we have filed with the Securities and Exchange Commission utilizing a "shelf" registration process. Under this shelf registration process, we are offering to sell our common stock using this prospectus supplement and the accompanying prospectus. In this prospectus supplement, we provide you with specific information about the shares of our common stock that we are selling in this offering. Both this prospectus supplement and the accompanying prospectus include important information about us, our common stock being offered, and other information you should know before investing. This prospectus supplement also adds, updates, and changes information contained in the prospectus. You should read both this prospectus supplement and the accompanying prospectus as well as additional information described under "Incorporation of Documents by Reference" on page S-56 before investing in shares of our common stock.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with different information. We are not making an offer to sell these securities in any state where the offer is not permitted. The information contained in this prospectus supplement and the accompanying prospectus is accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or the time of any sale of our common stock. In this prospectus supplement, "EPIX," "we," "us" and "our" refer to EPIX Medical, Inc.

PROSPECTUS SUPPLEMENT SUMMARY

The following information supplements, and should be read together with, the information contained or incorporated by reference in other parts of this prospectus supplement and in the accompanying prospectus. This summary highlights selected information from this prospectus supplement and the accompanying prospectus to help you understand our business. Because the following is only a summary, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus before deciding whether to invest in our common stock. You should pay special attention to the "Risk Factors" section beginning on page S-5 of this prospectus supplement to determine whether an investment in our common stock is appropriate for you.

Our Company

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. We plan to submit 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 2003.

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 magnetic resonance angiographic imaging of peripheral vascular disease.

We believe that MS-325 will significantly enhance the quality of MRA 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 2002, approximately 7.5 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.

Clinical Trial Results. We have completed enrollment in and reported preliminary results for a 780-patient Phase III clinical trial program to test the safety and efficacy of MS-325 for the imaging of peripheral vascular disease. Four Phase III trials were conducted 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 in the kidneys and in the pedal arteries in the feet. All four trials in the Phase III program for MS-325 met their primary endpoints.

MRI in the Diagnosis of Vascular Disease. The use of MRI has grown steadily over the past 10 years due to lower cost of procedures and improved imaging capabilities of MRI scanners. However, 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 contrast agents for MRI are inadequate for the diagnosis of vascular disease in many vascular beds due to the rapid leakage of the injectable contrast agent from the vasculature 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. None of the currently available MRI contrast agents are approved by the FDA for use in MRA. In 2002, approximately 2.2 million MRAs were performed in the U.S., an increase of 36% over 2001.

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.

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 preclinical studies, EP-2104R has been shown to enhance the ability of MRI to image clots. We plan to commence human trials of EP-2104R in 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 successful development and commercialization. Our most significant collaborations involve Schering Aktiengesellschaft, or 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, General Electric Medical Systems, 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. In addition to developing MS-325 for peripheral vascular disease, we are developing the product for imaging the coronary arteries of the heart. 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.

Corporate Information

We incorporated in Delaware in 1988 and commenced operations in 1992. Our principal executive offices are located at 71 Rogers Street, Cambridge, Massachusetts 02142-1118 and our telephone

number is (617) 250-6000. Our website is located at http://www.epixmed.com. Our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, which have been filed with the Securities and Exchange Commission, are available to you free of charge on our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the Commission. The information found on our website is not part of this prospectus supplement or the accompanying prospectus. Our common stock is quoted on the Nasdaq National Market under the symbol "EPIX."

The Offering

Common stock offered by EPIX	4,300,000 shares

Common stock to be outstanding after this offering	21,586,458 shares
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, including our research and development programs, and for general working capital. See "Use of Proceeds" on page S-18.
Risk factors	Investing in our common stock involves risks. Please read "Risk Factors" beginning on page S-5 of this prospectus supplement.
Nasdaq National Market symbol	EPIX

The information above is based on 17,286,458 shares of common stock outstanding as of June 30, 2003. It does not include:

3,919,877 shares of common stock subject to options outstanding as of June 30, 2003;

932,829 shares of common stock that have been reserved for issuance upon future grants under our stock option plans as of June 30, 2003;

59,720 shares of common stock available for sale under our employee stock purchase plan as of June 30, 2003; and

up to 645,000 shares of common stock issuable upon exercise of the underwriters' over-allotment option.

Summary Financial Data
(in thousands, except per share data)

The following table summarizes our historical financial data for the periods indicated. The following information is derived from, and qualified by reference to, the financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. You should read the financial data set forth below in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and with our financial statements and related notes thereto.

	Years Ended December 31,			Six Months Ended June 30,	
	2000	2001	2002	2002	2003
Statement of Operating Data:					
Revenues from research and license agreements and royalties	$ 6,924	$ 9,569	$ 12,270	$ 5,803	$ 7,318
Operating expenses:					
Research and development	25,833	22,904	29,084	14,414	13,282
General and administrative	4,835	5,506	6,001	3,049	3,165
Total operating expenses	30,668	28,410	35,085	17,463	16,447
Operating loss	(23,744)	(18,841)	(22,815)	(11,660)	(9,129)
Interest income, net	788	685	718	426	127

	Years Ended December 31,			Six Months Ended June 30,	
Loss before provision for income taxes	(22,956)	(18,156)	22,097	(11,234)	(9,002)
Provision for income taxes		1,092	94	44	66
Loss before cumulative effect of change in accounting principle	(22,956)	(19,248)	(22,191)	(11,278)	(9,068)
Cumulative effect of change in accounting principle	(4,364)				
Net loss	$ (27,320)	$ (19,248)	$ (22,191)	$ (11,278)	$ (9,068)
Weighted average shares:					
Basic and diluted	12,445	14,007	16,878	16,703	17,134
Net loss per share, basic and diluted:					
Loss before cumulative effect of change in accounting principle	$ (1.85)	$ (1.38)	$ (1.31)	$ (0.68)	$ (0.53)
Cumulative effect of change in accounting principle	(0.35)				
Net loss	$ (2.20)	$ (1.38)	$ (1.31)	$ (0.68)	$ (0.53)
Pro forma amounts assuming the accounting change is retroactively applied:					
Net loss	$ (22,956)	$	$	$	$
Net loss per share, basic and diluted	$ (1.85)	$	$	$	$

	As of June 30, 2003	
	Actual	As Adjusted[1]
Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 25,654	$ 95,179
Working capital	11,027	80,552
Total assets	27,514	97,039
Long-term obligations	14,137	14,137
Total stockholders' (deficit) equity	(1,976)	67,549

(1) As adjusted to reflect our receipt and application of an estimated $69.5 million of net proceeds from the sale of 4,300,000 shares of common stock in this offering, after deducting estimated underwriting discounts, commissions and offering expenses.

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the following risk factors, other information included in this prospectus supplement and the accompanying prospectus and 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, and you may lose some or all of your investment.

Risks Related to Our Business and Industry

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, 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 is currently our only product candidate in human clinical trials, and we cannot be certain that any of our other development projects will yield a product candidate suitable for entry into clinical trials. As a result, our initial revenues and profits from commercial sales of our products, if any, will be derived from sales 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, product development and marketing agreements with strategic collaborators. In particular, our revenue for the six months ended June 30, 2003 was $7.3 million, and consisted of $5.3 million from the product development portion of our strategic collaboration agreement with Schering AG and Pfizer, Inc., or Pfizer, $1.3 million from a patent licensing and royalty agreement with Bracco Imaging, S.p.A., or Bracco, and $682,000 of license fee revenue related to the strategic collaboration agreements for the development, manufacturing and marketing of MS-325 with Schering AG and Mallinckrodt Inc., a subsidiary of Tyco International Ltd., which we call 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 strategic 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 June 30, 2003 were approximately $123.2 million. These losses have primarily resulted from expenses associated with our research and development activities, including preclinical 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 substantial losses over at least the next several years as we expand 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 time frame 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 peripheral vascular disease imaging has occurred mainly in research and academic centers. If approved, 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 peripheral vascular system, and market acceptance both of MRA as an appropriate imaging technique for the peripheral 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.

If we do not raise additional funds necessary to fund our operations, 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, equipment lease financings and product development revenue, royalty and license payments from our strategic partners. We believe that we will need to raise substantial additional funds for research, development and other expenses, through equity or debt financings, strategic alliances or otherwise, prior to commercialization of any of our product candidates.

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 product candidates gain market acceptance;
- the timing and costs of product introductions;

the extent of our ongoing 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.

We estimate that cash, cash equivalents and marketable securities on hand as of June 30, 2003, together with further funds that may be available under the loan facility from Schering AG in May 2004, will be sufficient to fund our operations for the next 18 months. We believe that we will need to raise additional funds for research, development and other expenses through equity or debt financing, strategic alliances or otherwise, in order to reach a positive cash flow position. We have drawn $7.5 million of our $15.0 million loan facility available from Schering AG as part of our MRI research collaboration. We expect to be able to draw the remaining $7.5 million from the Schering AG loan facility in May 2004, 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, or if we receive a non-fileable letter from the FDA relating to our MS-325 NDA on or before March 1, 2004 and do not subsequently receive a fileable letter from the FDA. In the event that we are unable to draw the remaining $7.5 million from the Schering AG loan facility in May 2004, we estimate that cash, cash equivalents and marketable securities on hand as of June 30, 2003 will be sufficient to fund our operations for the next 12 months.

We have a limited manufacturing capability and we 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 do manufacture 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 sole 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 would 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 would 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, 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 peripheral vascular disease, which is our primary target indication, we believe that the technology is not as advanced for cardiac applications, which will be one of our next clinical development targets. Our initial NDA filing

for MS-325 will be related to peripheral vascular disease. Imaging sequences on scanners currently allow for the use of MS-325-enhanced MRA for diagnosing peripheral vascular disease, our lead indication. Based on feasibility studies we have conducted, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, is not developed to the point where there is clear visualization of the cardiac region, due to the effects of motion from breathing and from the beating of the heart. Although not our primary focus, we plan to continue to conduct 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 General Electric Medical Systems, Siemens Medical Systems and Phillips 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 product 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 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 plc, 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 six agents that are under clinical development for use with MRA: Schering AG's Gadovist, 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 High quality images Favorable safety profile	Requires high level of training Inadvisable for patients with cardiac pacemakers Less widely available
CTA	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 Fast Widely available Non-invasive	Operator dependent Lack of anatomic detail Bone precludes use in many vascular beds 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, General Electric Medical Systems, 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 that will compete against MS-325. Schering AG will be responsible for setting the price of MS-325 worldwide, and may not set prices in a manner that maximizes revenues to us. Although we are currently in compliance with the terms of these agreements, 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 agreements 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 General Electric Medical Systems, Siemens Medical Systems and Phillips Medical Systems, to develop software that can be used to enhance or suppress veins or arteries from MS-325-enhanced MRA images. 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 peripheral 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 MRA images and therefore may not be inclined to use the product. Our inability to market MS-325 successfully to 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 and patent applications, 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. If our license with MGH were to terminate, we would be unable to produce our product candidates, including MS-325, and our business, financial condition and results of operations would be materially adversely affected. 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 United States 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; four U.S. patents and their counterpart patents and applications in certain foreign

countries that we own; 13 U.S. patent applications, two international patent applications filed under the Patent Cooperation Treaty, and 12 U.S. provisional patent applications on 27 different subject matters as well as their counterpart applications in certain foreign countries. One of our issued patents covers aspects of the process by which MS-325 is manufactured. Two of our patents cover methods of imaging with MS-325. We have four 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, to 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 limitation in 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. In particular, we are aware that other companies that sell MRI contrast agents or MRI equipment have negotiated or settled intellectual property claims by 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. Although we are not aware that the validity of these patent claims has been established in litigation and we are not aware of the relevance of these claims to MS-325 and the "steady state" MRA, we anticipate that this individual may seek financial compensation related to the sale of MS-325.

If any judicial or administrative proceeding holds that we infringe any third party patents and that those patents are 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 any third party patent, 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 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 preclinical laboratory and animal tests; submission of an investigational new drug application, or IND to the FDA; 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. We have only limited experience in filing or pursuing applications necessary to gain regulatory approvals. Preclinical 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 peripheral 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 peripheral vascular disease in the renal arteries, and another to determine the efficacy of MS-325-enhanced MRA for the detection of peripheral 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 our Phase III clinical trial program and obtain FDA approval, we will not have a product to market.

In addition, we may encounter unanticipated delays or significant costs in our efforts to secure necessary approvals. 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 preclinical and clinical activities is subject to confirmation and

interpretation by regulatory authorities, which could delay, limit or prevent 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 preclinical 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 product candidates 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 will 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 would have a material adverse effect on our ability to market our products and consequently it would 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 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 would 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 the lives of some key officers, 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 this 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 efforts.

Risks Related to this Offering

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 first six months of 2003, the sale price of our common stock ranged from $14.32 to $6.21. The last reported sale price for our common stock on June 30, 2003 was $14.05. 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.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering.

Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase our profitability or our market value.

Our officers, directors and principal stockholders may exert significant control over our business and matters requiring stockholder approval; sales of shares by existing stockholders could adversely affect our stock price.

As of April 29, 2003, our directors, officers and stockholders holding more than 5% of our common stock beneficially owned or controlled approximately 34.4% of our outstanding common stock. Collectively, these stockholders may have the ability to significantly influence the outcome of all corporate matters requiring stockholder approval and they may vote their shares in a way with which you do not agree. In particular, this concentration of ownership may have the effect of delaying, deferring or preventing an acquisition of us and may adversely affect the market price of our common stock. In addition, shares held by our existing stockholders may be sold in the public market at any time and from time to time. If any of these stockholders sell substantial amounts of our common stock in the public market, the market price of our common stock could decline.

Because we do not intend to pay dividends, stockholders will benefit from an investment in our common stock only if it appreciates in value.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain our future earnings, if any, to finance further research and development and do not expect to pay any cash dividends in the foreseeable future. As a result, the success of an investment in our common stock will depend upon any future appreciation in its value. There is no guarantee that our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

If you purchase our common stock pursuant to this prospectus, depending on the terms of the offering, you will incur immediate dilution in the book value of your shares.

Based on our most recent balance sheet and the recent trading price of our common stock, you will incur an immediate dilution in the net tangible book value per share of our common stock purchased pursuant to this prospectus. The magnitude of this dilution will depend on the offering price per share, the total net proceeds received by us in the offering and the net tangible book value of our common stock immediately before the offering.

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 of control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These statements relate to future events or our future financial performance. In some cases,

you can identify forward-looking statements by terminology such as "may," "will," "intend," "expect," "anticipate," "believe," "estimate," "predict," "potential" or "continue" or the negative of such terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under "Risk Factors" beginning on page S-5 of this prospectus supplement, under "Risk Factors" beginning on page 3 of the accompanying prospectus and elsewhere in this prospectus supplement and the accompanying prospectus, that may cause our or our industry's actual results, levels of activity, performance or achievements to differ from those expressed or implied by such forward-looking statements. Before deciding to purchase our common stock, you should carefully consider the risks described in the "Risk Factors" sections of this prospectus supplement and the accompanying prospectus, in addition to other information set forth in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as may be required by law, we do not intend to update any of the forward-looking statements for any reason after the date of this prospectus supplement to conform such statements to actual results or if new information becomes available.

USE OF PROCEEDS

We estimate the net proceeds to us from the sale of our common stock in this offering will be approximately $69.5 million, after deducting estimated underwriting discounts, commissions and offering expenses payable by us in connection with this offering. If the underwriters exercise their over-allotment option in full, we will receive net proceeds from this offering of approximately $80.2 million.

We intend to use the net proceeds from this offering for general corporate purposes, including our research and development programs and general working capital. In addition, we may choose to repay outstanding indebtedness with a portion of the net proceeds, although we do not have any obligations or present intentions to do so. Pending the application of the net proceeds, we intend to invest the proceeds in investment grade, interest-bearing securities.

DILUTION

The net tangible book value of our common stock on June 30, 2003 was approximately $(2.0) million, or approximately $(0.11) per share. Net tangible book value per share is equal to the amount of our total tangible assets, less total liabilities, divided by the aggregate number of shares of common stock outstanding. Dilution per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of 4.3 million shares of common stock in this offering at an assumed public offering price of $17.16 per share, and after deducting estimated underwriting discounts, commissions and offering expenses, our net tangible book value at June 30, 2003 would have been approximately $67.5 million, or approximately $3.13 per share. This represents an immediate dilution of $14.03 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Assumed public offering price per share		$ 17.16
Net tangible book value per share as of June 30, 2003	$ (0.11)	
Increase per share attributable to new investors	17.27	
Net tangible book value per share as of June 30, 2003 after giving effect to this offering		3.13
Dilution per share to new investors		$ 14.03

CAPITALIZATION

The following table sets forth our capitalization as of June 30, 2003:

- on an actual basis; and
- on an as adjusted basis to give effect to our receipt of an estimated $69.5 million of net proceeds from the sale of our common stock pursuant to this offering, after deducting estimated underwriting discounts, commissions and offering expenses and application of those net proceeds as described under "Use of Proceeds."

This table should be read in conjunction with our financial statements and the notes thereto, which are incorporated by reference in this prospectus supplement and the accompanying prospectus.

