EPIX MEDICAL INC
Form 424B2
January 15, 2002

FILING PURSUANT TO RULE 424(B)(2)
REGISTRATION NO. 333-41782
REGISTRATION NO. 333-

PROSPECTUS SUPPLEMENT NO. 10
(TO PROSPECTUS DATED AUGUST 22, 2000)
EPIX MEDICAL, INC.
2,575,000 SHARES
COMMON STOCK

Epix Medical, Inc. is offering 2,575,000 shares of its common stock, $.01 par value per share, through this prospectus supplement and the accompanying prospectus at $12.50 per share. Our common stock is listed on the Nasdaq National Market under the symbol "EPIX." The last reported sale price of the common stock on the Nasdaq National Market on January 14, 2002 was $13.00 per share.

Robertson Stephens, Inc. has agreed to act as placement agent for the sale of up to 2,575,000 shares of our common stock. The placement agent is not required to sell any specific number or dollar amount of shares of common stock, but will use all reasonable efforts to arrange for the sale of all 2,575,000 of the shares.

INVESTING IN OUR COMMON STOCK INVOLVES RISKS.
SEE "RISK FACTORS" BEGINNING ON PAGE 5 OF THE ACCOMPANYING PROSPECTUS.

	PER SHARE	TOTAL
Public Offering Price	$12.50	$32,187,500
Commissions to Placement Agents	$ 0.75	$ 1,931,250
Proceeds to Epix Medical, Inc. (Before Expenses)	$11.75	$30,256,250

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

ROBERTSON STEPHENS
As Placement Agent
The date of this prospectus supplement is January 14, 2002.

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ABOUT THIS PROSPECTUS SUPPLEMENT

You should read this prospectus supplement along with the accompanying prospectus and the information incorporated by reference in these documents carefully before you invest. Such documents contain information you should consider carefully before making your investment decision. See "Incorporation of Documents by Reference" on page 38 of the accompanying prospectus. This prospectus supplement may add, update or change information in the prospectus. You should rely only on the information provided in this prospectus supplement, the accompanying prospectus or documents incorporated by reference in the accompanying prospectus. We have not authorized anyone to provide you with different information.

THE OFFERING

Common stock offered	2,575,000 shares
Common stock to be outstanding after the offering	16,811,852 shares
Use of proceeds	For general corporate and business purpose See "Use of Proceeds."
Dividend policy	We have never declared or paid any cash dividends on our capital stock. We intend retain any future earnings to finance the growth and development of our business and not anticipate paying any cash dividends i the foreseeable future.
Nasdaq National Market symbol	EPIX

We have 40,000,000 shares of authorized common stock and 1,000,000 shares of authorized Preferred Stock. As of December 31, 2001, options to purchase 3,373,476 shares of our common stock and warrants to purchase 26,665 shares of our common stock were outstanding.

USE OF PROCEEDS

We estimate the net proceeds from the sale of 2,575,000 shares of common stock offered by this prospectus supplement and the accompanying prospectus will be approximately $30,156,250, based upon an estimated offering price of $12.50 per share and after deducting the commission to be paid to the placement agents and the estimated offering expenses payable by us. The net proceeds to Epix from the sale of the shares of common stock offered by means of this prospectus supplement and the accompanying prospectus will be used in the manner described under "Use of Proceeds" on page 14 of the accompanying prospectus.

PLAN OF DISTRIBUTION

We are selling the shares of common stock through the placement agent. Subject to the terms and conditions contained in the placement agency agreement dated January 14, 2002, Robertson Stephens, Inc. has agreed to act as placement agent for up to 2,575,000 shares of common stock. The placement agent is not required to sell any specific number or dollar amount of shares, but has agreed to use all reasonable efforts to arrange for the sale of all 2,575,000 of the shares.

The placement agency agreement provides that the obligations of the placement agent are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of certain certificates, opinions and letters from us and our counsel.

The placement agent proposes to arrange for the sale to one or more purchasers of the shares of common stock offered pursuant to this prospectus supplement and the accompanying prospectus. We will pay the placement agent a commission equal to 6% of the gross proceeds of the sales of shares of common stock.

The following table shows the per share and total commissions we will pay to the placement agent in connection with the sale of the shares offered pursuant to this prospectus supplement and the accompanying prospectus.

Per share	$ 0.75
Total	$1,931,250

It is expected that the sale of the 2,575,000 shares will be completed on January 18, 2002. We estimate the total expenses of this offering which will be payable by us, excluding the commissions, will be approximately $100,000.

We have agreed to indemnify the placement agent against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribute to payments the placement agent may be required to make in respect thereof.

In order to facilitate the offering of the common stock, the placement agent may engage in transactions that stabilize, maintain or otherwise affect the market price of our common stock. Any of these activities may maintain the

market price of our common stock at a level above that which might otherwise prevail in the open market. The placement agent is not required to engage in these activities and if commenced, may end any of these activities at any time.

Robertson Stephens and its respective affiliates have in the past and may in the future perform financial services for us, for which they have received customary fees.

This is a brief summary of the material provisions of the Placement Agency Agreement and does not purport to be a complete statement of its terms and conditions. A copy of the Placement Agency Agreement is on file with the SEC and is incorporated by reference into the Registration Statement of which this prospectus supplement forms a part. See "Where You Can Find More Information" on page 37 of the accompanying prospectus.

VALIDITY OF COMMON STOCK

The validity of the shares of common stock we are offering will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. of Boston, Massachusetts, and for the placement agents certain legal matters related to this offering will be passed upon by Testa, Hurwitz & Thibeault, LLP of Boston, Massachusetts.

2,575,000 Shares
EPIX MEDICAL, INC.
Common Stock

PROSPECTUS
SUPPLEMENT

ROBERTSON STEPHENS

January 14, 2002

You should rely on the information contained in this prospectus supplement and attached prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement and attached prospectus. We are offering to sell, and seeking offers to buy, common shares only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement and attached prospectus is accurate only as of the date of this prospectus supplement and prospectus, regardless of the time of delivery of this prospectus supplement and attached prospectus or of any sale of our common shares.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the common shares or possession or distribution of this prospectus supplement and attached prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement and attached prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement and attached prospectus applicable to that jurisdiction.

PROSPECTUS

3,000,000 SHARES

EPIX MEDICAL, INC.

COMMON STOCK

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

- 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 August 21, 2000 the last reported sale price of our common stock on the Nasdaq National Market was $14.50 per share.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 5.

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 August 22, 2000

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PROSPECTUS SUMMARY

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 SEC. INVESTING IN OUR COMMON STOCK INVOLVES RISK, THEREFORE, CAREFULLY CONSIDER THE INFORMATION PROVIDED UNDER THE HEADING "RISK FACTORS" BEGINNING ON PAGE SIX.

OUR BUSINESS

We are a leading developer of targeted intravascular contrast agents intended for use with magnetic resonance imaging, known as MRI, for the diagnosis of human disease. Our principal product under development, MS-325, is an injectable intravascular contrast agent intended to enhance the quality of MR images and provide physicians with a superior method for diagnosing diseases affecting the vasculature. MS-325 is a small molecule, which produces an MRI signal because of the presence of gadolinium, a highly magnetically active element favored by clinicians for enhancing MR images. This molecule is designed with our proprietary technology to bind to albumin, the most common blood protein. In MS-325 images using standard MRI techniques, the blood gives off a strong magnetic signal and appears bright 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 and therefore provides the image acquisition time and signal strength needed to obtain a high contrast, high resolution image of the cardiovascular system. Like most currently available non-specific contrast agents, MS-325 is designed to be excreted safely through the kidneys over time.

We believe that MS-325 will simplify the diagnostic pathway for a number of diseases and in many cases replace highly invasive and expensive X-ray angiography, which is currently considered the definitive diagnostic exam for assessing cardiovascular disease. We have entered into strategic alliances with Schering Aktiengesellschaft, Mallinckrodt Inc. and Daiichi Radioisotope Laboratories, Ltd. for the development, manufacture and commercialization of MS-325 and other vascular contrast agents. We have also formed collaborations with the three major MRI scanner manufacturers, General Electric Medical Systems, Philips Medical Systems and Siemens to develop advanced imaging techniques designed to facilitate the use of MS-325-enhanced MRI.

In June 1999, we initiated a Phase III clinical trial to determine the efficacy of MS-325-enhanced MR angiography for the detection of aortoiliac occlusive disease, a common peripheral vascular disease. The trial is designed to compare the diagnostic accuracy of MS-325-enhanced MR angiography with that of X-ray angiography. In June 1998, the Company completed a Phase II clinical trial to test the safety and preliminary efficacy of MS-325 for the evaluation of peripheral vascular disease in the carotid, iliac and femoral arteries. This clinical trial favorably compared MS-325-enhanced MR angiography to conventional X-ray angiography, the current reference standard. We are currently conducting Phase II feasibility trials to test the safety and preliminary efficacy of MS-325 for the evaluation of coronary artery disease and recently completed enrollment of patients in Phase II trials for detection of malignant breast lesions as well as female sexual arousal dysfunction. Through our pre-clinical studies, we also intend to determine the potential utility of MS-325-enhanced MRI for a wide variety of applications, including myocardial perfusion imaging, low-field MR imaging, diagnosis or monitoring of muscular dystrophy, MRI-guided stent placement, lymphatic imaging, migraine imaging and diagnosis of diabetic angiopathy.

OUR COMPANY

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.

THE OFFERING

Common Stock offered in this prospectus.....	3,000,000 shares
Common Stock outstanding after the offering.....	15,999,244(1)
Use of Proceeds.....	For discovery and development programs and for other general corporate purposes.
Nasdaq National Market symbol.....	EPIX

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(1) Based on 12,999,244 shares outstanding as of July 14, 2000.

RISK FACTORS

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF FINANCIAL RISK. IN DECIDING WHETHER TO INVEST, YOU SHOULD CAREFULLY CONSIDER THE FOLLOWING RISK FACTORS AS WELL AS OTHER INFORMATION IN THIS PROSPECTUS, INCLUDING INFORMATION INCORPORATED BY REFERENCE FROM OTHER DOCUMENTS THAT WE FILE WITH THE SEC. IF ANY OF THESE RISKS ACTUALLY OCCUR, OUR BUSINESS, FINANCIAL CONDITION, OPERATING RESULTS OR CASH FLOWS COULD BE ADVERSELY AFFECTED. THIS COULD CAUSE THE TRADING PRICE OF OUR COMMON STOCK TO DECLINE, AND YOU COULD LOSE ALL OR PART OF YOUR INVESTMENT.

RISKS RELATING TO OUR BUSINESS AND INDUSTRY

WE ARE IN AN EARLY STAGE OF DEVELOPMENT AND HAVE NOT GENERATED REVENUES FROM COMMERCIAL SALES OF OUR PRODUCTS.

We currently have no products for sale, and we can not guarantee that we will ever have marketable products. All of our product candidates are in research or development. To date, we have financed our operations through public stock offerings, private sales of equity securities, equipment lease financings and license payments from our strategic partners. To achieve profitable 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. We can not assure you that we will successfully complete our product development efforts, that we will obtain required regulatory approvals in a timely manner, if at all, that we will be able to manufacture our product candidates at an acceptable cost and with acceptable quality or that we can successfully market any approved products.

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 December 31, 1999 were approximately $45.4 million and on March 31, 2000 they were $50.6 million. These losses have resulted primarily 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. We may never generate revenues from the sale of our products. Moreover, even if we generate product revenues, we may not be able to achieve or sustain profitability.

OUR FINANCIAL RESULTS FLUCTUATE QUARTERLY, WHICH COULD NEGATIVELY AFFECT OUR STOCK PRICE.

Our results of operations have varied and will continue to vary significantly from quarter to quarter and depend on, among other factors:

- the timing of fees and milestone payments that we receive from strategic partners;
- whether we form new strategic alliances;
- the timing of expenditures in connection with research and development activities, including clinical trials;
- 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.

Fluctuations in our results of operations may cause us to fail to meet investor expectations, resulting in a decline in the trading price of our stock price. As a result, you may lose all or part of your investment.

FOR THE FORSEEABLE FUTURE, WE WILL DEPEND ON OUR ONLY PRODUCT, MS-325, FOR REVENUES.

MS-325 is currently our only product candidate in human clinical trials and we can not guarantee 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, if any, will be derived from sales of MS-325. If MS-325 fails to achieve regulatory approval and market acceptance, our business, financial condition and results of operations will be materially adversely effected.

BECAUSE DEVELOPMENT OF OUR TARGETED CONTRAST AGENTS WILL INVOLVE A LENGTHY AND COMPLEX PROCESS, WE ARE NOT CERTAIN THAT WE WILL BE ABLE TO COMMERCIALIZE ANY OF OUR PRODUCTS CURRENTLY IN DEVELOPMENT.

Our product candidates are currently in research and development and will require additional research and development, extensive clinical testing and regulatory approval prior to any commercial sales. We cannot predict if or when we will be able to commercialize any of our products under development. We must complete clinical trials in the United States and demonstrate the safety and efficacy of MS-325, currently in Phase III clinical trials, prior to obtaining Food and Drug Administration approval. 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 trial proceeds. Our results from early clinical trials may not predict results that we will obtain in large scale clinical trials, as a number of companies have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. We may not conduct additional Phase II or Phase III clinical trials for MS-325 and such trials, if

begun, may not demonstrate any efficacy or will be completed successfully in a timely manner, if at all. 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 will be studied, the proximity of the patient to a clinical site and the eligibility criteria for the study. Delays in planned patient enrollment may result in increased costs, regulatory filing delays, or both. Furthermore, we, the FDA or other regulatory authorities may alter, suspend or terminate clinical trials at any time. If we do not successfully complete clinical trials, we will not have a product to market.