	June 30, 2003	
	Actual	As Adjusted
	(unaudited)	
	(in thousands)	
Long-term debt	$ 7,500	$ 7,500
Stockholders' (deficit) equity:		
Preferred stock, $0.01 par value, 1,000,000 shares authorized, no shares issued and outstanding		
Common stock, $.01 par value, 40,000,000 shares authorized, 17,286,458 shares issued and outstanding as of June 30, 2003; and 21,586,458 shares issued and outstanding as adjusted	173	216
Additional paid-in-capital	121,029	190,511
Accumulated deficit	(123,226)	(123,226)
Accumulated other comprehensive income	48	48
Total stockholders' (deficit) equity	(1,976)	67,549
Total capitalization	$ 5,524	$ 75,049

The information in the table above does not include:

- 3,919,877 shares of common subject to options outstanding at June 30, 2003, at a weighted average exercise price of $8.45 per share;
- 932,829 shares of common stock that have been reserved for issuance upon future grants, under our stock option plans as of June 30, 2003;
- 59,720 shares of common stock available for sale under our employee stock purchase plan as of June 30, 2003; and
- up to 645,000 shares of common stock issuable upon exercise of the underwriters' over-allotment option.

PRICE RANGE OF COMMON STOCK

Our common stock is quoted on the Nasdaq National Market under the symbol "EPIX." The following table sets forth, for the periods indicated, the high and low sale prices per share of our common stock as reported on the Nasdaq National Market since January 1, 2001.

	High	Low
2001		
First Quarter	$13.88	$7.88
Second Quarter	12.35	7.06
Third Quarter	12.45	6.60
Fourth Quarter	15.20	5.90
2002		
First Quarter	$16.20	$11.48
Second Quarter	15.50	8.25
Third Quarter	10.72	3.55
Fourth Quarter	9.95	4.25
2003		
First Quarter	$8.90	$6.21
Second Quarter	14.32	7.83
Third Quarter (through July 24, 2003)	19.16	13.55

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all future earnings for the operation and expansion of our business. We do not anticipate declaring or paying cash dividends on our common stock in the foreseeable future. Any future payment of cash dividends on our common stock will be at the discretion of our board of directors and will depend upon our results of operations, earnings, capital requirements, contractual restrictions and other factors deemed relevant by our board.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes. This discussion and analysis contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors including, but not limited to, those discussed in "Risk Factors" and elsewhere disclosed in this prospectus supplement and the accompanying prospectus.

Overview

Since commencing operations in 1992, we have been principally engaged in the research and development of 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 June 30, 2003 aggregating approximately $123.2 million.

We expect continued operating losses for the next several years as we incur expenses to support research and development efforts to obtain regulatory approvals for our product candidates.

Our initial product candidate, MS-325, is currently our only product candidate undergoing human clinical trials. We filed an IND application for MS-325 in July 1996. We initiated a Phase I clinical trial in 1996 and a Phase I dose escalation study in 1997, both of which have been completed. We completed a Phase II clinical trial in June 1998 to test the safety and preliminary efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease and also completed a Phase II trial in June 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. In 2001, we completed

enrollment in the first study of a two-arm Phase III clinical trial, which was initiated in June 1999, and was designed to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease. We announced the results of this trial in March 2002. In October 2002, we announced that we had completed patient enrollment in the second of the two trials designed to detect peripheral vascular disease in the aortoiliac arteries. We announced results of this trial in March 2003. In September 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 Phase III trials to our Phase III clinical trial program, one in the renal arteries and the other in the pedal arteries. In February 2003, we announced that we had completed patient enrollment in these studies. We announced the results of these two trials in July 2003. We plan to submit a NDA to the FDA in 2003.

In March 2000, we completed enrollment in a Phase II clinical trial to test the safety and feasibility of MS-325 for detecting breast cancer, and in March 2001, we completed enrollment in a Phase II feasibility trial, which we conducted in collaboration with Pfizer to explore the efficacy of MS-325-enhanced MRA in the diagnosis of female sexual arousal dysfunction. In April 2002, we completed enrollment in our MS-325-enhanced MRA Phase II feasibility trial for coronary artery disease.

We anticipate fluctuations in our quarterly 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 associated launch, 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.

In December 2001, the U.S. Securities and Exchange Commission, or the Commission, requested that all registrants discuss their most "critical accounting policies" in Management's Discussion and Analysis of Financial Condition and Results of Operations. The Commission indicated that a "critical accounting policy" is one that is both important to the portrayal of a company's financial condition and operating results and requires management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain.

Our significant accounting policies are more fully described in Note 3 in the Notes to Condensed Financial Statements section of our Quarterly Report on Form 10-Q for the period ended June 30, 2003 and in Note 2 of our Annual Report on Form 10-K for the year ended December 31, 2002. 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, are "critical accounting estimates and judgments."

Revenue Recognition

In 2000, we adopted SEC Staff Accounting Bulletin No. 101, or SAB 101, "Revenue Recognition in Financial Statements" retroactively to January 1, 2000, changing our method of recognizing revenue. Under SAB 101, we recognize revenues from non-refundable license fees and milestone payments not specifically tied to a separate earning process ratably over the period during which we have substantial continuing obligations to perform services under the contract. 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 can become reasonably estimable. These adjustments could have a material effect on our results of operations. Within the last year we have increased the estimated time period over which we will provide services under the Tyco/Mallinckrodt agreement several times from an original estimate of 89 months to a current estimate of 99 months, resulting in a reduction in revenue of approximately $163,000 for the first six months of 2003.

Payments received from Schering AG for development cost sharing obligations are recorded as revenue when the underlying costs are incurred. Non-refundable payments received for which revenue has not been earned are recorded as deferred revenue. Contract advances represent refundable amounts received in advance of services rendered.

Royalty revenues are recognized based on actual revenues as reported to us by Bracco. When actual results are not available, we estimate royalty revenues based on Bracco's estimates of 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 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, frequently one to three years. Typically, we enter into two types of vendor contracts, time based and patient based. Under a time based contract, using critical factors contained within the contract, typically 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 received. 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 because the alternative fair value accounting provided for under Statement of Financial Accounting Standards, or SFAS, No. 123, "Accounting for Stock-Based Compensation," as amended by SFAS No. 148, requires use of option valuation models that were not developed for use in valuing employee stock options. Under APB 25, when the exercise price is greater than or 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 would 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.

Results of Operations

Six Months Ended June 30, 2003 Compared to Six Months Ended June 30, 2002

Revenues

Revenues for the six months ended June 30, 2003 and 2002 were $7.3 million and $5.8 million, respectively. Revenues for the six-month period ended June 30, 2003 consisted of $5.3 million of product development revenue from Schering AG, $1.3 million of royalty and license fee revenue related to the Bracco agreement and $682,000 of license fee revenue related to the Schering AG and Tyco/Mallinckrodt strategic collaboration agreements for the development and marketing of MS-325. The increase in revenues of $1.5 million for the six months ended June 30, 2003 compared to the same period last year primarily related to product development revenue from the recently signed collaboration agreement with Schering AG for EP-2104R and to increased royalties from Bracco.

Research and Development Expenses

Research and development expenses for the six months ended June 30, 2003 were $13.3 million as compared to $14.4 for the same period in 2002. The decrease of $1.1 million was primarily attributable to decreased costs related to the completion of Phase III clinical trial program

for MS-325 and to lower spending on our thrombus program, partly offset by higher spending on our other MRI research programs.

General and Administrative Expenses

General and administrative expenses were $3.2 million for the six months ended June 30, 2003 as compared to $3.0 million for the six months ended June 30, 2002. The increase of $116,000 was primarily attributed to higher legal costs related to the Schering AG agreements and to directors and officers insurance. General and administrative expenses also include royalties payable to MGH, based on sales by Bracco of MultiHance. Royalty expenses totaled $50,000 and $33,000 for the six months ended June 30, 2003 and 2002, respectively.

Interest Income and Interest Expense

Interest income for the six months ended June 30, 2003 was $229,000 as compared to $618,000 for the six months ended June 30, 2002. The decrease of approximately $389,000 was primarily due to lower average levels of invested cash, cash equivalents and marketable securities and to lower interest rates. We classify net realized gains and losses in interest income. During the six months ended June 30, 2003 and 2002, there were no realized gains or losses on marketable securities. Interest expense for the six months ended June 30, 2003 and 2002 was $102,000 and $192,000, respectively. The decrease in interest expense resulted from lower interest rates during the six-month period ended June 30, 2003 applied to the royalty advances from Bracco.

Provision for Income Taxes

The provision for income taxes, which represents Italian income taxes related to the Bracco agreement, was $66,000 for the six months ended June 30, 2003 as compared to $44,000 for the six months ended June 30, 2002. The higher foreign income tax expense is directly attributed to higher royalty revenues from Bracco.

Year Ended December 31, 2002 Compared to Year Ended December 31, 2001

Revenues

Revenues for the years ended December 31, 2002 and 2001 were $12.3 million and $9.6 million, respectively. Revenues for 2002 consisted of $8.7 million of product development revenue from Schering AG, $1.6 million of royalty and license fee revenue related to the Bracco agreement and $2.0 million of license fee revenue related to the Schering AG and Tyco/Mallinckrodt strategic collaboration agreements for the development and marketing of MS-325. The increase in revenue of $2.7 million is primarily related to product development revenue from Schering AG.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2002 were $29.1 million as compared to $22.9 million for 2001. The increase in 2002 of $6.2 million was primarily attributable to increased costs associated with research and development personnel and clinical trials related to the advancement of MS-325 through Phase III clinical trials and to increased costs for personnel and other resources to support research and development for our potential discovery phase products.

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 $6.0 million for the year ended December 31, 2002 as compared to $5.5 million for the year ended December 31, 2001. The increase in 2002 of $495,000 was primarily due to increased MS-325 marketing costs and personnel costs. General and administrative expenses also included royalties payable to MGH based on sales by Bracco of MultiHance. Royalty expenses totaled $74,000 and $103,000 for the years ended December 31, 2002 and 2001, respectively.

Interest Income and Interest Expense

Interest income for the year ended December 31, 2002 was $1.1 million as compared to $1.0 million for the year ended December 31, 2001. The increase of approximately $100,000 was primarily due to realized gains from the sale of marketable securities and higher average levels of

invested cash, cash equivalents and marketable securities, partly offset by lower interest rates. Net realized gains on marketable securities, which are included in interest income, were $156,000 for the year ended December 31, 2002 as compared to none for year the ended December 31, 2001. Interest expense for the year ended December 31, 2002 was $362,000 as compared to $339,000 for the year ended December 31, 2001. This increase in interest expense in 2002 was the result of a full year of interest paid to Bracco under the Bracco agreement.

Provision for Income Taxes

The provision for income taxes, which represents Italian income taxes related to the Bracco agreement, was $94,000 for the year ended December 31, 2002 as compared to $1.1 million for the year ended December 31, 2001. The higher foreign income tax expense in 2001 of approximately $1.0 million is directly attributable to the receipt of $10.0 million from Bracco in September 2001 upon the execution of the worldwide license agreement with Bracco. Any future payments received from Bracco are subject to Italian income tax withholding.

Liquidity and Capital Resources

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities of $25.7 million at June 30, 2003 as compared to $28.1 million at December 31, 2002.

We used approximately $11.1 million of net cash to fund operations for the six months ended June 30, 2003 compared to $11.6 million for the six months ended June 30, 2002. A net loss of $9.1 million, combined with a reduction in deferred revenue of $1.3 million and contract advances of $741,000 resulting both from the annual reconciliation of advances from Schering AG and lower funding of research and development costs for MS-325 by Schering AG in the second quarter of 2003, primarily accounted for the net cash used in operations during the six-month period ended June 30, 2003.

Our investing activities resulted in net cash provided of $13.2 million for the six months ended June 30, 2003 as compared to net cash used of $27.2 million for the six months ended June 30, 2002. For the six months ended June 30, 2003, we generated cash from the sales and redemption of $13.3 million of available-for-sale marketable securities. During the same period last year, we purchased approximately $40.5 million of available-for-sale marketable securities, with most of the proceeds coming from our January 2002 common stock offering, and the sale or redemption of available-for-sale marketable securities of $14.0 million. Other investing activities included capital expenditures of $94,000 for the six months ended June 30, 2003 as compared to $701,000 for the six months ended June 30, 2002. Our capital expenditures primarily consist of purchases of property and equipment,

including lab equipment, computer equipment and software. We expect that our capital expenditures may increase in the future as we continue to enhance and expand our principal lab space.

Cash provided by financing activities was $8.8 million for the six months ended June 30, 2003. The primary sources of financing for the six months ended June 30, 2003 were the $7.5 million in loan proceeds from Schering arising from our MRI research collaboration completed in May 2003 and proceeds from stock option exercises of $1.3 million. This compares with net proceeds of approximately $31.0 million for the six months ended June 30, 2002, which came primarily from the issuance and sale of 2.575 million shares of our common stock in January 2002, pursuant to our previously filed shelf registration statement.

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 MRI research collaboration. We also receive royalty payments from Bracco on a quarterly basis for their sales of MultiHance and monthly interest income on our cash, cash equivalents and available-for-sale marketable securities. Additional future cash flows from our MS-325 collaboration with Schering AG depend on the successful filing of a NDA, the FDA's approval of that filing and product launch of MS-325, and includes up to $25.75 million in milestone payments from Schering AG and 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, and may include up to $15.0 million in milestone payments and royalties. 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 Eovist® product if it is approved for sale by the FDA or international regulatory authorities pursuant to a license agreement with Schering AG.

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 and $2.4 million we owe Daiichi in December 2003 under the terms of our

reacquisition agreement with Daiichi. Other potential future outflows depend on the successful filing of a NDA, FDA approval and product launch of MS-325, which include $5.0 million of milestone payments due Tyco/Mallinckrodt, 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 $2.5 million at June 30, 2003, upon termination of our license agreement with Bracco, plus up to an additional $3.0 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.

We estimate that cash, cash equivalents and marketable securities on hand as of June 30, 2003 together with further funds that may be available under the loan facility from Schering AG in May 2004 will be sufficient to fund our operations for the next 18 months**.** We believe that we will need to raise additional funds for research, development and other expenses through equity or debt financing strategic alliances or otherwise in order to reach a positive cash flow position. We have drawn $7.5 million of our $15 million loan facility available from Schering AG as part of our MRI research collaboration. We expect to be able to draw the remaining $7.5 million from the Schering AG loan facility in May 2004, 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 or if we receive a non-fileable letter from the FDA relating to our MS-325 NDA on or before March 1, 2004 and do not subsequently receive a fileable letter from the FDA. In the event that we are unable to draw the remaining $7.5 million from the Schering AG loan facility in May 2004, we estimate that cash, cash equivalents and marketable

securities on hand as of June 30, 2003 will be sufficient to fund our operations for the next 12 months. 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 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. In the second quarter of 2002, we signed a lease agreement that increased our future lease commitments by $3.4 million that will enable us to utilize our current principal scientific facilities through December 31, 2007. We also have a lease for nearby office space, which expires in October 2003. If we are unable to extend the lease, we expect that adequate alternative space will be available at acceptable terms.

Our major outstanding contractual obligations relate to our facilities leases and our present obligations to strategic partners. We did not include any commitments for obligations due on our commercial contracts or clinical trial programs since most of our commercial contracts or clinical trial programs contain termination clauses, exercisable by either party, which limit potential future obligations.

Below is a table that represents our contractual obligations and commercial commitments as of June 30, 2003:

		Payments due by period			
	Total	Remaining six months of 2003	2004	2005	2006 & beyond
Operating leases	$ 3,723,169	$ 682,660	$ 823,105	$ 746,184	$ 1,471,220
Accrued reacquisition costs	2,400,000	2,400,000			
Long-term debt	7,500,000				7,500,000
	$ 13,623,169	$ 3,082,660	$ 823,105	$ 746,184	$ 8,971,220

We have incurred tax losses to date and therefore have not paid significant federal or state income taxes since inception. As of December 31, 2002, we had net operating loss carryforwards of approximately $98 million available to offset future taxable income. These amounts expire at various times through 2022. 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 will 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.

BUSINESS

Overview

We are a leading developer of targeted contrast agents, designed to improve the diagnostic quality of images produced by magnetic resonance imaging. Our principal product under development, MS-325, is designed to provide visual imaging of the vascular system, through MRA. We believe that MS-325-enhanced MRA has the potential to improve the diagnosis of multiple diseases of the vascular system, including 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 magnetic resonance angiographic imaging of peripheral vascular disease. 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. We believe that MRA will be a less invasive method of imaging a patient's vascular anatomy for the evaluation of disease.

We have completed enrollment in and reported preliminary results for a Phase III clinical trial program designed to test the safety and efficacy of MS-325-enhanced MRA. All four trials in the Phase III program for MS-325 met their primary endpoints. We plan to submit a NDA for MS-325 to the FDA, in 2003. In collaboration with Schering AG, we expect to make analogous regulatory filings in Europe in 2004.

We have entered into strategic alliances with Schering AG, and Tyco/Mallinckrodt, for the development, manufacture and commercialization of MS-325 and other vascular contrast agents. We have also formed collaborations with the three leading MRI scanner manufacturers, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems to develop advanced imaging techniques and tools designed to facilitate the use of MS-325-enhanced MRA.

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 tissue in the body, its use in imaging the vascular system has been limited. Currently available MRI contrast agents were designed for general use and have not been approved by the FDA for use in MRA. The use of MRA with currently available contrast agents has been limited as a diagnostic tool for vascular disease by rapid leakage of the contrast agent into tissue outside the vascular system. As a result, the time available to image blood vessels with currently approved contrast agents, none of which is approved by the FDA for this use, 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.

As part of our thrombus program, we are developing a second targeted contrast agent that would enable MRI to illuminate blood clots by making them appear as identifiable bright spots on MRI images. Such a product could potentially change the method of diagnosis for many of the conditions associated with the formation of blood clots in the arteries and veins. We believe that the illumination of blood clots by a targeted contrast agent used in conjunction with MRI could lead to better medical outcomes due to earlier and more definitive diagnosis of diseases relating to clots. Early diagnosis is especially important for clots in the heart, neck, thigh and pelvis, which can be fatal because of their increased likelihood of migrating to the brain, heart or lungs. We believe that such a contrast agent could eliminate the need for procedures that require the use of large quantities of X-ray contrast dye and expose patients to radiation, and be more accurate than diagnostic tests that use radioactive drugs and ultrasound, which are all currently used to identify blood clots in the veins and arteries. We have

selected a compound, EP-2104R, for further development as a thrombus agent in our thrombus program. We designed EP-2104R to bind reversibly to fibrin, the dominant protein found in clots. In preclinical studies, EP-2104R has been shown to enhance the ability of MRI to image

clots. We expect to continue to apply resources to the thrombus program in the future and plan to commence human trials in 2004. In May 2003, we entered into a collaboration agreement with Schering AG for EP-2104R.

Cardiovascular Disease

The human cardiovascular system consists of the heart and the vasculature, a vast network of arteries and veins that carry blood throughout the body. Cardiovascular disease, a broad class of diseases affecting the heart and vasculature, is the number one cause of death in the U.S., with approximately 950,000 fatalities each year. One out of every 2.5 deaths in the U.S. is attributed to cardiovascular disease and it is estimated that over 61 million Americans suffer from some form of this disease.

Atherosclerosis is one of the most common forms of cardiovascular disease. This condition refers to the accumulation of fatty plaques in the inner lining of blood vessels, resulting in a thickening or hardening of affected vessels. As the disease progresses, the arteries can become weakened or increasingly narrowed, thereby reducing blood flow to vital organs, including the heart and brain. This condition is often characterized by the vascular region in which it is diagnosed. Coronary artery disease, for example, refers to disease in the arteries in the heart, while peripheral vascular disease refers to disease in the major vessels outside the heart: vessels of the head and neck, the aorta, arteries supplying blood to the kidneys and other organs, and the large vessels of the pelvis, legs, feet and arms. Recent research in cardiovascular disease has begun to highlight the systemic nature of this condition. Because the major risk factors tend to affect all vascular regions, many patients have multiple clinical symptoms of cardiovascular disease. Therefore, patients diagnosed with cardiovascular disease in one vascular region are at high risk of having disease in another vascular region.

Clinicians have also begun to realize the importance of characterizing atherosclerotic plaques once they have been identified. Even in arteries where significant narrowing has not yet occurred, vulnerable plaques may rupture, causing a blood clot to form, which can result in heart attack, stroke and death. We believe that the ability to characterize plaques may allow physicians to identify those regions of cardiovascular disease that present the most immediate threat to patients' health and that MS-325 will aid in the evaluation of the disease.

The consequences of cardiovascular disease can be severe and often include one or more of the following:

Aortic Aneurysm. The aorta is the main artery that carries blood from the heart to the rest of the body. Degenerative changes in the arterial wall often result in the enlargement or bulging of the lower part of this vessel, known as abdominal aortic aneurysm. Individuals with this condition are at serious risk that the aneurysm will rupture, causing life-threatening bleeding. There are an estimated 200,000 cases of abdominal aortic aneurysm diagnosed each year in the U.S. Because this condition can exist without symptoms for many years, many physicians have begun to consider the merits and cost-effectiveness of routine screening programs for this disease for patients deemed at risk.

Heart Attack and Chest Pain. The coronary arteries supply blood to the heart muscle, or myocardium. When these arteries are narrowed or clogged due to atherosclerotic buildup, the result can be chest pain, known as angina pectoris, or heart attack, known as myocardial infarction. This condition, known as coronary heart disease, is estimated to afflict 12.9 million Americans. Coronary heart disease is responsible for approximately 500,000 deaths each year in the U.S.

Hypertension. Hypertension, or high blood pressure, refers to the constriction of blood vessels, which causes the heart to work harder to supply blood to the body. This condition, which significantly elevates an individual's risk of heart attack or stroke, afflicts approximately fifty million individuals in the U.S. Renal hypertension, caused by blockages of the arteries that carry blood to the kidneys, can result in kidney failure and is estimated to account for up to ten percent of all cases of hypertension. Early diagnosis can be extremely helpful for patients with hypertension as a result of atherosclerosis in the renal arteries because it can be treated surgically or by other interventional procedures. However, conventional X-ray angiography, the current definitive diagnostic procedure for this condition, carries elevated risk for patients with renal impairment due to the toxicity of the X-ray dye used in that procedure.

Ischemic Stroke. Blocked arteries in the head and neck can prevent areas of the brain from receiving the necessary blood supply, potentially leading to ischemic stroke. Individuals with atherosclerosis are at increased risk of suffering such blockages due to atherosclerotic buildup in these arteries or, more commonly, from plaques originating in other areas which have broken off and lodged in these vessels. Approximately 85% of the 700,000 strokes each year in the U.S. are a result of atherosclerotic disease which leads to an obstruction of a blood vessel supplying blood to the brain.

Limb Loss. Atherosclerotic blockages in the arteries of the pelvis and legs can lead to ischemia, which is lack of oxygen, or infarction, which can cause death of tissue in these areas. Complications from atherosclerotic disease in these vessels include pain, limitations in mobility, and amputation of the extremities. Each year approximately 100,000 amputations are performed in the U.S. primarily due to the complications of cardiovascular disease.

Diagnosing Cardiovascular Disease

Cardiovascular disease is currently diagnosed using a number of different modalities, including pressure tests, conventional X-ray angiography, computed tomography, ultrasound, intravascular ultrasound, nuclear medicine and MRI. These modalities are often classified as either "screening" or "definitive" according to their role in the diagnostic pathway. Screening procedures are typically used early in the diagnostic evaluation to rule out certain conditions and assist physicians in determining subsequent diagnostic testing. Screening procedures tend to be relatively inexpensive and non-invasive. Physicians rely on definitive diagnostic procedures, however, to provide them with the information required to make final diagnosis and plan treatment. Because of the importance of this definitive information, physicians are willing to use costlier, more invasive modalities.

Screening for Vascular Disease

A patient with vascular disease may exhibit a wide range of symptoms, including: leg pain, gangrene, hypertension, stroke and transient ischemic attack, which is a brief episode of cerebral ischemia usually characterized by blurred vision, slurred speech, numbness or paralysis. The appropriate screening tests vary according to the particular disease indication. In the work-up of vascular disease of the legs or feet, for example, ultrasound is often performed to confirm the location of disease once it has been detected by non-imaging techniques. In general, traditional screening modalities for peripheral vascular disease most commonly ultrasound and renal nuclear exams tend to have poor image quality and frequently lead to inconclusive exams.

Screening for Coronary Artery Disease

Typically, a patient enters the diagnostic pathway for coronary artery disease after experiencing chest pain or shortness of breath. If the patient cannot be ruled out for this condition after the initial

work-up that includes a physical exam, patient history, electrocardiogram and exercise stress test, a cardiologist will often perform a stress echocardiogram and/or a nuclear stress perfusion study.

Stress Echocardiograms. Stress echocardiograms use ultrasound to measure motion of the walls of the heart under physical or pharmacological stress. In most cases, a lack of blood flow to a particular area of the heart will be highlighted by atypical motion of the heart wall. While a normal stress echocardiogram usually eliminates the possibility of blockages that significantly decrease blood flow, the test is often inconclusive and provides no information on the anatomy of the coronary arteries. We estimate that over 2.3 million stress echocardiograms were performed in the U.S. in 2002.

Nuclear Stress Perfusion Studies. Nuclear stress perfusion studies measure the flow of blood to cardiac tissue, and can be used either as the critical diagnostic test prior to conventional X-ray angiography or to confirm the impact on blood flow of an intermediate blockage identified through conventional X-ray angiography. Nuclear stress perfusion tests are non-invasive and use small quantities of radiation. A patient is injected with a radioactive agent and then a radiation sensitive camera is used to detect uptake of the agent in the heart muscle. A deficiency in blood flow to particular regions of the heart is shown in the resulting images. While the test can identify the effects of coronary artery disease, it provides no information about the anatomy of the coronary arteries and it cannot determine the location of blockages. We estimate that over 5.8 million nuclear stress perfusion studies were conducted in the U.S. in 2002.

Definitive Diagnosis of Atherosclerotic Disease

X-ray Angiography

Conventional X-ray angiography is currently considered to be the definitive diagnostic exam for imaging arterial anatomy in patients with suspected peripheral vascular disease or coronary artery disease. Invented in the 1920's, an X-ray angiogram involves the insertion of a catheter through a puncture of the femoral artery in the patient's groin. Once the catheter is placed in the artery, X-ray dye is injected into the bloodstream and an image is acquired of the relevant vascular region. Conventional X-ray angiography does not always provide sufficient information for clinical decision-making, particularly in the coronary arteries: while X-ray angiography identifies the location of arterial blockages, in many cases it cannot conclusively determine the impact of these blockages on blood flow. Therefore, for many blockages, additional studies must be performed to enable the physician to make a definitive diagnosis. Based on available procedure data, we estimate that over 4.6 million X-ray angiograms were performed in the U.S. in 2002, of which approximately 2.7 million were coronary angiograms. X-ray angiography has a number of undesirable characteristics for a diagnostic tool, including:

Invasiveness of procedure requires extended recovery time;

Significant risk of serious complications including limb loss, kidney failure, stroke and death;

Exposure of patients to potentially harmful ionizing radiation that can cause tissue damage;

Because X-ray dye is toxic in the kidneys, the large volumes of dye necessary to perform an X-ray angiogram may cause severe reactions;

Separate exams necessary to view both arteries and veins;

Separate exams necessary for each vascular region;

Provides only two-dimensional images;

Relatively expensive ($1,500-$3,000 for peripheral angiograms, $3,000-$6,000 for coronary angiograms);

Cost and invasiveness limit post-procedure patient follow-up; and

Inability to distinguish atherosclerotic plaques.

Computed Tomography

Another modality currently being investigated as a potential diagnostic tool for imaging blood vessels is computed tomography, or CT, which is primarily used to image solid organs. Although it does not require an arterial puncture, computed tomographic angiography, or CTA, requires the use of large quantities of toxic X-ray dye and exposes patients to radiation, which limits the number of vascular regions it can image in an exam. CTA has shown recent success in imaging the coronary arteries as a result of its speed, but its use remains limited. A specialized form of CT, electron beam CT, is approved in the U.S. for angiographic imaging but has had limited impact on clinical practice due to the low number of electron beam CT scanners installed and its use of toxic X-ray dye and radiation. CT is also being investigated for use in detecting calcium deposits in the coronary arteries, a surrogate often advocated as predictive of atherosclerotic disease in that region. While extremely sensitive, this technique lacks specificity for atherosclerosis and frequently results in the false diagnosis of disease. Approximately 670,000 CTA procedures were performed in the U.S. in 2002.

MRI

MRI has been established as the imaging technology of choice for a broad range of applications, including brain tumors, knee injuries and disorders of the head, neck and spine. MRI is performed by placing a portion of the patient's body in a magnetic field and applying safe, low-energy radio waves. The different organs and tissues in the body respond uniquely to the electromagnetic field within the MRI scanner, and

these responses can be captured and converted into high-resolution three-dimensional images. When a contrast agent is used, it is injected into a vein in the patient's arm prior to an MRI exam to amplify the signal from the desired anatomical structure. It is estimated that contrast agents are used in 26% of all MRI exams performed in the U.S. MRI scanners are characterized by the strength of the magnetic field they generate. Typical MRI scanners-those most commonly found in hospitals-generate a relatively strong magnetic field and therefore require significant infrastructure for installation. Low-field scanners, whose magnetic fields are less than one-third the strength of traditional scanners, are often found in out-patient settings due to their relatively low cost and infrastructure requirements. The trade-off for low-field MRI scanners is that a decrease in the strength of the magnetic field results in a decrease in the MRI signal detected, which typically results in reduced image quality.

While the use of MRA is expanding among experts, it has not made a significant impact on the diagnosis of cardiovascular disease to date, with the exception of arterial studies of the head and neck. Non-contrast MRA exams of the vascular system, which image blood flow, are often ineffective when used in patients with cardiovascular disease, because of the minimal blood flow or turbulent blood flow associated with this condition. Even for the imaging of carotid arteries in the neck, where flow-based MRA has had some clinical impact, the lack of direct anatomic data limits the ability of MRA to provide a quantitative measurement of stenosis required for accurate diagnosis. MRA exams using existing general use contrast agents are limited by the rapid diffusion of the agents out of the vascular system, which reduces the time during which an image can be acquired. Consequently, many experts believe MRI contrast agents that remain in the bloodstream for extended periods of time will be necessary to attain widespread use of MRI to image the vascular system. Of the 2.2 million MRAs performed in the U.S. in 2002, approximately 77% were for imaging cerebral and carotid arteries where MRA is less technically challenging than in other regions of the body. We believe that MS-325, by providing a longer imaging window, allowing visualization of multiple arterial beds and making MRA easier to perform, has the potential to become the contrast agent used in a significant portion of MRAs currently performed with general use contrast agents.

Plaque Characterization

Recent research suggests that plaques associated with regions of vessel wall inflammation may be at increased risk of rupture and are consequently more likely to present immediate risk to patients. The one modality currently used to characterize the content and/or shape of arterial plaques is known as intravascular ultrasound, or IVUS. An IVUS exam requires the insertion of a relatively large catheter, i.e., larger than an X-ray angiographic catheter, equipped with an ultrasound transducer through an arterial puncture in the femoral artery. These procedures, which are more invasive than conventional X-ray angiograms, are not commonly used in the U.S. due to the elevated risk of complications.

Summary

In summary, the current process for diagnosing cardiovascular disease is a complicated pathway that typically involves subjecting patients to risky and invasive procedures before a definitive diagnosis can be rendered. We therefore believe that there is significant clinical need for a highly accurate, minimally-invasive exam that provides more comprehensive diagnostic information about the cardiovascular system.

Our Approach To Cardiovascular MRI

Our lead product under development, MS-325, is an injectable intravascular contrast agent intended to enhance the quality of MRI images and provide physicians with a superior method for diagnosing cardiovascular disease. Unlike most currently available general use MRI contrast agents, which are non-specific and rapidly leak out of the arteries and veins, MS-325 binds reversibly to albumin, the most common protein in the blood. Because of its affinity for albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam and, therefore, provides the image acquisition time and signal strength needed to obtain a high resolution image of the cardiovascular system. These images are intended to provide sufficient anatomical detail for definitive diagnosis and surgical planning.

We believe that MS-325-enhanced MRA may facilitate several clinically valuable diagnostic procedures, as described below.

MS-325-Enhanced Angiography

We believe that MS-325-enhanced MRA will be used to diagnose cardiovascular disease and has the potential to replace a significant portion of the estimated 4.6 million conventional X-ray angiograms performed each year in the U.S. In particular, we believe MS-325-enhanced MRA has the following advantages over conventional X-ray angiography:

Safety. X-ray angiography is an invasive, catheter-based procedure that exposes patients to significant risk of serious complications due to femoral puncture and the insertion of a catheter. MS-325-enhanced MRA, on the other hand, is a minimally-invasive exam requiring only an intravenous injection of MS-325. In addition, MRA using MS-325 involves only safe, low-energy radio waves rather than potentially harmful radiation associated with conventional X-ray procedures.

Arterial and Venous Information in a Single Exam. Because MS-325 circulates in the blood for an extended period, it gives MRI the potential to capture image data of both arteries and veins in a single exam. While imaging arteries is necessary for identifying and locating disease, imaging of the veins plays a crucial role in identifying veinous structures suitable for use in bypass grafts and is useful for planning catheter-based interventional procedures. Veins can be separated from arteries in MS-325-enhanced MRAs using software being developed by various scanner manufacturers. X-ray technology requires separate exams to image arteries and veins.

Multiple Vascular Bed Imaging. Whereas X-ray angiography captures data over a limited vascular region, we expect MS-325-enhanced MRA to provide clinicians with the ability to capture images of many vascular areas in a single exam. We believe that a multiple vascular bed MR angiogram with a single injection of MS-325 will be particularly well suited for the diagnosis of cardiovascular disease, given the systemic nature of this condition.

Three-dimensional Images. MS-325-enhanced MRA captures three-dimensional data that can be manipulated by physicians for optimal visualization of the vessels being examined. These three-dimensional data sets will allow physicians to rotate, zoom in and "fly through" images in order to identify cardiovascular disease.

Cost-Effectiveness. Because it will be performed outside the surgical setting, MS-325-enhanced MRA is likely to cost significantly less than X-ray angiography. We estimate that a multiple vascular bed MRA exam with MS-325 will cost between $500 and $1,000, roughly one-third the cost of an X-ray angiogram of a single vascular region.