IF MRI MANUFACTURERS DO NOT ENHANCE THEIR HARDWARE AND SOFTWARE, WE WILL NOT BE ABLE TO MARKET OUR CONTRAST AGENTS FOR CARDIAC INDICATIONS.

Existing MRI scanners do not have the capability to perform coronary angiography without improvements in current MRI hardware and software. The success of cardiac applications of MS-325 therefore depends on advancements in MRI hardware and software. Although several leading MRI manufacturers, academic centers and others are developing advanced hardware and software, we do not know when, or if, these techniques will enable MS-325 to provide clinically relevant images in the cardiac indications that we are pursuing. If MRI manufacturers do not enhance their scanners to perform coronary angiography, we will not be able to market MS-325 for that application and the potential market for our products will be substantially reduced.

IF MRI TECHNOLOGY BECOMES OBSOLETE, WE WILL NOT HAVE A MARKET FOR OUR PRODUCT CANDIDATES.

Several well-established medical imaging modalities compete with MRI, including X-ray angiography, computer assisted tomography, nuclear medicine and ultrasound. Other companies are actively developing the capabilities of the competing modalities to enhance their effectiveness in cardiovascular system imaging. If developments by others render MS-325 or our future product candidates obsolete or non-competitive, we will not have a market for our product candidates.

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 products, when and if approved for marketing by the United States Food and Drug Administration, 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 35% to 45% 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 cardiac 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 our product candidates compared to imaging with other modalities. Our MRI contrast agents represent a new approach to imaging the cardiovascular system and market acceptance both of MRI as an appropriate imaging technique for the cardiovascular system and of our product candidates is critical to our success. If our products do not achieve market acceptance, we may not generate sufficient revenues to achieve or maintain profitability.

OUR COMPETITORS HAVE GREATER FINANCIAL RESOURCES, SUPERIOR PRODUCTS, MANUFACTURING CAPABILITIES 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. Many of these competitors have substantially greater capital and other resources than we have 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 developed. In addition, these companies may be more successful than we are in developing, manufacturing and marketing products. Our strategic partners or customers may choose to use competing technologies or products. As a result, we may not be able to compete successfully in the future.

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.

Under the terms of a license agreement that we have with Massachusetts General Hospital, 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, sub-licensing, royalty and other obligations on us. If we fail to comply with these and other requirements our license could convert from exclusive to non-exclusive or terminate entirely. It is unlikely that we would be unable to obtain this technology elsewhere. Any such event would have a material adverse effect on our business, financial condition and results of operations.

WE DEPEND ON OUR STRATEGIC COLLABORATORS FOR SUPPORT IN PRODUCT DEVELOPMENT AND THE REGULATORY APPROVAL PROCESS, AND, IF WE EXPERIENCE PROBLEMS WITH OUR COLLABORATORS, WE MAY NOT GET REGULATORY APPROVAL.

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 several strategic alliances, including a collaboration agreement with Schering AG, to develop and commercialize MS-325 worldwide, excluding Japan, and other MRI vascular agents worldwide, a development and license agreement with Daiichi for the development and commercialization of MS-325 in Japan and an agreement with Mallinckrodt, Inc. (a Delaware corporation) and Mallinckrodt, Inc. (a New York corporation) granting 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. Schering AG, Mallinckrodt and Daiichi currently manufacture imaging agents for other modalities that will compete against MS-325. Schering AG will be responsible for setting the price of the product worldwide, except Japan, and Daiichi will be responsible for setting the product price in Japan. However, Schering AG or Daiichi may not set prices in a manner that maximizes revenues for us. In addition, Daiichi may exercise its right to terminate our agreement on short notice under certain circumstances. Our failure to receive milestone payments, a reduction or discontinuance of efforts by our partners, or the termination of these alliances would have a material adverse effect on our business, financial condition and results of operations.

We may not successfully enter into additional strategic alliances for the development and commercialization of future product candidates. In addition, any future alliances may not be on terms favorable to us or may not be successful. 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 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. However, the patent positions of pharmaceutical and biopharmaceutical firms, including us, generally include complex legal and factual questions. The issued patents that we own or license, or any patents that we obtain in the future, may not effectively protect our technology or provide a competitive advantage. In addition, any of our patents, patent applications or licensed patents may be challenged, invalidated or circumvented in the future.

Many of our competitors actively pursue patent protection for activities and discoveries similar to our activities and discoveries. These competitors, many of which have made substantial investments in competing technologies, could seek to assert that our products or chemical processes infringe on their existing patents and/or will not seek new patents that claim to cover aspects of our technology. Furthermore, patent applications in the United States are maintained in secrecy until patents are issued, and patent applications 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 pharmaceuticals are numerous. Therefore, we may not be aware of all competitive patents, either pending or issued, that relate to our products or processes used or those products or processes that we propose to use. If our patents fail to protect our business, we may not be able to compete effectively.

WE MAY INCUR SUBSTANTIAL COSTS AS A RESULT OF LITIGATION OR OTHER PROCEEDINGS RELATING TO OUR PATENT AND OTHER INTELLECTUAL PROPERTY RIGHTS.

The pharmaceutical and biotechnology industries are characterized by extensive litigation regarding patents and other intellectual property rights. We intend to protect and defend our intellectual property vigorously. We may need to bring costly and time-consuming litigation to enforce our issued patents, to protect our trade secrets and know-how, or to determine the enforceability, scope and validity of the proprietary rights of others. 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 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 could be breached or we may not have adequate remedies for any breach. Furthermore, our competitors could independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our proprietary technology, and we might not be able to meaningfully protect our rights in unpatented proprietary technology. 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 commercial success will also depend on our ability to operate without infringing upon the patents of others in the United States and abroad. There are 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.

EXTENSIVE GOVERNMENT REGULATION MAY DELAY OR PREVENT US FROM MARKETING MS-325 OR 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, it is possible that accidents will happen that

would expose us to legal risk and/or financial loss. 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.

The regulatory approval process for new MRI contrast agents, including required preclinical studies and clinical trials, 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 assure you 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. 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. 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.

We and our strategic partners 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.

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 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.

Additional financing may not be available on terms acceptable to us, or at all. If we cannot fund our capital requirements, it would have a material adverse effect on our business, financial condition and results of operations. If adequate funds are not available, we may have to curtail operations significantly or obtain funds by entering 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. 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.

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 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 Mallinckrodt fails to fulfill its manufacturing responsibilities satisfactorily, Schering 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 may not be able to find an alternative manufacturer. In addition, Schering 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.