Patient Monitoring. After a therapeutic intervention for cardiovascular disease such as angioplasty or bypass graft, optimal patient management often includes follow-up exams, to look for recurring blockages, or restenosis, as well as proper functioning of grafts. Due to the risk, discomfort and expense associated with X-ray angiography, follow-up imaging currently is limited. As a result, undiagnosed restenosis and other complications can lead to increased patient management costs and poorer outcomes. We estimate that there are currently over two million patients who have undergone a coronary angioplasty procedure and over two million patients who have undergone a coronary bypass graft who are potential candidates for a periodic reexamination. In addition, we believe that MS-325-enhanced MRA may have potential utility to monitor the success of therapeutic treatments designed to affect the proliferation, or angiogenesis, of micro-vessels designed to help cure coronary artery disease.

Plaque Characterization. MS-325-enhanced MRA research has demonstrated potential utility for visualizing the walls of arteries as well as the interior, or lumen, of these vessels. This unique feature may allow precise determination of plaque shape. We believe that MS-325-enhanced MRA may further enable clinicians to identify regions of inflammation in vessel walls due to the elevated concentration of albumin in these areas. We therefore believe that MS-325-enhanced MRA may potentially help clinicians identify those plaques whose shape and proximity to vessel wall inflammation make them more likely to pose health risks to patients.

Low-Field MR Angiography

We believe that the extended blood residence time of MS-325 will prove particularly beneficial in facilitating the use of low-field MRI scanners for diagnosing cardiovascular disease. These scanners, which account for approximately 36% of the installed base of MRI scanners in the U.S., offer several potential advantages over traditional scanners: they are relatively inexpensive, they use open configurations for improved patient comfort, they can be portable, they are compatible with nearby electronic equipment, and they can enable MRI for patients with pacemakers. However, low-field scanners do not currently provide the resolution required for clinically useful vascular studies. Because of its high signal at low magnetic field strengths, MS-325 may enable low-field MRI scanners to perform high-resolution imaging of the vasculature. This would potentially allow relatively inexpensive MRI exams to be performed in outpatient settings, such as physician offices and freestanding imaging centers.

Integrated Cardiac Exam

We believe that MS-325, coupled with anticipated advances in software and hardware for MRI equipment, will enable physicians to use MRI to perform a minimally-invasive, integrated cardiac exam for the diagnosis of coronary artery disease. Such a procedure would be designed to provide information on coronary artery anatomy, including location of arterial blockages, as well as cardiac perfusion and cardiac function data, in one sitting early in the diagnostic work-up. Because the procedure is intended to provide physicians with more comprehensive diagnostic information at an earlier stage of the diagnostic work-up, physicians would be able to make a more informed diagnosis, and therefore arrange for appropriate patient treatment, sooner than would otherwise be possible, thereby potentially achieving better patient outcomes at a lower cost. We believe that over half of the patients in the U.S. who enter the diagnostic pathway for coronary artery disease each year would be candidates for such an integrated cardiac exam.

Other Cardiovascular Applications

We are currently investigating the potential utility of MS-325-enhanced MRI for a number of additional applications related to cardiovascular disease, including myocardial perfusion imaging which measures blood flow to cardiac tissue.

Beyond Cardiovascular

MRI Additional Applications

We believe MS-325-enhanced MRA will find significant clinical utility beyond the diagnosis of cardiovascular disease. Because of its potential for high-resolution imaging of the vasculature, for example, MS-325 may be useful in diagnosing several conditions involving damaged or abnormal microvessels such as cancer. In addition, as it is targeted to albumin, MS-325-enhanced MRA may play a role in diagnosing conditions which result in regions of atypical albumin concentration such as inflammation due to infection or due to rheumatoid diseases such as arthritis or lupus.

Technology Platform

Our product candidates are small molecule chelates, which are soluble metal-organic complexes, containing a magnetically active metal element, gadolinium, which elicits a strong MRI signal. We have designed our product candidate molecules based on their chemical, pharmacological and biophysical attributes and profile. Our compounds must be safe, easily eliminated from the body, and display a useful distribution pattern in the body. At the same time, these agents must elicit the strongest possible effect on the local magnetic properties of tissue. Our scientists specialize in discovering and patenting useful ways to combine these two disparate areas of investigation. Specifically, we believe our ability to design targeted MRI contrast agents is a result of our expertise in targeting, MRI signal generation and image acquisition and 3-D visualization.

Targeting

We develop metal complexes that are engineered to bind to particular proteins in the body. This binding causes increased concentration and retention of the contrast agent in the specific tissues and fluids that contain the targeted molecules. Our objectives in designing such agents are to choose the best target the protein or cell type that most precisely characterizes the relevant disease state and to identify a chemical structure that binds to that target without binding to other molecules in the body. The chemical structure of MS-325, for example, is designed to bind selectively to albumin, the most common blood protein, which keeps the agent localized within the bloodstream. In designing our MR agent for use in our thrombus program, we have used combinatorial chemistry to select a family of highly specific peptides that bind to fibrin, the dominant protein inside clots, without binding to

fibrinogen, a similar, but far less clot-specific protein in blood. We have considerable expertise in peptide synthesis and in labeling the peptides with strongly enhancing clusters of gadolinium.

MRI Signal Generation

A key part of our biophysical technology platform is receptor-induced magnetic enhancement, or RIME. Developed by Dr. Randall Lauffer, our founder and Chief Scientific Officer, while at MGH, RIME is now exclusively licensed by us under patents held by MGH. The binding of a RIME agent to its receptor reduces the rate at which the agent rotates in solution. This reduced rotation rate leads to a complex magnetic effect whereby the agent's signal-enhancing characteristics are substantially increased, resulting in a stronger signal during MR scans. For MS-325, RIME effects result in an up to 10-fold increase in signal relative to non-specific gadolinium agents. We also have technology for the synthesis of discrete, compact clusters of gadolinium chelates to increase the signal from a single targeting molecule. This involves the use of both chemistry and biophysics to maintain the RIME effect.

Image Acquisition and 3-D Visualization

We have also developed significant expertise in the translation of raw MRI data into clinically useful three-dimensional images. MRI is the most flexible of the major medical imaging technologies. The hardware and software of most MRI scanners allow an enormous range of data acquisition methods, and, increasingly, methods for displaying and interpreting the resulting medical images. Through our research and development, extensive academic collaborations and industrial partnerships, we have built a deep understanding of the relationships between the contrast agent biophysics, scanner engineering, and medical practice. Our expertise allows us not only to create the best images for our agents in development, but is critical for optimizing the clinical usefulness of future MRI agents.

Our Products and Development Programs

MS-325

Our lead product candidate, MS-325, is a targeted intravascular contrast agent intended for use with MRI. 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 MR images. MS-325 is designed with our proprietary technology to bind reversibly to albumin, the most common blood protein. 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 image acquisition time and signal strength required to obtain a high resolution image of multiple regions of the vascular system. Like most currently available general use contrast agents, MS-325 is designed to be safely eliminated through the kidneys over time.

Lead Indication MRA of Peripheral Vascular Disease

We have completed enrollment in and reported preliminary results for a four-part Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease. All four trials in the Phase III program for MS-325 met their primary endpoints.

In September 2001, we completed enrollment in the first of two Phase III trials designed to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease, a common form of vascular disease in the lower abdomen and pelvic regions. We reported preliminary results of this trial in March 2002 at the American College of Cardiology conference. The trial met its primary clinical endpoint, which was an improvement in accuracy of MS-325-enhanced MRA versus

that of non-contrast MRA, with each of three blinded radiologist readers showing improvement in accuracy with a p-value less than 0.001. In our Phase III studies, as in many other such studies, the statistical significance of clinical results is determined by a widely used statistical method that establishes the p-value of clinical results. A p-value less than 0.001 means that the likelihood of the improvement in accuracy occurring by chance is less than one in one thousand. The trial demonstrated that MS-325-enhanced MRA compared favorably to conventional X-ray angiography, the current reference standard, achieving 88% accuracy in identifying clinically significant arterial narrowing or stenoses caused by atherosclerotic disease. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 90%.

In October 2002, we completed enrollment in the second of the two Phase III trials for the detection of aortoiliac occlusive disease. We reported preliminary results of this trial in March 2003 at the European Congress of Radiology. The trial met its primary clinical endpoint which, was an improvement in the accuracy of MS-325-enhanced MRA versus that of non-contrast MRA, with each of three blinded radiologist readers showing improvement in accuracy with a p-value less than 0.001. This trial demonstrated that MS-325-enhanced MRA compared favorably to conventional X-ray angiography, the current reference standard, achieving 84% accuracy in identifying clinically significant stenoses caused by atherosclerotic disease. In determining the reference standard in the trial the X-ray inter-reader accuracy agreement was 90%.

In September 2001, we expanded our Phase III clinical trial program for MS-325 in order to broaden our lead indication to peripheral vascular disease from the previous indication of aortoiliac occlusive disease. This expansion resulted from discussions with the FDA during which we agreed to add other vascular beds broadly representative of atherosclerotic disease in the vascular system to our then current Phase III clinical trial program. In late 2001, we filed two additional protocols with the FDA, one to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in renal arteries supplying blood to the kidneys, and another to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in pedal arteries supplying blood to the feet. We expect that a broad vascular disease indication will include the entire vasculature excluding the heart.

In February 2003, we completed enrollment in the final two Phase III trials designed to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the renal arteries in the kidney and in the pedal arteries in the feet. In July 2003, we reported preliminary results of the final two Phase III trials.

The Phase III trial in the renal arteries in the kidney met its primary clinical endpoint, which was an improvement in accuracy of MS-325-enhanced MRA versus that of non-contrast MRA, with each of three blinded radiologist readers showing clinically significant improvement in accuracy. The improvements in accuracy were statistically significant for all three readers with a p-value less than 0.001. The trial demonstrated that MS-325-enhanced MRA compared favorably to conventional X-ray angiography, the current reference standard, achieving 77% accuracy in identifying clinically significant arterial narrowing or stenoses caused by atherosclerotic disease. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 84%.

The Phase III trial in the pedal arteries in the feet met its primary clinical endpoint, which was an improvement in the accuracy of MS-325-enhanced MRA versus that of non-contrast MRA, with each of three blinded radiologist readers showing clinically significant improvement in accuracy, The improvements in accuracy were statistically significant for two of the three readers with a p-value less than 0.01. This trial demonstrated that MS-325-enhanced MRA compared favorably to conventional X-ray angiography, the current reference standard, achieving 76% accuracy in identifying clinically significant stenoses caused by atherosclerotic disease. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 79%.

The four Phase III trials indicated that MS-325 was safe and well tolerated by patients in the studies. The overall rate of adverse events in the renal and pedal trials was comparable to the adverse event rate in the placebo arm of a previously reported trial, with adverse events from the use of MS-325 including nausea, tingling, itching, taste perversion and headache.

In June 2001, we completed a Phase II clinical trial. This Phase II trial compared the diagnostic accuracy of five different doses of MS-325-enhanced MRA with that of X-ray angiography in the aortoiliac vascular bed. The results of this trial strongly supported the 0.03 mmol/kg dose selected for use in the Phase III aortoiliac occlusive disease studies and favorably compared MS-325-enhanced MRA to conventional X-ray angiography achieving 87% accuracy versus conventional X-ray angiography, in identifying clinically significant stenoses caused by atherosclerotic disease. The results indicated that MS-325 was safe and well-tolerated by patients in this study.

In June 1998, we completed a Phase II clinical trial to test the safety and preliminary efficacy of MS-325 for the evaluation of vascular disease in the carotid, iliac and femoral arteries. In this Phase II study, MS-325-enhanced MRA compared favorably to conventional X-ray angiography, achieving 82% accuracy versus conventional X-ray angiography in identifying clinically significant stenoses caused by atherosclerotic disease and was safe. The results indicated that MS-325 was safe and well-tolerated by patients in this study. In addition, we have completed two Phase I clinical trials to date; the first in February 1997, and the second in February 1998.

Coronary Artery Disease

We have conducted a Phase II feasibility trial in 106 patients to test the safety and preliminary efficacy of MS-325-enhanced MRA for the evaluation of coronary artery disease. As with the completed first two Phase III aortoiliac trials, our coronary trial compares MS-325-enhanced MRA to X-ray angiography, the current reference standard, to determine the location and degree of plaque blockages. Clinical use of MRA for imaging the coronary arteries is particularly difficult at present due to the problem of cardiac motion that results from both the beating of the heart and breathing. We have joined with several leading MRI manufacturers, academic centers and other research organizations to develop hardware and software solutions to the problem of cardiac motion. We received promising early images from this study indicating that MS-325 may be useful in assessing coronary artery blockages. We plan to conduct further studies of the use of MS-325 in coronary imaging following submission of our NDA.

Potential Additional Applications

We are currently evaluating results from clinical and pre-clinical studies performed in the areas of breast cancer, female sexual arousal dysfunction and myrocardial perfusion to determine the potential utility of MS-325 for additional applications.

Breast Cancer. In March 2000, we completed enrollment for a 45-patient multi-center Phase II feasibility trial designed to test the safety and preliminary efficacy of MS-325-enhanced MRI for detecting malignant breast lesions in women with breast abnormalities. In this trial, we evaluated MS-325-enhanced MRI in 20 patients using low field MRI scanners and 25 patients using high field MRI systems. Data from the sub-population of the 20 patients using low field MRI scanners showed marked and persistent contrast enhancement in both benign and malignant lesions, demonstrating that MS-325 provides a strong signal enhancement of breast lesions and enables high quality imaging at field strengths associated with open MRI and lower field magnetic resonance systems that we believe will be appropriate for breast cancer clinics. We believe that MS-325 has potential utility as part of a non-invasive imaging procedure that would assist physicians in identifying breast cancer in patients who have had mammograms that do not yield conclusive information or who are at high risk of developing breast cancer. Commencement of additional clinical studies for the breast cancer application is contingent upon the future outlook and development of the breast imaging market.

Female Sexual Arousal Dysfunction. In March 2001, we completed enrollment in a Phase II feasibility trial in 25 patients, which we conducted in collaboration with Pfizer to explore the efficacy of MS-325-enhanced MRI in the diagnosis of female sexual arousal dysfunction. Preliminary results from this trial indicate that MS-325-enhanced MRI is able to measure changes in pelvic blood volume and organ volume during sexual arousal. We believe that this technique may be useful in assessing how different diseases affect sexual response in women as well as examining the effects of potential treatments in restoring impaired sexual response. Commencement of additional clinical studies for this application is contingent upon future outlook and development of the market.

Myocardial Perfusion. We are currently evaluating results from pre-clinical studies to assess the utility of MS-325-enhanced MRA to detect myocardial perfusion.

Thrombus Program

Background

Thromboembolic disease refers to a class of relatively common disorders involving the formation of blood clots, or thrombi, in the veins and arteries. Common forms of these disorders include heart attacks and strokes resulting from clots which cause a sudden blockage in the blood flow to the heart or brain. Another common condition caused by clot formation in the pelvis or legs is deep vein thrombosis, or DVT. This disease afflicts approximately two million Americans each year. The most severe consequences of DVT tend to occur when a clot dislodges from the vessel wall to form an embolus, which can then pass to and obstruct arteries in the lung. This condition, known as pulmonary embolism, or PE, affects an estimated 600,000 patients each year in the U.S. In addition, blood clots in the carotid artery can lead to stroke, while clots in the coronary arteries can result in heart attack. We estimate that blood clots are responsible for over 400,000 deaths each year in the U.S.

The most common method currently used for detecting blood clots in the chamber of the heart is ultrasound imaging of the heart or echocardiography. Clots in the heart are important to detect because they can dislodge and travel to the brain, causing stroke. Clots in the heart chambers are detected using an invasive technique known as transesophogeal echocardiography, or TEE, which involves sedation of the patient and the insertion of a probe down the patient's throat to the level of the heart. There are approximately one million TEE exams performed annually in the U.S. Clots in the coronary arteries often lead to heart attacks. There is currently no diagnostic imaging method for the specific detection of clots in the coronary arteries. There are over one million heart attacks annually in the U.S. caused by blood flow restrictions in the coronary arteries, many of which involve blood clots.

The current method for diagnosing DVT involves a series of venous ultrasound exams sometimes followed by X-ray venography. The ultrasound procedure, while non-invasive, is effective primarily for diagnosing DVT in the thighs. It is ineffective for a significant portion of the patient population who do not have symptoms and those who have clots forming below the knee, in the pelvis and in the vena cava, the primary vein returning blood to the heart. It is estimated that over 3.3 million ultrasound procedures are performed each year in the U.S. to detect DVT. X-ray venography, the current clinical standard for diagnosis, requires the injection of X-ray contrast dye into the foot and carries a significant risk of complications, including the formation of new clots.

The diagnosis of PE presents an even greater challenge for clinicians with recent research suggesting that PE diagnosis is missed more than 50% of the time. The primary diagnostic technique for PE, a nuclear scan, is indeterminate in a large number of patients. Approximately one million such exams were performed in the U.S. in 2001. In the event of an indeterminate exam, the clinician must either infer the diagnosis from the presence or absence of DVT or must perform a pulmonary angiogram. Pulmonary angiography is a highly invasive catheter-based procedure which subjects the patient to significant risk of morbidity and mortality. Clots in the carotid and coronary arteries are

diagnosed in much the same way as atherosclerotic blockages, with X-ray angiography providing definitive diagnosis in most patients.