IF THE SUPPLIERS FROM WHOM WE PURCHASE COMPONENTS OF MS-325 RAISE PRICES OR REDUCE QUANTITIES, THE COST TO PRODUCE MS-325 COULD INCREASE SIGNIFICANTLY.

We currently procure the raw materials for the various components of MS-325 from a broad variety of vendors and, wherever possible, maintain relationships with multiple vendors for each component. There are a number of components of MS-325 for which the largest suppliers may have significant control over the market price due to controlling market shares. If any one of our suppliers decided to increase prices significantly or reduce quantities of components of MS-325 available for sale to us, it could have a material adverse effect on our ability to commercialize MS-325 and on our business, financial condition and results of operations.

PRODUCT LIABILITY CLAIMS COULD INCREASE OUR COSTS AND ADVERSELY EFFECT OUR RESULT 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 FOR OUR PRODUCTS AFTER THEY ARE APPROVED FROM THIRD PARTY PAYORS IN THE U.S. AND ABROAD, WE WILL NOT BE ABLE TO COMMERCIALIZE OUR PRODUCTS.

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 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 can not 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 key technical and senior management personnel, many of whom would be difficult to replace and some of whom perform important functions for us beyond those functions suggested by their respective job title or description. 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. 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.

RISKS RELATING 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 the shares of our common stock is affected by:

- 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
- general market conditions.

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 development stage companies. These broad market fluctuations may adversely affect the market price of our common stock. In the past, following periods of volatility in the market price of a particular company's securities, shareholders have often brought class action securities litigation against that company. Such litigation, if brought against us, could result in substantial costs and a diversion of management's attention and resources.

WE DO NOT HAVE AN EXACT PLAN FOR THE USE OF THE NET PROCEEDS OF THIS OFFERING AND WILL THEREFORE HAVE BROAD DISCRETION AS TO THE USE OF THESE PROCEEDS, WHICH WE MAY NOT USE EFFECTIVELY.

We may allocate the net proceeds from this offering in ways which you and other stockholders may not approve. We have no exact plan with respect to the use of the net proceeds of this offering and have not committed these proceeds to any particular purpose apart from expenses of the business and general working capital and possible future acquisitions. Accordingly, our management will have broad discretion in applying the net proceeds of this offering and may use the proceeds in ways with which you and our other stockholders may disagree. We may not be able to invest these funds effectively which would adversely affect our financial condition.

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" in our Annual Report on Form 10-K for the year ended December 31, 1999 and under "Business" in the Form 10-K, incorporated in this prospectus by reference. Such statements are based on current expectations that involve a number of uncertainties including those set forth in the risk factors above. 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.

USE OF PROCEEDS

We intend to use the net proceeds of this offering, if any, for general corporate and business purposes, general working capital and possible future acquisitions. 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 this offering, progress of our research, drug discovery and development programs, the results of preclinical 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.

Further, we have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain earnings, if any, to support the development of our business and do not anticipate paying cash dividends for the foreseeable future. In addition, our current long-term debt agreement prohibits the payment of cash dividends.

DILUTION

The pro forma net tangible book value of the common stock, which reflects the purchase of 1,112,075 shares of our common stock by Schering Berlin Venture Corporation on June 20, 2000 pursuant to a stock purchase agreement dated June 9, 2000, as of March 31, 2000 was approximately $26.1 million, or $2.03 per share. After giving effect to our sale of 3,000,000 shares of common stock in this public offering at an assumed public offering price of $17.25 per share, and after deducting the estimated underwriting discount and offering expenses, the adjusted pro forma net tangible book value as of March 31, 2000 would have been $77.8 million, or $4.91 per share.

The pro forma net tangible book value per share before this offering has been determined by dividing the pro forma net tangible book value (total tangible assets less total liabilities) by the pro forma number of shares of common stock outstanding as of March 31, 2000. This offering will result in an increase in net tangible book value per share of $2.88 to existing stockholders and dilution in net tangible book value per share of $12.34 to new investors who purchase shares in this offering. Dilution is determined by subtracting the pro forma net tangible book value per share after this offering from the assumed public offering price of $17.25 per share. The following table illustrates this dilution:

Assumed public offering price		$17.25
Pro forma net tangible book value per share as of March 31, 2000	$2.03	
Increase attributable to new investors	2.88	
Pro forma net tangible book value per share after this offering		4.91
Dilution in pro forma net tangible book value to new investors		$12.34

The following table summarizes, as of March 31, 2000, on a pro forma basis to reflect the June 9, 2000 sale of 1,112,075 shares of common stock to Schering Berlin Venture Corporation, the differences between the total consideration paid and the average price per share paid by the existing stockholders and the new investors with respect to the number of shares of common stock purchased from us based on an assumed public offering price of $17.25 per share:

	SHARES		TOTAL CONSIDERATION	
	NUMBER	PERCENT	AMOUNT	PERCENT
New investors	3,000,000	18.94%	$ 51,700,338	40.17%
Existing stockholders	12,843,488	81.06	$ 77,007,949	59.83%

Total.....	15,843,488	100%	$128,708,287	100%

These tables assume no exercise of stock options and warrants outstanding as of March 31, 2000.

BUSINESS

CARDIOVASCULAR DISEASE BACKGROUND

The human cardiovascular system consists of the heart and a vast series 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 United States, with over 950,000 fatalities in 1998. One out of every 2.4 deaths in the United States is attributed to cardiovascular disease and it is estimated that over 58 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 deposits, or 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 coronary arteries, while peripheral vascular disease refers to disease in the major vessels outside the coronary arteries: vessels of the head and neck, the aorta, the renal arteries, and the large vessels of the pelvis, legs and arms.

Recent research in cardiovascular disease has begun to highlight the pervasive, or multi-focal nature, of this condition. Because the major risk factors tend to affect all vascular regions, many patients have multiple clinical manifestations of cardiovascular disease. Therefore, patients diagnosed with cardiovascular disease in one vascular region are at high risk of having similar disease in another vascular region. Clinicians have also begun to realize the importance of characterizing atherosclerotic plaques once they have been identified. We believe that the ability to characterize plaques may allow physicians to identify those regions of cardiovascular disease which present the most immediate threat to patients' health.

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

LIMB LOSS. Atherosclerotic blockages in the arteries of the pelvis and legs--the iliac, femoral, popliteal, and tibial arteries--can lead to ischemia (lack of oxygen) or infarction (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 United States primarily due to some form of cardiovascular disease.

AORTIC ANEURYSM. The aorta is the main blood vessel that carries blood from the heart to the rest of the body. Degenerative changes in the vessel wall often result in the enlargement or bulging of the lower part 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

United States. Because this condition can be asymptomatic for many years, many physicians have begun to consider the merits and cost-effectiveness of routine screening programs for this disease.

HEART ATTACK. The coronary arteries supply blood to the heart muscle (myocardium). When these arteries are narrowed or clogged due to atherosclerotic buildup, the result can be chest pain (angina pectoris) or heart attack (myocardial infarction). This condition, known as coronary artery disease, is estimated to afflict 7 million Americans. Coronary artery disease is responsible for a significant portion of the nearly 500,000 heart attack deaths each year, making it the number one cause of death in the United States.

HYPERTENSION. The renal arteries are the vessels which carry blood to the kidneys. Blockage of these arteries can result in kidney failure and in addition is estimated to account for up to ten percent of all cases of 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 50 million individuals in the United States. Early diagnosis can be extremely helpful for patients with renovascular hypertension because it can be treated with various revascularization procedures; however, X-ray angiography, the current definitive diagnosis for this condition, carries elevated risk for patients with renal impairment due to the toxicity of the X-ray contrast dye.

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 elevated 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 80% of the 600,000 strokes each year in the United States are a result of atherosclerotic disease.

DIAGNOSING CARDIOVASCULAR DISEASE--THE LIMITS OF CURRENT PRACTICE

Cardiovascular disease is currently diagnosed using a number of different imaging technologies, or modalities, including X-ray angiography, computed tomography, ultrasound, intravascular ultrasound, nuclear medicine and magnetic resonance imaging, or 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. These procedures tend to be relatively inexpensive and non-invasive. Definitive diagnostic procedures, on the other hand, are relied upon to give physicians the information required to make final diagnosis and plan treatment. Because of the importance of this definitive information, physicians are willing to resort to costlier, more invasive modalities.

SCREENING FOR PERIPHERAL VASCULAR DISEASE. A patient with peripheral vascular disease may exhibit a wide range of symptoms including: leg pain; gangrene; hypertension; stroke and transient ischemic attack, 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 peripheral vascular disease of the lower limb, 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,

leading to exams which are frequently inconclusive.

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, then a cardiologist will often perform a stress echocardiogram and/or a nuclear stress perfusion study.

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 reflected in atypical motion of the heart wall. The test is non-invasive and costs between $300 and $900. While a normal stress echocardiogram usually eliminates the possibility of blockages which significantly decrease blood flow, the test is often inconclusive and provides no information on the anatomy of the coronary arteries. We estimate that over 1.6 million stress echocardiograms were performed in the United States in 1998.

NUCLEAR STRESS PERFUSION STUDIES, which measure the flow of blood to cardiac tissue, can be used either as the critical diagnostic test prior to X-ray angiography or to confirm the impact on blood flow of an intermediate blockage identified through X-ray angiography. These tests are non-invasive, use small quantities of radiation and cost between $600 and $1,400. 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 on the resultant images. While the test can identify the effects of coronary artery disease, it provides no information on the anatomy of the coronary arteries and it cannot determine the location of blockages. We estimate that over 3.8 million nuclear stress perfusion studies were conducted in the United States in 1998.

DEFINITIVE DIAGNOSIS OF PLAQUE BLOCKAGES. 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 relevant artery, X-ray contrast dye is injected into the bloodstream and an image is acquired of that vascular region. 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 4.3 million X-ray angiograms were performed in the United States in 1998, of which approximately 2.1 million were coronary angiograms. X-ray angiography has a number of undesirable characteristics for a diagnostic modality including:

- Invasive procedure results in significant risk of serious complications including limb loss, renal failure, and death;

- Exposure of patients to potentially harmful ionizing radiation;

- Separate exams are necessary to view both arteries and veins;

- Separate exams are necessary for each vascular region;

- Provides only 2-dimensional images;

- Relatively expensive ($1,000-$3,000 for peripheral angiograms, $2,000-$6,000 for coronary angiograms);

- Cost and invasive nature limit patient post-procedure follow-up; and

- Inability to characterize plaques.

Another modality currently being investigated as a potential diagnostic tool for imaging blood vessels is computed tomography, or CT, which is a modality primarily used to image solid organs. Although it does not require an arterial puncture, CT requires the use of large quantities of toxic X-ray contrast dye and exposes patients to radiation, which limits the number of vascular regions it can image in an exam. CT has shown limited success in imaging the coronary arteries due to cardiac motion. A specialized form of CT, electron beam CT, is approved in the United States 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 contrast dye and radiation. CT is also being investigated for use in detecting calcium deposits in the coronary arteries, which has been advocated as predictive of atherosclerotic disease in that region. While extremely sensitive, this technique is limited by its high level of false positives.

MRI has been established as the imaging modality of choice for a broad range of applications, including brain tumors, knee injuries and many spinal disorders. 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 3-dimensional images. A contrast agent is often 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 35-40% of all MRI exams.

MR 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 installations. 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 the decreased cost and infrastructure requirements. The trade-off for low-field MR scanners is that a decrease in the strength of the magnetic field results in a decrease in the MR signal detected, which typically results in reduced resolution.

MRI has not made a significant impact on the diagnosis of cardiovascular disease to date with the exception of certain carotid artery studies. Non-contrast agent MRI exams of the vascular system, which image blood flow rather than anatomy, are often ineffective when used in patients with cardiovascular disease because of the minimal or turbulent blood flow associated with this condition. Even for the imaging of carotid arteries, where flow-based MRI has had some clinical impact, the lack of direct anatomic data limits the ability of MRI to provide a quantitative measurement of stenosis required for accurate diagnosis. MRI exams using existing non-specific 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 which remain in the bloodstream for extended periods of time will be necessary to obtain sufficient contrast for widespread

use of MRI to image the vascular system.

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 then X-ray angiograms, are not commonly used in the United States due to the elevated risk of complications.

In summary, the current process for diagnosing cardiovascular disease is a complicated pathway which 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, non-invasive exam which provides more comprehensive diagnostic information about the cardiovascular system.

OUR APPROACH TO DIAGNOSING CARDIOVASCULAR DISEASE

Our principal product under development, MS-325, is an injectable intravascular contrast agent intended to enhance the quality of MR images and provide physicians with a superior method for diagnosing diseases affecting the vasculature. Unlike most currently available MRI contrast agents, which are non-specific and therefore leak rapidly out of the bloodstream, MS-325 binds reversibly to albumin, the most common blood protein. Because of its affinity for albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam and, consequently, provides the image acquisition time and signal strength needed to obtain a high contrast, 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 MRI may facilitate several clinically valuable diagnostic procedures:

MS-325-ENHANCED ANGIOGRAPHY

We believe that MS-325-enhanced MR angiography will be used to diagnose cardiovascular disease and has the potential to replace a significant portion of the estimated 4.3 million X-ray angiograms performed each year in the United States. In particular, we believe MS-325-enhanced MR angiography has the following advantages over conventional X-ray angiography:

SAFETY. X-ray angiography is an invasive, catheter-based procedure which exposes patients to significant risk of serious complications due to femoral puncture. MS-325-enhanced MR angiography, on the other hand, is a non-invasive exam requiring only intravenous injection of MS-325.