Thrombus Development Program

We are developing a second targeted contrast agent that would enable MRI to illuminate blood clots. This agent could potentially change the diagnostic work-up for many of the conditions associated with thromboembolic disease, including patients with clots in the heart and brain as well as for diagnosing clots in patients with DVT or PE. We believe that the use of this new approach could lead to better medical outcomes due to earlier and more definitive diagnosis. Early diagnosis is especially important for clots in the heart, brain, neck, thigh and pelvis. Because of their increased likelihood of migrating to the lungs once inside the pulmonary vasculature, these clots can be fatal. We believe that an MRI contrast agent for the detection of clots could eliminate the need for the CT, ultrasound and nuclear medicine studies currently used to identify thrombotic disease, and could potentially provide a non-invasive definitive diagnosis for the presence of blood clots.

We have selected a compound, EP-2104R, for further development as a thrombus agent. In pre-clinical studies, EP-2104R has been shown to enhance the ability of MRI to image clots. We designed EP-2104R based on a family of highly specific peptides that bind reversibly to fibrin, the dominant protein inside clots. The selected peptide is linked to a proprietary gadolinium group, which for the first time, will provide a sufficiently strong signal to allow imaging of clots during MRI exams. We believe that our proprietary technology platform could enable MRI to differentiate old and new clot formation, potentially identifying those clots that pose the most risk to patients. We expect to continue to devote significant resources to this program in the future and plan to commence human trials in 2004.

Our Business Strategy

Our objective is to become a worldwide leader in MRI contrast agents by pursuing a strategy based on commercializing MS-325 and developing new applications for our proprietary technology platform. Our key business objectives are to:

Obtain regulatory approval and support the commercialization of MS-325 for our lead cardiovascular imaging indication of peripheral vascular disease. As previously discussed in the section "Our Product and Development Programs Lead Indications MRA of Peripheral Vascular Disease," we have announced preliminary results of our four-part Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease. All four trials met their primary endpoints.

Establish the clinical utility of MS-325 in other cardiovascular imaging indications. We plan to study the safety and efficacy of MS-325-enhanced MRA for the evaluation of coronary artery disease. In a Phase II trial in 106 patients, we compared MS-325-enhanced MRA to conventional X-ray angiography, the current reference standard. In addition, we are currently evaluating the results of preclinical trials for such applications as myocardial perfusion imaging.

Develop EP-2104R for thromboembolic disease imaging. In our thrombus program, we are developing EP-2104R as an MRI contrast agent for imaging clots. We plan to commence human trials in 2004.

Maximize the value of strategic alliances. We have established collaborations with Schering AG, Tyco/Mallinckrodt, General Electric Medical Systems, Philips Medical Systems, Siemens Medical Systems and Pfizer. We entered into these alliances, and will seek to enter into future strategic alliances with pharmaceutical, imaging agent and MRI equipment industry leaders, in order to

obtain access to resources and infrastructure to leverage our strengths. See "Strategic Alliances and Collaborations."

Maximize the value of our proprietary technology platform. We plan to build on our leadership in developing targeted contrast agents for MRI through further research and development programs in cardiovascular imaging and therapeutics. We

have established a collaboration for MRI research with Schering AG in which we and Schering AG are exclusively combining our research programs in the field of MRI to discover novel MRI product candidates for clinical development. We are initiating exploratory research programs utilizing our skills and intellectual property to discover product candidates for the treatment or prevention of cardiovascular disease.

Strategic Alliances and Collaborations

Our business strategy includes entering into alliances with leaders in the pharmaceutical, diagnostic imaging and MRI equipment industries to facilitate the development, manufacture, marketing, sale and distribution of our products. To date, we have formed strategic alliances and collaborations with Schering AG, Tyco/Mallinckrodt, General Electric Medical Systems, Philips Medical Systems, Siemens Medical Systems and Pfizer.

Co-Development, Sales & Marketing

Schering AG. In June 2000, we entered into a strategic collaboration agreement for MS-325 pursuant to which we granted Schering AG an exclusive license to co-develop and market MS-325 worldwide, exclusive of Japan. In December 2000, we amended this strategic collaboration agreement to grant to Schering AG the exclusive rights to develop and market MS-325 in Japan. Generally, each party to the agreement will share equally in MS-325 costs and profits. Under the agreement, we will assume responsibility for completing clinical trials and filing for FDA approval in the U.S. Schering AG will lead clinical and regulatory activities for the product outside the U.S. In addition, we granted Schering AG an exclusive option to develop and market an unspecified cardiovascular MRI blood pool agent from our product pipeline. In connection with this strategic collaboration and the amendment to our strategic collaboration agreement with Tyco/Mallinckrodt, as further described below, Schering AG paid us an up-front fee of $10.0 million, which we then paid to Tyco/Mallinckrodt. Under the agreement, Schering AG also paid us $20.0 million in exchange for shares of our common stock through its affiliate, Schering Berlin Venture Corporation, or Schering BV. We may receive up to an additional $18.75 million in milestone payments under the strategic collaboration agreement, of which $2.5 million will be earned upon NDA filing and up to $1.25 million will be earned upon product approval. Under the terms of the December 2000 amendment, Schering AG paid us an up-front fee of $3.0 million and may be required to pay us an additional $7.0 million upon our achievement of certain milestones. Following commercial launch of MS-325, we will also be entitled to receive a royalty on products sold outside the U.S. and a percentage of Schering AG's operating profit margin on products sold in the U.S.

Also, under the strategic collaboration agreement with Schering AG, we have options to acquire certain participation rights with respect to two of Schering AG's MRI imaging products currently in clinical trials, SHU555C and Gadomer-17. We are entitled to exercise these options on a region-by-region basis upon the payment of certain fees. Once we exercise the SHU555C option, we will enter into a definitive agreement with Schering AG with respect to SHU555C, pursuant to which Schering AG will be responsible for the conduct of all development, marketing and sales activities in connection with SHU555C. Once we exercise the Gadomer-17 option, we will enter into a definitive agreement with Schering AG with respect to Gadomer-17, pursuant to which we will share development costs incurred from the date of the option exercise, as well as profits, equally with Schering AG and we will be obligated to make milestone payments to Schering AG. Under the terms

of the strategic collaboration agreement, either party may terminate the agreement upon thirty days notice if there is a material breach of the contract or if either party fails to meet certain milestones. In addition, Schering AG may terminate the agreement at any time on a region-by-region basis or in its entirety, upon six months written notice to us; and we may terminate the agreement with respect to development of MS-325 in the European Union, or EU, at any time after June 9, 2001 upon ninety days written notice to Schering AG, if Schering AG has failed to meet its obligations in connection with the regulatory approval of MS-325 in the EU.

In May 2003, we announced a broad alliance with Schering AG for the discovery, development and commercialization of molecularly-targeted contrast agents for MRI. The alliance is comprised of two areas of collaboration with one agreement providing for exclusive development and commercialization collaboration of EP-2104R, our product candidate for the detection of thrombus, as well as any other product candidate that we and Schering determine to develop for detection of thrombus using MRI, and the second agreement covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. As a result of the alliance, Schering AG has an option to the late stage development and worldwide marketing rights for EP-2104R and for all development candidates emerging from the MRI research collaboration.

Under the terms of the EP-2104R agreement, we are responsible for execution of a clinical feasibility program in humans. At the end of the feasibility program, Schering AG may exercise an option to develop and commercialize EP-2104R under which Schering AG will receive an exclusive, worldwide license for EP-2104R and become responsible for all further development, manufacturing, marketing and sales. Schering AG will make fixed payments to us totaling approximately $9.0 million over two years to cover our expenditures in the feasibility program. In

addition, if Schering AG exercises its option to develop and commercialize EP-2104R, Schering AG will pay us up to $15.0 million in additional payments upon the occurrence of certain development and commercial events, as well as royalties on sales attributable to the EP-2104R development effort. The royalty rate will depend on the level of annual net sales. In addition to funding for our feasibility program and milestone and base royalty payments, we have the right to increase our royalty rate by repaying to Schering AG a portion of the costs of clinical development.

Under the terms of the MRI three-year joint research agreement, we and Schering AG are exclusively combining our existing research programs in the field of diagnosing human disease using MRI to discover novel MRI product candidates for clinical development. Schering AG will fund a portion of our related personnel costs and third party research costs of up to $2.0 million per annum and has made available to us a loan facility of up to $15.0 million with principal repayment beginning in 2007. The loan facility carries a variable, market-based interest rate. We have drawn $7.5 million of the $15.0 million loan facility available from Schering AG. The remaining $7.5 million of the Schering AG loan facility may be available starting May 2004 subject to specified covenants and conditions contained in the loan agreement. Also under the MRI research agreement, Schering AG has the first option to obtain exclusive, worldwide rights for the product candidates, and, upon exercising the option, would become responsible for all future development, manufacturing, marketing and sales. We would receive a base royalty on net sales with the option to increase the royalty by participating in development funding. If Schering AG does not exercise its option, we may license the product, and Schering AG would receive a base royalty on net sales and milestone payments.

On May 8, 2000, we granted to Schering AG a worldwide, royalty-bearing license to patents covering Schering AG's development project, Eovist injection, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 8, 2000, Schering AG granted us a non-exclusive, royalty-bearing license to certain of its Japanese patents. We agreed to withdraw our invalidation claim of Schering AG's Japanese patent 1,932,626 in the Japanese Patent Office pursuant to this license agreement. See "Patents and Proprietary Rights." Schering AG had been an opposing party in our European patent case prior to the licensing agreement. On May 9, 2000, the Opposition

Division of the European Patent Office maintained our European patent in a slightly amended form. The patent is owned by MGH and is exclusively licensed to us. The remaining opposing parties initially elected to appeal the May 9, 2000 decision. However, in September 2001, we settled this patent dispute with the opposing parties by entering into a non-exclusive royalty bearing license agreement with Bracco. See "Patents and Proprietary Rights" for further discussion of this settlement.

Tyco/Mallinckrodt. In June 2000, in connection with the exclusive license that we granted to Schering AG, we amended our strategic collaboration with Tyco/Mallinckrodt to grant Tyco/Mallinckrodt a non-exclusive, worldwide license to manufacture MS-325 for clinical development and commercial use in accordance with a manufacturing agreement entered into in June 2000 between Tyco/Mallinckrodt and Schering AG, and to enable us to enter into the strategic collaboration agreement with Schering AG described above. In connection with this amendment, we paid Tyco/Mallinckrodt an up-front fee of $10.0 million and are obligated to pay up to an additional $5.0 million in milestone payments, of which $2.5 million will be paid upon NDA filing and $2.5 million will be paid upon product approval. We will also pay Tyco/Mallinckrodt a share of our MS-325 operating profit margins in the U.S. and a percentage of the royalty that we receive from Schering on MS-325 gross profits outside the U.S.

In October 1999, we entered into a Non-Negotiable Promissory Note and Security Agreement with Tyco/Mallinckrodt, our strategic partner, under which we were eligible to borrow our share of MS-325 development costs, on a quarterly basis, up to a total of $9.5 million. The loan was secured by a first priority security interest in all of our intellectual property. In June 2000, pursuant to the amended collaboration agreement with Tyco/Mallinckrodt and the new strategic collaboration with Schering AG, Schering AG assumed the development cost sharing obligation for MS-325 from Tyco/Mallinckrodt as of January 1, 2000. As a result, we amended the terms of the loan to allow funding for our portion of development costs through December 31, 1999. The loan was repaid in full when it matured on October 1, 2002.

Daiichi. In March 1996, we entered into a development and license agreement with Daiichi pursuant to which we granted Daiichi an exclusive license to develop and commercialize MS-325 in Japan. Under this arrangement, Daiichi assumed primary responsibility for clinical development, regulatory approval, marketing and distribution of MS-325 in Japan. We retained the right and obligation to manufacture MS-325 for development activities and commercial sale under the agreement. In December 2000, we reacquired the rights to develop and commercialize MS-325 in Japan from Daiichi. Under the terms of this reacquisition agreement with Daiichi, we agreed to pay Daiichi a total amount of $5.2 million. In January 2001, we paid Daiichi $2.8 million in up-front fees and we expect to pay an additional $2.4 million by December 31, 2003. Daiichi will also receive a royalty from us based on net sales of MS-325 in Japan. Simultaneously with our reacquisition from Daiichi of the MS-325 development and marketing rights in Japan, we assigned these rights to Schering AG as described above.

MRI Equipment Manufacturers

To date, we have formed collaborations with the three major MRI scanner manufacturers, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems, to develop advanced imaging techniques designed to facilitate the use of MS-325-enhanced MRA. We believe it is extremely important to collaborate with equipment manufacturers to develop software and advanced imaging techniques capable of taking full advantage of the unique properties of MS-325 to diagnose cardiovascular disease.

General Electric Medical Systems. In January 1998, we announced the formation of a collaboration with General Electric Medical Systems to accelerate the development of cardiovascular MRI. In particular, the collaboration focuses on reducing the effects of cardiac motion on MR images, providing

user-friendly computer tools as a means of visualizing arteries and veins in three-dimensional space and optimizing MRI, for intravascular MRI contrast agents, including MS-325. Under the terms of this non-exclusive agreement, research is performed at several centers in addition to our facilities, including General Electric's corporate research facility in Schenectady, NY, General Electric Medical Research in Milwaukee, WI, and several academic centers.

Philips Medical Systems. We agreed in November 1998 to collaborate with Philips Medical Systems in advancing the development of contrast-based cardiovascular MRI technologies. Under the terms of this non-exclusive collaboration agreement, we are combining our resources with Philips Medical Systems to optimize imaging technology and improve three-dimensional visualization of arteries and veins in patients undergoing MRA. Research and development is being carried out at several international Philips research centers, as well as at our facilities.

Siemens Medical Systems. In September 1999, we announced a non-exclusive collaboration with Siemens Medical Systems to optimize MRI technology and improve visualization of arteries and veins in patients undergoing MRA. The collaboration also focuses on expanding the use of MRI in diagnosing cardiovascular disease and providing user-friendly tools for easy visualization of the cardiovascular system in three-dimensional space. Research and development is being carried out at our facilities and at Siemens' Iselin, NJ facilities.

Potential New Applications

Pfizer. In September 1998, we entered into an exclusive agreement with Pfizer to explore the potential utility of MS-325-enhanced MRA in the diagnosis of female sexual arousal dysfunction. As part of this collaboration, we and Pfizer undertook a Phase II feasibility trial to explore the efficacy of MS-325-enhanced MRA in the detection and monitoring of female sexual arousal dysfunction. We completed enrollment in the trial in March 2001. Under the terms of this collaboration, Pfizer has full responsibility for funding the trial. Pfizer currently markets Viagra® for erectile dysfunction in men.

Competition

The healthcare industry is characterized by extensive research efforts and rapid technological change and there are many companies that are working to develop products similar to ours. There are currently no FDA-approved targeted vascular contrast agents for use with MRI. However, there are a number of general use MRI agents approved for marketing in the U.S. and in certain foreign markets that, if approved for MR angiography, are likely to compete with MS-325. Such products include Magnevist and Gadovist by Schering AG, Dotarem by Guerbet, S.A., Omniscan by Amersham plc, ProHance and MultiHance by Bracco and OptiMARK by Tyco/Mallinckrodt. We are aware of six agents under clinical development: Schering AG's Gadovist, Gadomer-17 and SHU555C, Guerbet's Vistarem, Bracco's B-22956/1 and Advanced Magnetics' Code 7228 that have been or are being evaluated for use in MRA. We are aware of no MRI contrast agent other than our prototype being developed for use in imaging blood clots. We cannot assure you that our competitors will not succeed in the future in developing products that are more effective than any that we are developing. We believe that our ability to compete within the MRI contrast agent market depends on a number of factors including the success and timeliness with which we complete FDA trials, the breadth of applications, if any, for which our products receive approval, and the effectiveness, cost, safety and ease of use of our products in comparison to the products of our competitors. Our success will also depend on physician acceptance of MRI as a primary imaging modality for certain cardiovascular and other applications.

We have many competitors, including pharmaceutical, biotechnology and chemical companies. A number of competitors, including two of our strategic partners, are actively developing and marketing product candidates that, if commercialized, would compete with our product candidates. Many of these competitors have substantially greater capital and other resources than we do and may represent significant competition for us. Such companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. Such companies may be more successful than us in developing, manufacturing and marketing products. Furthermore, there are several well-established medical imaging modalities that currently compete, and will continue to compete, with MRI, including X-ray angiography, CT, nuclear medicine and ultrasound. Other companies are actively developing the capabilities of the competing modalities to

enhance their effectiveness in cardiovascular system imaging. For example, we are aware of at least one radiopharmaceutical agent, Schering AG's AcuTect®, which has been approved for imaging acute venous thrombosis. Other nuclear medicine agents, including Draxis Health's FibrImage®, are in clinical testing for DVT and other clot imaging applications. In addition, several ultrasound contrast agents, including Dupont's Definity®, Amersham's Optison® and Alliance Pharmaceutical's Imagent® are approved in the U.S. and may be used for myocardial perfusion imaging. Several other ultrasound contrast agents are undergoing clinical testing for myocardial perfusion imaging including Amersham's Sonazoid®, Point Biomedical's PB-127 and Acusphere's AI-700. 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.

Patents and Proprietary Rights

We consider the protection of our proprietary technologies to be material to our business prospects. We pursue a comprehensive patent program in the U.S. and in other countries where we believe that significant market opportunities exist.

We own or have exclusively licensed patents and patent applications relating to critical aspects of our core technology as well as many specific applications of this technology. Our patents and applications relating to our technology consist of the following:

- Two U.S. patents exclusively licensed from MGH as well as their cognate patents and applications in certain foreign countries.