NO IONIZING RADIATION. MR angiography with MS-325 involves only safe, low-energy radio waves rather than potentially harmful ionizing radiation.

ARTERIAL AND VENOUS INFORMATION IN A SINGLE EXAM. MS-325-enhanced MRI offers the ability to capture image data of both arteries and veins in a single exam. Venographic imaging plays a crucial role in identifying veins suitable to be harvested for use in bypass grafts as well as planning the route for catheter-based interventional procedures. X-ray technology requires separate exams to image arteries and veins.

WHOLE-BODY IMAGING. Whereas X-ray angiography captures data over a limited vascular region, we expect MS-325-enhanced MR angiography to provide clinicians with the ability to capture images of the entire vascular system. We believe that a whole-body MR angiography exam 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.

3-DIMENSIONAL IMAGES. MS-325-enhanced MR angiography captures 3-dimensional data which can be manipulated by physicians to get the best possible view of the vessels in question. These 3-dimensional data sets will allow physicians to spin, 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 MR angiography is likely to be significantly less costly than X-ray angiography. We estimate that an MRI exam with MS-325 will cost between approximately between $500 and $1,000, roughly one-third the cost of an equivalent X-ray angiogram.

PATIENT MONITORING. After an intervention for cardiovascular disease such as angioplasty or bypass graft, optimal patient management could include follow-up exams, or re-looks, to determine the re-forming of 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, which can lead to increased patient management costs and poorer outcomes due to undiagnosed restenosis and other complications. We estimate that there are currently over 2 million patients who have undergone a coronary angioplasty procedure and over 2 million patients who have undergone a coronary bypass graft who are potential candidates for a periodic re-look. In addition, we believe that MS-325-enhanced MRI may have potential utility to monitor the success of treatments designed to affect the proliferation, or angiogenesis, of microvessels.

PLAQUE CHARACTERIZATION. Angiographic images with MS-325-enhanced MRI have demonstrated the ability to visualize the walls of arteries as well as the interior, or lumen, of these vessels, potentially allowing precise determination of plaque shape. We believe that MS-325-enhanced MR angiography may allow 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 MR angiography 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 25% of the installed base of MRI scanners, pose 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 out-patients settings, such as physician offices and free-standing 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 non-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. Of the estimated 6.75 million patients in the United States who enter the diagnostic pathway for coronary artery disease each year, we believe that over half 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 and MRI-guided stent placement. In addition, we intend to initiate a preclinical study to assist physicians in identifying healthy veins that can be harvested for bypass surgery.

BEYOND CARDIOVASCULAR MRI--ADDITIONAL APPLICATIONS

We believe MS-325-enhanced MRI 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 is being investigated for possible use in diagnosing several conditions involving damaged or abnormal microvessels. In addition, as a marker of albumin, MS-325-enhanced MRI may play a role in diagnosing conditions which result in regions of atypical albumin concentration. We are pursuing applications for MS-325 beyond cardiovascular disease in order to fully leverage the broad diagnostic potential of this technology.

BREAST CANCER

Although inexpensive and widely used as a screening tool, mammography yields inconclusive results in up to 10% of all exams. In addition, mammography fails to detect tumors in approximately 10% of all asymptomatic women who suffer from this disease. While MRI promises improved image

quality and detection when compared with mammography, it is not widely used today for breast cancer diagnosis. 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 sub-optimal or indeterminate mammograms. We estimate that there are currently as many as 1.9 million such mammograms performed each year in the United States. In addition, we believe that MS-325 is particularly well suited for imaging with the lower-field or open MRI scanners, allowing cost-effective detection of breast cancer lesions in high-risk women where early detection with high sensitivity imaging is required. Based on the guidelines used by the National Cancer Institute in the Breast Cancer Prevention Trial, more than 25 million women in the United States are characterized as being at high risk of developing breast cancer. We also believe that MS-325-enhanced MRI in open scanners may provide the potential for real-time imaging of biopsies and interventions.

FEMALE SEXUAL AROUSAL DYSFUNCTION

Clinicians have begun to recognize the role of compromised vasculature in many patients with sexual dysfunction. We have undertaken a Phase II feasibility trial, in conjunction with Pfizer Inc., to assess the potential utility of MS-325-enhanced MRI in diagnosing female sexual arousal dysfunction by monitoring pelvic blood volume in women. It is estimated that 30 million or more women in the United States suffer from some form of sexual dysfunction.

OTHER NON-CARDIOVASCULAR APPLICATIONS

Further applications currently being investigated in preclinical studies include: detection of glioma and ocular melanoma, diagnosis/monitoring of muscular dystrophy, lymphatic imaging, migraine imaging and diagnosis of diabetic angiopathy.

DEVELOPMENT PROGRAMS

MS-325

BACKGROUND

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 by containing gadolinium, a highly magnetically active element favored by clinicians for enhancing MR images. This molecule is designed with our proprietary technology to bind to albumin, the most common blood protein. In MS-325 images using standard MRI techniques, the blood gives off a strong magnetic signal and appears bright 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 and therefore provides the image acquisition time and signal strength needed to obtain a high contrast, high resolution image of the cardiovascular system. Like most currently available non-specific contrast agents, MS-325 is designed to excrete safely through the kidneys over time.

LEAD INDICATION--AORTOILIAC OCCLUSIVE DISEASE

In June 1999, we initiated a Phase III clinical trial to determine the efficacy of MS-325-enhanced MR angiography for the detection of aortoiliac occlusive disease, a common peripheral vascular disease. Evaluation for aortoiliac occlusive disease is a critical component of two common procedures performed on the peripheral vascular system: abdominal aortography, particularly for the identification of abdominal aortic aneurysm, and leg arteriography, also known as peripheral run-off, for the detection of atherosclerosis. The trial, a multi-center, comparative, two-arm study with a target enrollment of 600 patients, is designed to compare the diagnostic accuracy of MS-325-enhanced MR angiography with that of X-ray angiography. This trial is expected to include up to 50 clinical sites worldwide.

In June 1998, we completed a Phase II clinical trial to test the safety and preliminary efficacy of MS-325 for the evaluation of peripheral vascular disease in the carotid, iliac and femoral arteries. This Phase II trial was conducted at seven clinical sites and involved the blinded administration of MS-325 at several dosing levels in a total of 81 patients. In the trial, MS-325-enhanced MR angiography was compared to conventional X-ray angiography, the current reference standard, to determine the location and degree of plaque blockages. The results for identification of plaque blockages, combining all doses, indicate that MS-325 demonstrated 82% accuracy, 80% sensitivity and 82%

specificity in the peripheral vasculature relative to X-ray angiography. In this study, MS-325 was well tolerated by patients at all dose levels, with no severe side effects reported.

CORONARY ARTERY DISEASE

We are currently conducting a Phase II feasibility trial to test the safety and preliminary efficacy of MS-325 for the evaluation of coronary artery disease. This trial is being conducted at multiple sites and is expected to enroll up to 105 patients. As with the completed Phase II peripheral vascular disease trial, MS-325-enhanced MR angiography is being compared to X-ray angiography, the current reference standard, to determine the location and degree of plaque blockages. Clinical use of MR angiography for imaging the coronary arteries is particularly difficult at present due to the problem of cardiac motion which results from both the beating of the heart and respiration. 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. Promising early images from this study have been obtained which indicate that MS-325 may increase coronary vessel contrast.

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, MS-325-enhanced MRI was evaluated on 20 patients using low field MRIs and 25 patients using high field MRIs. Although the analysis of the data from the complete patient group is not yet complete, data from a sub-population of the twenty patients using low field MRIs 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 MR and lower field magnetic resonance systems. 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.

FEMALE SEXUAL AROUSAL DYSFUNCTION

In September 1998, we undertook a Phase II feasibility trial in 16 patients 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 during sexual arousal. We believe that this technique may prove 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.

ADDITIONAL APPLICATIONS

We are currently conducting preclinical studies to determine the potential utility of MS-325-enhanced MRI for a wide variety of applications. Applications currently being investigated include: myocardial perfusion imaging, low-field MR imaging, diagnosis/monitoring of muscular dystrophy, MRI-guided stent placement, lymphatic imaging, migraine imaging and diagnosis of diabetic

angiopathy. We intend to initiate preclinical studies to identify veins suitable to be harvested for use in bypass grafts as well as planning the route for catheter-based interventional procedures and the detection of glioma and ocular

melanoma.

EP-862 PROTOTYPE CLOT IMAGING AGENT

BACKGROUND

Thromboembolic disease refers to a class of relatively common disorders involving the formation of blood clots or, thrombi, in the veins and arteries. The most common form of this disease, deep vein thrombosis, or DVT, is characterized by the presence of thrombi in the deep veins of the leg and calf. This disease afflicts approximately 2 million Americans each year. The most severe consequences of DVT tend to occur when a thrombus 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 United States. 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 United States.

The current method for diagnosing DVT involves a series of venous ultrasound exams typically 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 may be asymptomatic and those who have clots forming below the knee, in the pelvis and in the vena cava. It is estimated that over 2.1 million ultrasound procedures are performed each year in the United States to detect DVT. The X-ray venography, which represents the current gold 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. In fact, research suggests that this 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. Nearly 1 million such exams were performed in the United States in 1998. In the event of an indeterminate exam, the clinician must either infer the diagnosis from the presence/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.

DEVELOPMENT PROGRAM

We are seeking to develop a targeted contrast agent that would enable MRI to illuminate blood clots. Such a product could potentially change the diagnostic work-up for many of the conditions associated with thromboembolic disease, including PE and DVT. 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 thigh, pelvis and vena cava:because of their increased likelihood of migrating to the lungs once inside the pulmonary vasculature, these clots can be fatal. We believe that such a contrast agent 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 but clinically equivalent alternative to pulmonary angiography. We further 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.

EP-862, our prototype clot-imaging agent is based on a family of highly specific peptides that bind 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. In November 1999, we announced that EP-862 had been shown in preclinical testing to

detect sub-millimeter blood clots in an animal model. EP-862 is being further optimized for clot imaging before human studies are initiated.

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:

ESTABLISH THE SAFETY AND CLINICAL UTILITY OF MS-325 FOR MULTIPLE CARDIOVASCULAR IMAGING INDICATIONS. In June 1999, we initiated a Phase III clinical trial to determine the efficacy of MS-325-enhanced MR angiography for the detection of aortoiliac occlusive disease. We continue to enroll patients in our Phase II feasibility trial to assess the safety and preliminary efficacy of MS-325-enhanced MR angiography for the evaluation of coronary artery disease. In each of these clinical trials, we compared MS-325-enhanced MR angiography to X-ray angiography, the current reference standard for these indications. In addition, we are currently conducting preclinical studies for such applications as myocardial perfusion imaging and MRI-guided stent placement.

ESTABLISH THE CLINICAL UTILITY OF MS-325 BEYOND CARDIOVASCULAR IMAGING. We are committed to leveraging the unique diagnostic properties of MS-325 across as many clinical applications as possible. We are therefore seeking to establish the clinical utility of MS-325-enhanced MRI in diagnosing many conditions other than cardiovascular disease. We recently completed enrollment for a Phase II feasibility study designed to evaluate the safety and efficacy of MS-325-enhanced MRI in identifying malignant breast lesions in women with breast abnormalities. We have also undertaken a Phase II feasibility trial, in conjunction with Pfizer Inc., to assess the potential utility of MS-325-enhanced MRI in diagnosing female sexual arousal dysfunction by monitoring pelvic blood volume in women. We are currently conducting preclinical studies to evaluate the potential use of MS-325-enhanced MRI for such applications as: diagnosis/monitoring of muscular dystrophy, lymphatic imaging, migraine imaging and diagnosis of diabetic angiopathy.

DEVELOP EP-862 FOR THROMBOEMBOLIC DISEASE IMAGING. We are currently developing thrombosis-specific MRI contrast agents based on its proprietary technology platform. In November 1999, we announced that our prototype clot imaging agent, EP-862, had been shown in preclinical testing to detect sub-millimeter blood clots.

MAXIMIZE THE VALUE OF STRATEGIC ALLIANCES. At the end of June 2000, we had established collaborations with Schering AG, Mallinckrodt, Daiichi, General Electric Medical Systems, Philips Medical Systems, Siemens, 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.

STRATEGIC ALLIANCES

Our 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 with Schering AG, Mallinckrodt, Daiichi, General Electric Medical Systems, Philips Medical Systems, Siemens, and Pfizer.

CO-DEVELOPMENT, SALES & MARKETING

SCHERING AG

In June 2000, we entered into a strategic collaboration agreement pursuant to which we granted Schering AG an exclusive license to co-develop and market MS-325 worldwide, exclusive of Japan.

Generally, both of us will share equally in MS-325 costs and profits. Under the agreement, we will assume responsibility for completing clinical trials and filing for Food and Drug Administration approval in the United States and Schering AG will lead clinical activities for the product outside the United States. In addition, we granted Schering AG an exclusive option to develop and market a cardiovascular MRI blood pool agent from our pipeline. In connection with this strategic collaboration, Schering AG paid an up front fee of $10 million and made a $20 million dollar equity investment in us at $17.98 per share. We may receive up to an additional $20 million under this agreement in milestones. Under the agreement, we also have the option to participate in the development and marketing of two Schering AG products currently in clinical trials, SHU555C and Gadomer-17. Schering AG will fund the development costs of SHU555C. We can obtain a royalty from the worldwide sales of SHU555C through the payment of an upfront fee upon certain conditions related to the marketing approval of SHU555C and MS-325. We also have the exclusive rights to worldwide co-development and profit-sharing for Gadomer-17. After completion of Schering AG-funded Phase II studies, we may exercise this right through payment of an up-front fee and milestone payments. We will share the development costs and profits of Gadomer-17 equally with Schering AG. Our agreement will remain in effect as long as Schering AG is selling our products in any area to which they are entitled to distribution. The agreement may be terminated by either party 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 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 European Union.