- Four U.S. patents owned by us as well as their cognate patents and applications in certain foreign countries.

- Thirteen U.S. utility applications in prosecution, two international patent applications filed under the Patent Cooperation Treaty, and 12 U.S. provisional utility applications on 27 different subject matters as well as their cognate applications in certain foreign countries.

Our two licensed U.S. patents relate to our technology, including albumin binding with metal chelates, and liver targeting metal chelates. We have been issued a patent in Europe similar to one of those U.S. patents.

Legal proceedings between Bracco, Schering AG and others against us and MGH involving national patents derived from European Patent No. 222,886, the European patent referred to above, have been terminated. A Settlement and Release Agreement as to litigation between the parties and a License Agreement from us to Bracco for European Patent No. 222,886 and its worldwide counterparts was executed on September 25, 2001. We received various payments, including royalties on a quarterly basis pursuant to the license with Bracco. Previously, on May 8, 2000, we granted to Schering AG a worldwide royalty-bearing license to our patents covering Schering AG's development project, Eovist, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 8, 2000,

Schering AG granted us a non-exclusive royalty-bearing license to its Japanese Patent Nos. 1,932,626 and 1,968,413, and its Japanese Application corresponding to PCT Intl. Pub. No. WO99/16474. We have agreed to withdraw our invalidation claim of Schering AG's Japanese Patent No. 1,932,626 in the Japanese Patent Office pursuant to this license agreement. As a result of the Settlement and License Agreements with Bracco and Schering AG, we are not aware of any legal actions involving this patent family.

We have received an additional U.S. patent covering certain novel metal chelates, U.S. Patent No. 5,582,814, granted December 10, 1996, expiring April 15, 2014. We have also received a patent in the U.S. covering certain aspects of the process by which we manufacture MS-325, U.S. Patent No. 5,919,967, granted July 6, 1999, expiring April 11, 2017. We have received two additional patents, U.S. Patent No. 6,548,044, granted April 15, 2003, expiring November 21, 2020, and U.S. Patent No. 6,549,798, granted April 15, 2003, expiring February 7, 2021, that cover methods of using MS-325 and other blood pool contrast agents. These patent terms are exclusive of any possible patent term extension. Finally, we have patent applications pending in the U.S., Japan and Europe covering various aspects of our technology.

Our patent protection for MS-325 currently will expire in 2006 in the U.S. and Europe. If certain currently pending patent claims issue, this protection will expire in 2015. Protection for aspects of our manufacturing process for MS-325 in the U.S. will currently expire in 2017, and will also expire in 2017 in Europe and Japan if certain currently pending patent claims issue. We may apply for patent term extension under the Hatch/Waxman provisions, which may extend our patent protection in the U.S.

In addition, from 1999 through 2001, we filed five new U.S. patent applications for additional products and processes involving compounds, compositions, and methods for imaging. In 2002, we filed three U.S. patent applications, two international patent applications under the Patent Cooperation Treaty, and five U.S. provisional patent applications. We have filed four U.S. patent applications relating to EP-2104R and its methods of use. If certain currently pending patent claims issue, patent protection for EP-2104R will not expire until 2022. In 2003, we filed four U.S. patent applications and 10 U.S. provisional patent applications.

An issued patent grants to the owner the right to exclude others from practicing inventions claimed therein. In the U.S., a patent filed before June 8, 1995 is enforceable for 17 years from the date of issuance or 20 years from the deemed date of filing the underlying patent applications, whichever is longer. Patents based on applications filed on or after June 8, 1995 expire 20 years from the deemed date of filing. This rule is sometimes regarded as unfavorable to pharmaceutical companies, where the time period between patent filing and commercialization of the patented product may be extended many years because of the lengthy development cycle and regulatory process.

The patent positions of pharmaceutical and biopharmaceutical firms involve complex legal and factual questions. There can be no assurance that our issued patents, or any patents that may be issued in the future, will effectively protect our technology or provide a competitive advantage. There can be no assurance that any of our patents or patent applications will not be challenged, invalidated or circumvented in the future.

Our commercial success will also depend on our ability to operate without infringing upon the patents of others in the U.S. and abroad. If we are found to infringe any third-party patents, and those patents are upheld as valid and enforceable in a judicial or administrative proceeding, we could be prevented from practicing the subject matter claimed in such patents, or would be required to obtain licenses from the patent owners of each such patent, or to redesign our products or processes, to avoid infringement. There can be no assurance that such licenses would be available or, if available, would be available on terms acceptable to us or that we would be successful in any attempt to redesign our products or processes to avoid infringement. Accordingly, an adverse determination in a judicial or administrative proceeding or failure to obtain necessary licenses could prevent us from manufacturing

and selling our products, which may have a material adverse effect on our business, financial condition and results of operations.

There may be pending or issued patents, held by parties not affiliated with us, relating to technologies used by us in the development or use of certain of our product candidates. There can be no assurance that our current or future activities will not be challenged, that additional patents will not be issued containing claims materially constraining our proposed activities, that we will not be required to obtain licenses from third parties, or that we will not become involved in costly, time-consuming litigation regarding patents in the field of contrast agents and other technologies, including actions brought to challenge or invalidate our own patent rights.

Many of our competitors are continuing to actively pursue patent protection for activities and discoveries similar to ours. There can be no assurance that these competitors, many of which have substantially greater resources than us and have made substantial investments in competing technologies, will not in the future seek to assert that our products or chemical processes infringe their existing patents and/or will not seek new patents that claim to cover aspects of our technology. Furthermore, patent applications in the U.S. and in foreign countries are maintained in secrecy for a specified period after filing. Publication of discoveries in the scientific or patent literature tends to lag behind actual discoveries and the filing of related patent applications. In addition, patents issued and patent applications filed relating to biopharmaceuticals are numerous. Therefore, there can be no assurance that we are aware of all competitive patents, either pending or issued, that relate to products or processes used or proposed to be used by us.

We have entered into a license agreement with MGH pursuant to which MGH has granted us an exclusive worldwide license to the patents and patent applications which relate to our only product candidate, MS-325. The MGH license imposed certain due diligence obligations with respect to the development of products covered by the license, all of which have been fulfilled to date. The MGH license requires us to pay royalties on our net sales of MS-325 until 2006. We must also pay MGH a percentage of all royalties received from our sublicensees until 2006. Accordingly, we will be required to make payments to MGH on profits generated under the Schering AG collaboration, if any. Our failure to comply with these requirements could result in the conversion of the license from being exclusive to non-exclusive in nature or termination of the license agreement itself. Any such event would have a material adverse effect on our business, financial condition and results of operations.

We entered into a collaboration agreement in 1997 with Dyax Corp., or Dyax, for research relating to our thrombus program. Under the terms of this agreement, we share rights to certain thrombus inventions with Dyax in return for royalty rights upon commercialization of certain products arising from the thrombus program.

The pharmaceutical and biotechnology industries have been characterized by extensive litigation regarding patents and other intellectual property rights. Litigation may be necessary to enforce any patents issued to us and/or determine the scope and validity of others' proprietary rights. We may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office or by foreign agencies to determine the priority of inventions. Any involvement in litigation surrounding these issues could result in extensive costs to us as well as be a significant distraction for management. Such costs could have a material adverse effect on our business, financial condition and results of operations.

We also rely upon trade secrets, technical know-how, and continuing technological innovation to develop and maintain our competitive position. We typically require our employees, consultants, and advisors to execute confidentiality and assignment of invention agreements in connection with their employment, consulting or advisory relationships with us. These agreements require disclosure and assignment to us of ideas, developments, discoveries and inventions made by employees, consultants and advisors. There can be no assurance, however, that these agreements will not be breached or that

we will have adequate remedies for any breach. Furthermore, no assurance can be given that competitors will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our proprietary technology, or that we can meaningfully protect our rights in unpatented proprietary technology. We intend to vigorously protect and defend our intellectual property. Costly and time-consuming litigation brought by us may be necessary to enforce our issued patents, to protect our trade secrets or know-how owned by us, or to determine the enforceability, scope, and validity of the proprietary rights of others.

Manufacturing

We do not have, nor do we currently have plans to develop, full-scale manufacturing capability for MS-325. We rely on, and we intend to continue to rely on, Tyco/Mallinckrodt as the sole manufacturer of MS-325 for 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, commercialization and development of MS-325, and the cost to produce MS-325 could increase significantly. Schering AG may not be able to find an alternative manufacturer, or Schering AG may not be able to manufacture MS-325 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.

Government Regulation

The manufacture and commercial distribution of pharmaceuticals are subject to extensive governmental regulation in the U.S. and other countries. Pharmaceuticals, including contrast-imaging agents for use with MRI, are regulated in the U.S. by the FDA under the Food, Drug and Cosmetic Act, or FD&C Act, and require FDA approval prior to commercial distribution. Pursuant to the FD&C Act, pharmaceutical manufacturers and distributors must be registered with the FDA and are subject to ongoing FDA regulation, including periodic FDA inspection of their facilities and review of their operating procedures. Noncompliance with applicable requirements can result in failure to receive approval, withdrawal of approval, total or partial suspension of production, fines, injunctions, civil penalties, recalls or seizure of products and criminal prosecution, each of which would have a material adverse effect on our business, financial conditions and results of operations.

In order to undertake clinical trials and market pharmaceutical products for diagnostic or therapeutic use in humans, the procedures and safety standards established by the FDA and comparable agencies in foreign countries must be followed. In the U.S., a company seeking approval to market a new pharmaceutical must obtain FDA approval of a new drug application, or NDA. Before a NDA may be filed, however, a certain procedure is typically followed. This includes:

- performance of preclinical laboratory and animal studies;
- submission to the FDA of an application for an IND, which must become effective before human clinical trials may commence;
- completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the pharmaceutical for its intended use;

submission to the FDA of a NDA; and

approval of the NDA by the FDA prior to any commercial sale or shipment of the agent.

Preclinical studies include laboratory evaluation of product chemistry and animal studies to assess the potential safety and efficacy of the product and its formulation. The results of the preclinical

studies and the protocol for the proposed clinical trial are submitted to the FDA as part of an IND, and unless the FDA objects, the IND will become effective 30 days following its receipt by the FDA. Clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol together with information about the clinical investigators who will perform the studies and the institutions at which the trials will be performed are submitted to the FDA as part of the IND.

An independent institutional review board, or IRB, at each institution at which the trial will be conducted will also be asked by the principal investigator at that institution to approve, according to FDA regulations governing IRBs, the trials that will be performed at that institution. The IRB will consider, among other things, ethical factors, the protection of human subjects and the possible liability of the institution and the adequacy of the informed consent.

Clinical trials under the IND are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the pharmaceutical into humans, the pharmaceutical is tested for safety, dosage tolerance, metabolism, distribution, excretion and clinical pharmacology in healthy adult subjects. Imaging agents may also be subject to a Phase Ib trial under which an agent's imaging characteristics in humans are first evaluated. Phase II involves a detailed evaluation of the safety and efficacy of the agent in a range of doses in patients with the disease or condition being studied. Phase III clinical trials typically consist of evaluation of safety and efficacy in a larger patient population and at more institutions.

The process of completing clinical testing and obtaining FDA approval for a new product is likely to take a number of years. When the study for a particular indication as described in the IND is complete, and assuming that the results support the safety and efficacy of the product for that indication, we intend to submit a NDA to the FDA. The NDA approval process can be expensive, uncertain and lengthy. Although the FDA is supposed to complete its review of a NDA within 180 days of the date that it is filed, the review time is often significantly extended by the FDA, which may require more information or clarification of information already provided in the NDA. During the review period, an FDA advisory committee likely will be asked to review and evaluate the application and provide recommendations to the FDA about approval of the pharmaceutical. In addition, the FDA will inspect the facility at which the pharmaceutical is manufactured to ensure compliance with GMP and other applicable regulations. Failure of a manufacturer to comply or come into compliance with GMP requirements could significantly delay FDA approval of the NDA. The FDA may grant an unconditional approval of an agent for a particular indication or may grant approval conditioned on further post-marketing testing and/or surveillance programs to monitor the agent's efficacy and side effects. Results of these post-marketing programs may prevent or limit the further marketing of the agent. In addition, further studies and a supplement to the initially approved NDA will be required to gain approval for the use of an approved product in indications other than those for which the NDA was approved initially.

After a NDA is approved, we would continue to be subject to pervasive and continuing regulation by the FDA, including record keeping requirements, reporting of adverse experience from the use of the agent and other requirements imposed by the FDA. FDA regulations also require FDA approval of a NDA supplement for certain changes if they affect the safety and efficacy of the pharmaceutical, including, but not limited to, new indications for use, labeling changes, the use of a different facility to manufacture, process or package the product, changes in manufacturing methods or quality control systems and changes in specifications for the product. Our failure to receive approval of a NDA supplement could have a material adverse effect on our business, financial condition and results of operations. The advertising of most FDA-regulated products is subject to FDA and Federal Trade Commission jurisdiction, but the FDA has sole jurisdiction over advertisements for prescription drugs. We are and may be subject to regulation under state and Federal law regarding occupational safety, laboratory practices, handling of chemicals, environmental protection and hazardous substance control.

We also will be subject to existing present and possible future local, state, federal and foreign regulation. Failure to comply with regulatory requirements could have a material adverse effect on our business, financial condition and results of operations.

Approval and marketing of pharmaceutical products outside of the U.S. are subject to regulatory requirements that vary widely from country to country. The time required to obtain regulatory approval from comparable regulatory agencies in each foreign country may be longer or shorter than that required for FDA approval. In addition, in certain foreign markets we may be subject to governmentally mandated prices for our products.

Regulations regarding the approval, manufacture and sale of our product candidates are subject to change. We cannot predict what impact, if any, such changes might have on our business, financial condition or results of operations.

Our research, development and manufacturing processes require the use of hazardous substances and testing on certain laboratory animals. As a result, we are also subject to federal, state, and local laws, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials and waste as well as the use of and care of laboratory animals. These laws and regulations are all subject to change. We cannot predict what impact, if any, such changes might have on our business, financial condition or results of operations.

Reimbursement

We expect that sales volumes and prices of our products will be dependent in large measure on the availability of reimbursement from third-party payors and that individuals seldom would be willing or able to pay directly for all the costs associated with procedures which in the future may incorporate the use of our products. We expect that our products will be purchased by hospitals, clinics, doctors and other users that bill various third-party payors, such as Medicare, Medicaid and other government insurance programs, and private payors including indemnity insurers, Blue Cross Blue Shield plans and managed care organizations, or MCOs, such as health maintenance organizations. Most of these third-party payors provide coverage for MRI for some indications when it is medically necessary, but the amount that a third-party payor will pay for MRI may not include a separate payment for a contrast imaging agent that is used with MRI. Reimbursement rates vary depending on the procedure performed, the third-party payor, the type of insurance plan and other factors.

In 2001, the Centers for Medicare and Medicaid Services, formerly HCFA, created additional payment codes for contrast-enhanced MRA procedures performed in outpatient settings, where we expect the majority of MRA procedures to occur, improving the reimbursement situation for such agents. Certain new contrast agents may also be eligible for additional pass-through payments. For inpatients, Medicare pays hospitals a prospectively determined amount for the entire patient stay based on a Medicare beneficiary's discharge diagnosis related group, or DRG. This payment usually includes payment for any procedure, including MRI, that is performed while a beneficiary is in the hospital. No additional payment has been made for contrast agents used during the procedure. Other third-party payors may pay a hospital an additional amount for an MRI procedure performed on an in-patient according to another methodology such as a fee schedule or a percentage of charge. Such payment may or may not include a payment for a contrast-imaging agent.

Third-party payors carefully review and increasingly challenge the prices charged for procedures and medical products. In the past few years, the amounts paid for radiology procedures in particular have come under careful scrutiny and have been subject to decreasing reimbursement rates. In addition, an increasing percentage of insured individuals are receiving their medical care through MCOs which monitor and often require preapproval of the services that a member will receive. Many MCOs are paying their providers on a capitated basis which puts the providers at financial risk for the services provided to their patients by paying them a predetermined payment per member per month.

The percentage of individuals, including Medicare beneficiaries, covered by MCOs is expected to grow in the U.S. over the next decade. We believe that the managed care approach to healthcare and the growth in capitated arrangements and other arrangements under which the providers are at financial risk for the services that are provided to their patients may facilitate the market acceptance of our products, as we believe that the use of our products will significantly lower the overall costs and improve the effectiveness of managing patient populations. We cannot assure you, however, that our products will be available, will lower costs of care for any patients or will be utilized by providers, or if reimbursement will be available.

In foreign markets, reimbursement is obtained from a variety of sources, including governmental authorities, private health insurance plans and labor unions. In most foreign countries, there are also private insurance systems that may offer payments for alternative therapies. Although not as prevalent as in the U.S., health maintenance organizations are emerging in certain European countries. We may need to seek international reimbursement approvals, although we can not assure you that any such approvals will be obtained in a timely manner or at all. Failure to receive international reimbursement approvals could have a material adverse effect on market acceptance of our product candidates in the

international markets in which such approvals are sought.

We believe that reimbursement in the future will be subject to increased restrictions such as those described above, both in the U.S. and in foreign markets. We believe that the overall escalating cost of medical products and services has led to, and will continue to lead to, increased pressures on the health care industry, both foreign and domestic, to reduce the cost of products and services, including products offered by us. There can be no assurance, in either the U.S. or foreign markets, that third party reimbursement will be available or adequate, that current reimbursement amounts will not be decreased in the future or that future legislation, regulation, or reimbursement policies of third-party payors will not otherwise adversely affect the demand for our product candidates or our ability to sell our product candidates on a profitable basis, particularly if MRI exams enhanced with our contrast agents are more expensive than competing vascular imaging techniques that are equally effective. The unavailability or inadequacy of third-party payor coverage or reimbursement could have a material adverse effect on our business, financial condition and results of operations.

Employees

As of July 23, 2003, we employed 84 persons on a full-time basis, of which 67 were involved in research and development and 17 in administration and general management. Thirty-one of our employees hold Ph.D. or M.D. degrees. We believe that our relations are good with our employees. None of our employees are a party to a collective bargaining agreement.

MANAGEMENT

The following table provides information about our executive officers and directors as of June 30, 2003.

Name	Age	Position
Christopher F.O. Gabrieli	43	Chairman of the Board
Stanley T. Crooke, M.D., Ph.D.	58	Director
Peter Wirth	52	Director
Michael D. Webb	45	Chief Executive Officer and Director
Randall B. Lauffer, Ph.D.	45	Chief Scientific Officer and Director
Alan P. Carpenter, Jr., Ph.D, J.D.	50	Executive Vice President, Research and Development
Stephen C. Knight, M.D.	43	President and Chief Operating Officer
Peyton J. Marshall, Ph.D.	48	Senior Vice President and Chief Financial Officer
Gregg Mayer	46	VP, Strategic Marketing and Corporate Communication
Robert Weisskoff, Ph.D.	41	VP, Business Development and Head of Imaging

Christopher F.O. Gabrieli has been a member of the Board of Directors of EPIX since 1994, and he is the Chairman of the Board of Directors. Mr. Gabrieli is the Chairman of Massachusetts 2020, a non-profit public policy organization. He is a member of the general partners of Bessemer Venture Partners III L.P. and Bessemer Venture Partners IV L.P. and related venture capital partnerships, where he worked from 1986 to 2000. Mr. Gabrieli is a director of Isis Pharmaceuticals, Inc., where he was a co-founder.

Stanley T. Crooke, M.D., Ph.D. has been a member of the Board of Directors of EPIX since 1996. Dr. Crooke is the Founder, Chairman and Chief Executive Officer of Isis Pharmaceuticals Inc., a pharmaceuticals company founded in 1989. Dr. Crooke also is an adjunct professor at University of California, San Diego and San Diego State University. Prior to founding Isis Pharmaceuticals, Inc., he was the President of Research and Development for SmithKline Beckman Corporation. Dr. Crooke serves on the boards of directors of Antisense Therapeutics Limited and Axon Instruments, Inc.

Peter Wirth, Esq. has been a member of the Board of Directors of EPIX since August 2001. Mr. Wirth is currently an Executive Vice President and the Chief Legal Officer of Genzyme Corporation in Cambridge, MA, where he has senior management responsibility for the legal and corporate development functions, for the Genzyme Molecular Oncology business unit and for Genzyme's small molecule and polymer drug discovery and development group. Prior to joining Genzyme in 1996, he was a partner at the law firm of Palmer & Dodge, LLP in Boston.

Michael D. Webb has been a member of the Board of Directors of EPIX since 1994 and has served as EPIX's Chief Executive Officer since December 1994 and EPIX's Secretary since November 1996. Mr. Webb worked for Ciba-Corning Diagnostics, a medical instrument company, from April 1989 to December 1994, most recently as Senior Vice President, Worldwide Marketing and Strategic Planning. From 1984 to 1989, Mr. Webb was a senior consultant at Booz-Allen & Hamilton, Inc., specializing in healthcare and life sciences. Mr. Webb holds a Bachelors degree in Biochemistry from the University of Kansas and an MA in International Relations from Sussex University in the UK. He also has an

M.B.A. in Marketing and Finance from the Kellogg Graduate School of Management at Northwestern University.

Randall B. Lauffer, Ph.D. has been a member of the Board of Directors of EPIX since 1988 and is EPIX's Chief Scientific Officer. Dr. Lauffer founded EPIX in November 1988 and served as Chief Executive Officer until December 1994 and as Chairman of the Board of Directors until October 1996. From November 1983 to March 1992, Dr. Lauffer was a member of the faculty of Harvard Medical School, serving most recently as Assistant Professor of Radiology from 1987 to 1992. During this time

he was also Director of the NMR Contrast Media Laboratory at Massachusetts General Hospital as well as an NIH Postdoctoral Fellow and an NIH New Investigator. Dr. Lauffer is the primary inventor of EPIX's core technology and is the originator of several types of MRI technology, including liver-enhancing agents, vascular agents, tissue blood flow agents, and strategies to increase the magnetic efficiency of MRI agents in the body. He has written over 50 scientific publications and two books, and is named on several U.S. patents. Dr. Lauffer holds a Ph.D. degree in inorganic chemistry from Cornell University.

Alan P. Carpenter, Jr., Ph.D., J.D. joined EPIX in February 2001 with over 20 years of experience in the medical imaging pharmaceutical industry. Dr. Carpenter worked with New England Nuclear, E.I. duPont and DuPont Pharmaceuticals in several Research and Development, Clinical, Project Management and Business Development positions; including five years as Vice President of Research and Development for the Medical Imaging Division. Dr. Carpenter is an inventor on several patents and patent applications relating to a variety of imaging agents, including those covering various aspects of Cardiolite®; the leading myocardial perfusion imaging agent, as well as Definity; an ultrasound contrast imaging agent approved by the FDA. He has had a lead role in the submission and approval of four NDAs during his career. Dr. Carpenter received his Ph.D. in Analytical Chemistry from the University of Massachusetts at Amherst in 1978 and his J.D. from the Massachusetts School of Law in 1995 and is a registered patent attorney with the USPTO.

Stephen C. Knight, M.D. joined EPIX in July 1996, as Vice President of Business Development and was later promoted to Senior Vice President of Finance and Business Development. In July 1998, Dr. Knight assumed the role of Chief Financial Officer. In November 1999, he was named President and Chief Operating Officer of EPIX. From April 1991 to June 1996, Dr. Knight was a senior consultant with Arthur D. Little, specializing in biotechnology, pharmaceuticals and valuation. Dr. Knight was also a consultant at APM, Inc., a consulting company. Prior to 1990, Dr. Knight performed research at AT&T Bell Laboratories, the National Institute of Neurological and Communicative Diseases and Stroke, and at Yale University. Dr. Knight is the Chairman of Veritas Medicine, Inc., where he was a co-founder. Dr. Knight holds an M.D. from the Yale University School of Medicine and an M.B.A. degree from the Yale School of Organization and Management.

Peyton J. Marshall, Ph.D. joined EPIX in November of 2002 as Senior Vice President and Chief Financial Officer. Prior to joining EPIX, Dr. Marshall was Chief Financial Officer of The Medicines Company from 1997 through its initial public offering and the launch of its lead product until the company's headquarters moved to New Jersey in 2002. From 1995 to 1997, Dr. Marshall was based in London as a Managing Director and head of European Corporate Financing and Risk Management Origination at Union Bank of Switzerland, an investment banking firm. From 1986 to 1995, Dr. Marshall held various investment banking positions at Goldman Sachs and Company, an investment banking firm, including head of European product development from 1987 to 1993 and Executive Director, Derivatives Origination from 1993 to 1995. From 1981 to 1986, Dr. Marshall held several product development positions at The First Boston Corporation, an investment banking firm, and was an Assistant Professor of Economics at Vanderbilt University. Dr. Marshall holds an A.B. in economics from Davidson College and a Ph.D. in economics from the Massachusetts Institute of Technology.

Gregg Mayer joined EPIX as Vice President of Marketing in April 1998 with 14 years of in-vitro diagnostics experience, adding his roles as MS-325 Business Manager and Corporate Communications thereafter. At Chiron Diagnostics from May 1992 until joining EPIX, Mr. Mayer was most recently Director of U.S. Marketing, Immunodiagnostics and managed strategies for automated laboratory systems and immunoassays. As Worldwide Marketing Manager, Immunodiagnostics, Mr. Mayer directed strategic development priorities for cardiovascular disease, endocrine disorders, bone disease and therapeutic drug monitoring, bringing more than 30 products through the development pipeline. At Abbott Diagnostics from 1984 to 1992, Mr. Mayer started his healthcare career in sales and was global

Senior Product Manager for transplant immunosuppression and therapeutic drug monitoring products. Mr. Mayer holds a B.B.A. from The University of Texas at Austin and earned an M.B.A. in marketing, international business and finance from the JL Kellogg Graduate School of Management at Northwestern University.

Robert Weisskoff, Ph.D. joined EPIX full time as Senior Director of Imaging Development in October 1998, after serving as a consultant to EPIX since 1996. In September 2000, he was promoted to Vice President of Business Development and Head of Imaging. Prior to joining EPIX, Dr. Weisskoff spent eight years at Massachusetts General Hospital, and was the Associate Director of the MGH-NMR Center and Associate Professor of Radiology at Harvard Medical School. From 1988-1990, Dr. Weisskoff led the technology development for ultra-high speed MRI for the first commercial Echo Planar scanner at Advanced NMR Systems. Dr. Weisskoff holds an A.B. in Physics from Harvard, a Ph.D. in Physics from the Massachusetts Institute of Technology, and an M.B.A. from Columbia University.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to the terms and conditions of the underwriting agreement, the underwriters named below have severally agreed to purchase from us the number of shares set forth opposite their names on the table below at the public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus. SG Cowen Securities Corporation is acting as representative of the several underwriters named below:

Name	Number of Shares
SG Cowen Securities Corporation	
Wells Fargo Securities, LLC	
Needham & Company, Inc.	
WR Hambrecht+Co, LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters to purchase the shares of common stock offered hereby are conditional and may be terminated at their discretion based on their assessment of the state of the financial markets. The obligations of the underwriters may also be terminated upon the occurrence of other events specified in the underwriting agreement. The underwriters are severally committed to purchase all of the shares of common stock being offered by us if any shares are purchased.

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriting fee is an amount equal to the offering price to the public less the amount paid per share by the underwriters to us. The underwriters may offer the common stock to securities dealers at the price to the public less a concession not in excess of $ per share. Securities dealers may reallow a concession not in excess of $ per share to other dealers. After the shares of common stock are released for sale to the public, the underwriters may vary the offering price and other selling terms from time to time.

We have granted to the underwriters an option, exercisable not later than 30 days after the date of this prospectus supplement, to purchase up to an aggregate of 645,000 additional shares of common stock at the public offering price set forth on the cover page of this prospectus supplement less the underwriting discounts and commissions. The underwriters may exercise this option only to cover over-allotments, if any, made in connection with the sale of the common stock offered hereby. If the underwriters exercise their over-allotment option, the underwriters have severally agreed to purchase shares of common stock from us in approximately the same proportion as shown in the table above.

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Payable by EPIX Medical, Inc.	
	No Exercise	Full Exercise
Per share	$	$
Total		

We estimate that the total expenses of this offering, excluding underwriting discounts and commissions, will be approximately $.

We have agreed to indemnify the underwriters against certain civil liabilities, including liabilities under the Securities Act and liabilities arising from breaches of representations and warranties contained in the underwriting agreement, and to contribute to payments the underwriters may be required to make in respect of any such liabilities.

Our directors and executive officers have agreed with the underwriters that, for a period of 90 days following the date of this prospectus supplement, they will not dispose of or hedge any shares of common stock or any securities convertible into or exchangeable for shares of common stock, subject to customary estate planning exceptions. SG Cowen Securities Corporation may, in its sole discretion, at any time without prior notice, release all or any portion of the shares from the restrictions in any such agreement.

The representative of the underwriters has advised us that the underwriters do not intend to confirm sales to any account over which they exercise discretionary authority. The underwriters are delivering this prospectus supplement only in printed form.

The representative of the underwriters may engage in over-allotment, stabilizing transactions, syndicate covering transactions, penalty bids and passive market making in accordance with Regulation M under the Securities Exchange Act. Over-allotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate covering transactions involve purchases of the shares of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the shares of common stock originally sold by such syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Penalty bids may have the effect of deterring syndicate members from selling to people who have a history of quickly selling their shares. In passive market making, market makers in the shares of common stock who are underwriters or prospective underwriters may, subject to certain limitations, make bids for or purchases of the shares of common stock until the time, if any, at which a stabilizing bid is made. These stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the shares of common stock to be higher than it would otherwise be in the absence of these transactions. These transactions may be effected on the Nasdaq National Market or otherwise and, if commenced, may be discontinued at any time.

Our common stock is listed on the Nasdaq National Market under the symbol "EPIX".

LEGAL MATTERS

Certain legal matters in connection with the legality of the common stock offered by this prospectus supplement will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Hale and Dorr LLP, Boston, Massachusetts.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with them, which means that we can disclose to you important information contained in other documents filed with the SEC by referring you to those documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus. Information we later file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, or the Exchange Act, subsequent to the date of this prospectus

supplement through the termination of this offering. Please read the following documents incorporated by reference to this prospectus supplement and the accompanying prospectus:

our annual report on Form 10-K for the year ended December 31, 2002 filed with the SEC on March 28, 2003;

our proxy statement for our 2003 Annual Meeting of Shareholders filed with the SEC on April 29, 2003;

our quarterly report on Form 10-Q for the quarter ended March 31, 2003 filed with the SEC on May 13, 2003;

our quarterly report on Form 10-Q for the quarter ended June 30, 2003 filed with the SEC on July 28, 2003;

our current reports on Form 8-K filed on July 24, 2003, July 18, 2003, May 28, 2003, April 24, 2003, April 1, 2003, March 11, 2003 and February 4, 2003;

the description of our common stock contained in "Description of Capital Stock" in the registration statement on Form S-1 filed with the SEC on January 30, 1997 (File No. 333-17581) and any amendments or reports filed to update such description; and

all documents filed by us under Section 13(a), 13(c), 14, or 15(d) of the Exchange Act between the date of this prospectus supplement and the termination of the registration statement of which this prospectus supplement is a part.

If the information in incorporated documents conflicts with information in this prospectus supplement you should rely on the most recent information. If the information in an incorporated document conflicts with information in another incorporated document, you should rely on the most recent incorporated document.

You may request a copy of these filings at no cost, by writing or telephoning us at the following address: EPIX Medical, Inc., 71 Rogers Street, Cambridge, Massachusetts 02142, Attention: Investor Relations (telephone number: (617) 250-6000). If you have any other questions regarding us, please contact our Investor Relations Department in writing at the above address or at the above telephone number or visit our website at http://www.epixmed.com.

PROSPECTUS

5,000,000 SHARES

Common Stock

This prospectus will allow us to issue common stock over time.

We will provide a prospectus supplement each time we issue common stock;

The prospectus supplement will inform you about the specific terms of that offering and also may add, update or change information contained in this document;

You should read this document and any prospectus supplement carefully before you invest.

Our common stock is listed on the Nasdaq National Market under the symbol "EPIX." On December 18, 2002, the last reported sale price of our common stock on the Nasdaq National Market was $7.05 per share.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE "RISK FACTORS" ON PAGE 3.

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

The Date of this Prospectus is January 15, 2003

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ABOUT THIS PROSPECTUS

The following is only a summary. We urge you to read the entire prospectus, including the more detailed financial statements, notes to the financial statements and other information incorporated by reference from our other filings with the Securities and Exchange Commission, or SEC. Investing in our common stock involves risk. Therefore, carefully consider the information provided under the heading "Risk Factors" beginning on page 3.

BUSINESS

We are a leading developer of targeted contrast agents, which are substances injected into blood vessels to improve the visual images produced by magnetic resonance imaging, or MRI. MRI is a technique widely used in the identification of a variety of diseases. It is a non-invasive procedure that does not disturb body tissue and provides 3-dimensional images of, among other things, the body's arteries and veins, collectively known as the vascular system, that enable physicians to diagnose and manage disease. Our principal product under development, MS-325, is designed to provide visual imaging of multiple diseases of the heart and blood vessels, including diseases of the blood vessels outside the heart, known as peripheral vascular disease, as well as diseases that affect the coronary arteries and reduce blood flow to the heart. Our primary target indication for MS-325 is peripheral vascular disease. We believe that MS-325 will significantly enhance the quality of MRI and provide physicians with a clinically superior, minimally-invasive and cost-effective method for diagnosing peripheral vascular disease. We also believe that MS-325 will simplify, and, in many cases replace, X-ray angiography, a highly invasive and expensive catheter-based procedure currently used for the detection of peripheral vascular disease. We are currently in Phase III clinical trials to test the safety and efficacy of MS-325 enhanced magnetic resonance angiography, or MRA, which is a type of MRI that is specific to the vascular system. We

believe that magnetic resonance angiography will be a less invasive method of imaging and determining a patient's internal blood vessel anatomy for the evaluation of peripheral vascular disease.

The use of MRI has grown steadily over the past 10 years due to reduced cost and improved imaging capabilities. MRI now provides an effective method of diagnosis for a broad range of applications. MRI manufacturers have improved both their hardware and software, reducing the time per procedure dramatically, while 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. Prior attempts to employ contrast agents to make such vascular MRI more useful as a diagnostic tool have had limited success. Unlike most currently available non-specific MRI contrast agents, MS-325 is specifically designed to enhance the quality of magnetic resonance images of the arteries and veins and provide physicians with a superior method for diagnosing diseases in these vessels. 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. This molecule is designed with our proprietary technology to bind to albumin, the most common protein in the blood. In MS-325-enhanced images generated with standard MRI techniques, the blood produces a strong magnetic signal and appears bright against the dark background of surrounding tissue. Because of its attraction to albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam and therefore provides the extended image time and signal strength required to obtain a high contrast, high resolution image of the vascular system. Like most currently available non-specific contrast agents, MS-325 is designed to be excreted safely through the kidneys over time.

We have entered into strategic alliances with Schering Aktiengesellschaft, or Schering AG, and Tyco International Ltd., formerly Mallinckrodt, Inc., and referred to here as Tyco/Mallinckrodt, for the development, manufacture and commercialization of MS-325 and other vascular contrast agents. We have also formed collaborations with the three leading MRI scanner manufacturers, General Electric

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

Although we are seeking to develop another targeted contrast agent that would enable MRI to illuminate blood clots as described in more detail below, MS-325 is currently our only product candidate in human clinical trials. Our initial commercial product revenues and profits will depend on the successful completion of our Phase III clinical trials, Food and Drug Administration, or FDA, approval of MS-325, the successful manufacturing of the product by our partner Tyco/Mallinckrodt and sales by our partner Schering AG.

As noted above, and as part of our thrombus program, we are seeking to develop a targeted contrast agent in addition to MS-325 that would enable MRI to illuminate blood clots. Such a product could potentially change the method of diagnosis for many of the conditions associated with the formation of blood clots in the arteries and veins. The most common form of these conditions is deep vein thrombosis, which is characterized by the presence of blood clots in the deep veins of the leg and calf. The most severe consequences of deep vein thrombosis is pulmonary embolism, which tends to occur when a blood clot dislodges from the vessel wall to obstruct the arteries in the lung. We believe that the illumination of blood clots by a targeted contrast agent used in conjunction with MRI could lead to better medical outcomes due to earlier and more definitive diagnosis. Early diagnosis is especially important for clots in the thigh, pelvis and vena cava, which can be fatal because of their increased likelihood of migrating to the lungs. We believe that such a contrast agent could eliminate the need for procedures that require the use of large quantities of X-ray contrast dye and expose patients to radiation, diagnostic tests that use radioactive drugs and ultra sound, which are all currently used to identify blood clots in the veins and arteries. We further believe that our proprietary technology could enable MRI to differentiate old and new clot formation, thereby potentially identifying those clots that pose the most risk to patients. In November 1999, we announced that our prototype agent, EP-862, had been shown in pre-clinical testing to detect sub-millimeter blood clots in animals. Although we are unlikely to develop EP-862 as a thrombus agent, we have continued to advance the thrombus program by identifying several other improved prototype agents. We expect to continue to apply resources to the thrombus program in the future and hope to file an Investigational New Drug application, or IND, with the FDA, which, if approved, will allow us to begin human safety trials.

We incorporated in Delaware in 1988 and commenced operations in 1992. Our principal executive offices are located at 71 Rogers Street, Cambridge, Massachusetts 02142-1118 and our telephone number is (617) 250-6000. Our Web site is located at http://www.epixmed.com. We do not intend for the information contained in our Web site to be considered a part of this prospectus.

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the following risk factors, other information included in this prospectus, any supplement to this prospectus and 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, and you may lose some or all of your investment.

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, 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 is currently our only product candidate in human clinical trials, and we cannot be certain that any of our other development projects will yield a product candidate suitable for entry into clinical trials. As a result, our initial revenues and profits from commercial sales of our products, if any, will be derived from sales 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, product development and marketing agreements with strategic collaborators. In particular, our revenue for the year ended December 31, 2001 was $9.6 million, and consisted of $5.7 million from the product development portion of our strategic collaboration agreement with Schering AG, $2.1 million from a patent licensing and royalty agreement entered into with Bracco Imaging, S. p. A. and $1.8 million of license fee revenue related to the strategic collaboration agreements for the development 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 and equipment lease financings.

Although we are currently in compliance with the terms of our strategic 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 do not expect to 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, 2002 were approximately $109 million. These losses have primarily resulted from expenses associated with our research and development activities, including preclinical and clinical trials, and general and

administrative expenses. We anticipate that our research and development expenses will increase significantly in the future, and we expect to incur substantial losses over at least the next several years as we expand our research and development efforts, pre-clinical testing and clinical trials and 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 time frame 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 30% of all MRI exams, there are no FDA approved targeted vascular agents in use. Furthermore, clinical use of MRI for vascular imaging has been limited and use of MRI for peripheral vascular disease imaging has occurred mainly in research. Market acceptance, and thus sales of our product candidates, will depend on several factors, including:

safety;

price;

ease of administration;

effectiveness; and

the rate of adoption of up-to-date MRI technology.

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 MRI enhanced with MS-325 compared to imaging with other technologies. MS-325 represents a new approach to imaging the peripheral vascular system, and market acceptance both of MRI as an appropriate imaging technique for the peripheral vascular system, and of MS-325, is critical to our success. If MS-325 or any of our other products do not achieve market acceptance, we may not generate sufficient revenues to achieve or maintain profitability.

If we do not raise additional funds necessary to fund our operations, 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, equipment lease financings and royalty and license payments from our strategic partners. We believe that we will need to raise substantial additional funds for research, development and other expenses, through equity or debt financings, strategic alliances or otherwise, prior to commercialization of any of our product candidates. 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 United States 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 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.

We estimate that existing cash, cash equivalents and marketable securities will be sufficient to fund our operations through November 2003. We believe that we will need to raise additional funds for research, development and other expenses through equity or debt financing, strategic alliances or otherwise, in order to achieve commercial introduction of any of our product candidates. Additional funding may not be available to us on favorable terms, if at all. Debt financing, if available, may involve covenants which could restrict our business activities. To the extent that we raise additional capital through the sale of equity or securities convertible into equity, the issuance of such securities could result in dilution to our existing stockholders. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to enter into arrangements with strategic partners or others that may require us to relinquish rights to certain of our technologies, product candidates, products or potential markets. If we are required to relinquish such rights, the ultimate value of these product candidates to us may be reduced.

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 do manufacture small amounts of MS-325 for research and development efforts, we intend to rely on Tyco/Mallinckrodt as the primary manufacturer of MS-325 for Phase III clinical trials, as well as 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, we will not be able to complete development of our contrast agent for the evaluation of cardiac indications.

Although magnetic resonance imaging hardware and software is sufficient for the evaluation of peripheral 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 target indication. Our initial NDA filing for MS-325 will be related to peripheral vascular disease. Peripheral vascular disease, as it relates to our primary target indication, occurs in areas of the body where imaging sequences on scanners currently allow for the use of MS-325-enhanced magnetic resonance angiography for diagnostic purposes, which covers the entire body's vascular system, except for the heart. Based on feasibility studies we have conducted, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, is not developed to the point where there is clear visualization of the cardiac region, due to the effects of motion from the beating of the heart. Although not our primary focus, we plan to continue to conduct feasibility studies for cardiac indications using available software and hardware that can be adopted for coronary and cardiac perfusion data acquisition. We have entered into research collaborations with General Electric Medical Systems and Phillips 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 product manufacturers are not able to enhance their scanners to perform cardiac indications, 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 FDA-approved targeted vascular

contrasts agents for use with MRI, there are a number of non-specific MRI agents approved for marketing in the United States and certain foreign markets that are likely to compete with MS-325 if MS-325 is approved for Magnetic Resonance Angiography or MRA. Collectively, these non-specific agents are referred to as "extracellular" agents, and include: Magnevist® by Schering AG, Dotarem® by Guerbet, S.A., Omniscan® by Amersham Health, ProHance® by Bracco Imaging S.p.A. and OptiMark® by Tyco/Mallinckrodt. Extracellular agents are broadly-accepted in the market as general purpose 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 use becomes entrenched in the marketplace. Additionally, we believe that some of these general purpose agents are in clinical trials for an MRA indication. However, these general purpose agents are not specifically designed for vascular imaging and because they "leak" out of the 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 under clinical development, specifically for use with MRA: Schering AG's Gadomer-17 and SHU555C, Guerbet's P792 (Vistarem), Bracco's B-22956/1 and Advanced Magnetic's 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, or DSA, X-ray angiography, CT angiography, 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	3-dimensional images Minimally-invasive Favorable safety profile High quality images	Requires high level of training Inadvisable for patients with certain conditions (i.e. pacemakers, etc.) 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 2-dimensional images Expensive Patient recuperation time
Ultrasound	Low cost Fast Widely available Non-invasive	Operator dependent Lack of anatomic detail Bone precludes use in many vascular beds 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, may 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 United States 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, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems. Two of our key agreements include a collaboration agreement with Schering AG, to develop and commercialize MS-325 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 fail to meet certain performance targets in clinical trials. 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 in their respective territories, or they may not successfully market MS-325. 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 are currently in Phase III clinical trials, 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.

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 and patent applications, 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 a comprehensive patent program for our product candidates in the United States 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 the critical 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; two U.S. patents and their counterpart patents and applications in foreign countries that we own; eight patent applications and six provisional patent applications on fourteen different subject matters as well as their counterpart patents and applications in foreign countries. One of our issued patents covers the process by which MS-325 is manufactured. 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 patent applications in the United States with foreign counterparts and foreign applications are maintained in secrecy until patents are issued or published, and patent applications in foreign countries are maintained in secrecy for a specified 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 would 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;
- 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 United States 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. If any judicial or administrative proceeding upholds 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 any third party patent, 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 abroad. 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 preclinical laboratory and animal tests; submission of an investigational new drug application or IND; completion of human clinical trials; submission of a new drug application, or 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. Preclinical 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 can not 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 large-scale 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. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the clinical protocol under which MS-325 is studied, the proximity of the patient to a clinical site and the eligibility criteria for the study. 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 peripheral 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 peripheral vascular disease in the renal (kidney) arteries, and another to determine the efficacy of MS-325 enhanced MRA for the detection of peripheral vascular disease in the pedal (feet) arteries. Although providing us with greater market potential for the sale of MS-325 upon approval, we expect that this change to our Phase III clinical trial program, and the associated delay in the start up of new clinical centers, will result in an approximate fifteen month delay to our NDA submission date from our previous forecast, and an increase in costs associated with the program. If we do not successfully complete our Phase III clinical trial program, we will not have a product to market.

In addition, we may encounter unanticipated delays or significant costs in our efforts to secure necessary approvals. 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 preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent FDA 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 United States 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 preclinical 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, manufacturing and marketing of our product candidates 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 if and when 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 will not be able to commercialize 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 would have a material adverse effect on our ability to market our products and consequently it would 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 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 would 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 the lives of some key officers, 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 this 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 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 2001, the closing price of our common stock ranged from $14.60 to $6.24. Our common stock reached a high of $15.86 and traded as low as $4.11 during the first three quarters of 2002. The last reported sales price for our common stock on December 18, 2002 was $7.05. 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.

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 of control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These statements can be identified by the use of forward-looking terminology such as "may," "will," "could," "expect," "anticipate," "estimate," "continue" or other similar words. These statements discuss future expectations,

contain projections of results of operations or of financial condition or state trends and known uncertainties or other forward-looking information. Examples of forward-looking statements can be found in the discussion set forth under "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" in the Form 10-K for the year ended December 31, 2001 filed with the SEC on March 29, 2002 and incorporated in this prospectus by reference. Such statements are based on current expectations that involve a number of uncertainties. When considering forward-looking statements, you should keep in mind that the risk factors noted above and other factors noted throughout this prospectus or incorporated by reference could cause our actual results to differ significantly from those contained in any forward-looking statement. We do not intend to update any forward-looking statements to conform to actual results unless required by law.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the common stock offered by this prospectus, if any, for general corporate purposes including research and development and for the acquisition of, or investment in, companies, technologies or assets that complement our business. However, we have no present understandings, commitments or agreements to enter into any potential acquisitions or to make any investments.

The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from the sale of common stock offered by this prospectus, progress of our research, drug discovery and development programs, the results of pre-clinical and clinical studies, the timing of regulatory approvals, technological advances, determinations as to commercial potential of our compounds and the status of competitive products. In addition, expenditures will also depend upon the establishment of collaborative research arrangements with other companies and other factors. Pending application of the net proceeds, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities. Additional information about the use of net proceeds from the sale of common stock offered by this propsectus may be set forth in the prospectus supplement relative to the specific offering.

PLAN OF DISTRIBUTION

We may offer the common stock:

directly to purchasers;

to or through underwriters;

through dealers, agents or institutional investors; or

through a combination of such methods.

Regardless of the method used to sell the common stock, we will provide a prospectus supplement that will disclose:

the identity of any underwriters, dealers, agents or investors who purchase the common stock;

the material terms of the distribution, including the number of shares sold and the consideration paid;

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

the amount of any compensation, discounts or commissions to be received by the underwriters, dealers or agents;

any public offering price;

the terms of any indemnification provisions, including indemnification from liabilities under the federal securities laws; and

the nature of any transaction by an underwriter, dealer or agent during the offering that is intended to stabilize or maintain the market price of the common stock.

Sale Through Agents

We may designate agents to solicit purchases for the period of the agent's appointment or to sell the common stock on a continuing basis. Unless we inform you otherwise in the applicable prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of the agent's appointment.

Sale Through Underwriters Or Dealers

If underwriters are used in an offering of the common stock, we will execute an underwriting agreement with such underwriters and will set out the name of each underwriter and the terms of the transaction (including any underwriting discounts and other terms constituting compensation of the underwriters and any dealers) in a prospectus supplement. In the event that we use an underwriter in connection with an offering of common stock pursuant to this registration statement, we will file a post-effective amendment to the registration statement or a Current Report on Form 8-K in order to file any underwriting agreement with such underwriter or underwriters. If an underwriting syndicate is used, the managing underwriter(s) will be set forth on the cover of a prospectus supplement. Common stock may be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement that names the underwriter the nature of any such relationship.

If dealers are used in an offering of the common stock, we will sell the common stock to the dealers as principals. The dealers then may resell such common stock to the public at varying prices, which they determine at the time of resale.

Compensation of Underwriters, Dealers and Agents

Underwriters, dealers and agents that participate in the distribution of the common stock may be underwriters as defined in the Securities Act of 1933 and any discounts or commissions they receive from us, as well as any profit on their resale of the common stock, may be treated as underwriting discounts and commissions under the Securities Act. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers or agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

Direct Sales

We may sell the common stock directly. In that event, no underwriters or agents would be involved. We may sell the common stock directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of that common stock.

Delayed Delivery Contracts

If we so indicate in a prospectus supplement, we may authorize underwriters, dealers or agents to solicit offers from selected types of institutions to purchase common stock from us at the public offering price under delayed delivery requirements. These contracts would provide for payment and delivery on a specified date in the future. Institutions with which such contracts may be made include commercial and savings

banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement relating to such contracts will set forth the price to be paid for common stock under the contracts, the commission payable for solicitation of the contracts and the date or dates in the future for delivery of the common stock under the contracts.

Stabilization Activities

During and after an offering through underwriters, the underwriters may purchase and sell the common stock in the open market. These transactions may include over-allotment and stabilizing transactions and purchases to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, in which selling concessions allowed to syndicate members or other broker-dealers for the offered common stock sold for their account may be reclaimed by the syndicate if the offered common stock is repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the offered common stock, which may be higher than the price that might otherwise prevail in the open market. If commenced, these activities may be discontinued at any time. Such stabilization activities will only be conducted in conjunction with a firm commitment underwritten offering.

Passive Market Making

Any underwriters who are qualified market makers on the NASDAQ National Market may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering,

before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of highest independent bid for the security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid then must be lowered when certain purchase limits are exceeded.

LEGAL MATTERS

The validity of the issuance of the common stock offered in this prospectus is being passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

Our financial statements, appearing in our Annual Report on Form 10-K for the year ended December 31, 2001, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file at the SEC's Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public at the SEC's web site at "http://www.sec.gov." In addition, our stock is listed for trading on the Nasdaq National Market. You can read and copy reports and other information concerning us at the offices of the National Association of Securities Dealers, Inc. located at 1735 K Street, Washington, D.C. 20006.

This prospectus is only part of a Registration Statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933 and therefore omits certain information contained in the Registration Statement. We have also filed exhibits and schedules with the Registration

Statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may:

inspect a copy of the Registration Statement, including the exhibits and schedules, without charge at the public reference room, or

obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 until the sale of all of the shares of common stock. The documents we are incorporating by reference are:

our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2002, June 30, 2002 and September 30, 2002;

our Annual Report on Form 10-K for the fiscal year ended December 31, 2001;

our Forms 8-K filed on November 14, 2002, March 18, 2002, January 25, 2002, January 16, 2002 and January 14, 2002;

our Definitive Proxy Statement filed on April 30, 2002; and

the description of our common stock contained in "Description of Capital Stock" in the Registration Statement on Form S-1 filed with the SEC on January 30, 1997 (File No. 333-17581), including any amendment or report filed for the purpose of updating such description.

You may request a copy of these filings at no cost by writing or telephoning our Investor Relations Officer at the following address and phone number:

EPIX Medical, Inc.
71 Rogers Street
Cambridge, Massachusetts 02142
(617) 250-6000

This prospectus is part of a Registration Statement that we filed with the SEC. You should rely only on the information incorporated by reference in or provided in this prospectus and the Registration Statement. We have not authorized any other person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of this document.