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 will assume 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. However, Daiichi may, under certain circumstances, elect to formulate MS-325 purchased from us into a final product. The agreement imposes certain development due diligence obligations on both parties and marketing due diligence obligations on Daiichi. The agreement may be terminated by Daiichi upon 30 days prior written notice if Daiichi determines in its reasonable opinion that MS-325 lacks clinical efficacy, presents serious side effects or otherwise exhibits unacceptable properties. In connection with this strategic alliance, we received an up-front fee from Daiichi in the amount of $3.0 million and earned a $900,000 milestone payment in June 1997. Daiichi will be required to make future payments to us up to an aggregate amount of $2.4 million upon the

achievement of certain MS-325 development milestones. Daiichi also made a $5.0 million equity investment in us and is required to make royalty payments to us on net sales of MS-325 in Japan.

MANUFACTURING

MALLINCKRODT

In June 2000, we amended our strategic collaboration with Mallinckrodt to grant 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 Mallinckrodt and Schering AG, and to enable us to enter into the agreement with Schering AG. In connection with this amendment, we paid Mallinckrodt an up-front fee of $10 million and may pay up to an additional

$5 million in milestones. We will also pay Mallinckrodt a share of operating margins in the US and a royalty on gross profits outside the US.

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, to develop advanced imaging techniques designed to facilitate the use of MS-325-enhanced MRI. We believe it is extremely important to collaborate with equipment manufacturers to develop MRI 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 3-dimensional space, and optimizing MRI sequences 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; the National Institute of Health and several academic centers.

PHILIPS MEDICAL SYSTEMS

In November 1998, we agreed with Philips Medical Systems to collaborate in advancing the development of contrast-based cardiovascular MRI technologies. Under the terms of this non-exclusive collaboration agreement, the companies will combine their resources to optimize imaging technology and improve 3-dimensional visualization of arteries and veins in patients undergoing MR angiography. Research and development is to be carried out at several international Philips research centers, as well as at our facilities.

SIEMENS

In September 1999, we announced a non-exclusive collaboration with Siemens to optimize MR imaging technology and improve visualization of arteries and veins in patients undergoing MR angiography. The collaboration will also focus on expanding the use of MRI in diagnosing cardiovascular disease and providing user-friendly tools for easy visualization of the cardiovascular system in 3-dimensional space. Research and development will be carried out at our facilities and at Siemens' Iselin, NJ facilities.

NEW APPLICATIONS

PFIZER

In September 1998, we and Pfizer entered into an exclusive agreement to explore the potential utility of MS-325-enhanced MRI 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 MRI in the detection and monitoring of female sexual arousal dysfunction. Under the terms of this collaboration, Pfizer has full responsibility for funding the trial. Pfizer currently markets Viagra-Registered Trademark- for erectile dysfunction in men.

TECHNOLOGY PLATFORM

Our product candidates are small molecule chelates (soluble metal-organic complexes) containing a magnetically active metal element, gadolinium, which elicits a strong MRI signal. The design of these molecules derives from the unique and highly complex intersection of chemistry, pharmacology, and biophysics. Our compounds must be safe, excretable 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 three areas:

TARGETING

We develop metal complexes that are engineered to bind to particular proteins and receptor molecules in the body. This binding causes increased concentration and retention of the contrast agent in the specific tissues and fluids that contain the targeted receptor molecules. The challenge in designing such agents is two-fold: one must both choose the best target--the protein or cell type that most precisely characterizes the relevant disease state--and identify a targeting region that binds to that target without binding to other molecules in the body. The targeting region 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. For EP-862, we have used combinatorial chemistry technology to select a family of highly specific peptides which bind to fibrin, the dominant protein inside clots, without binding to fibrinogen, a similar, but far more common 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. RIME was developed by Dr. Randall Lauffer, our founder and Chief Scientific Officer, while at Massachusetts General Hospital, and is now exclusively licensed by us under patents held by the Massachusetts General Hospital. The binding of a RIME agent to its receptor reduces the rate at which the agent rotates, in solution. This reduction in 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 challenges in 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 3-dimensional images. MRI is the most flexible of the major medical imaging modalities. The hardware and software of most MRI scanners allow an enormous range of 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 the agents we have already designed, but is critical for optimizing the usefulness of future MRI agents.

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 non-specific MRI agents approved for marketing in the United States and in certain foreign markets that are likely to compete with MS-325 if approved for MR angiography. Magnevist-Registered Trademark- by Schering-AG, Dotarem-Registered Trademark- by Guerbet, S.A., Omniscan-Registered Trademark- by Nycomed Imaging ASA ("Nycomed"), ProHance-Registered Trademark- by Bracco S.p.A. ("Bracco") and OptiMARK-Registered Trademark- by Mallinckrodt are all such products. We are aware of three competing agents under clinical development, Nyomed's NC100150, Schering AG's Gadomer-17 and SHU555C, that are being evaluated for use in MR angiography. We believe two additional MRI contrast agents, Bracco's B-22956/1 and Advanced Magnetics' Code 7228 may be in preclinical testing for this indication. We are aware of no MRI contrast agent other than EP-862 that is being developed for use in imaging blood clots. We can not assure you that our competitors will not succeed in the future in developing products that are more effective than any that are being developed by us. We believe that our ability to compete within the MRI contrast agent market is dependent 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 be based 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 products 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 may be developed by us, and 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. Several other nuclear medicine

agents, including Draxis Health's FibrImage and Schering AG's P748, are in clinical testing for DVT and PE, respectively. We believe another radiopharmaceutical under clinical development by Schering AG, P-773, is being investigated for use in imaging atherosclerotic plaque. In addition, while no ultrasound contrast agent has yet been approved for myocardial perfusion imaging, several of these agents are undergoing clinical testing for this indication, including Molecular Biosystems' Optison, DuPont's Definity, Alliance Pharmaceutical's Imagent, Nycomed's Sonazoid, and Sonus Pharmaceuticals' Echogen. Finally, we are aware of one ultrasound agent, ImaRx's MRX-408, under preclinical development for imaging DVT. We cannot guarantee that we will be able to compete successfully in the future or that developments by others will not render MS-325, EP-862 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 United States and in other countries where we believe that significant market opportunities exist.

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

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

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

- Seven applications in prosecution on seven different subject matters as well as their cognate patents and applications in foreign countries.

Our two U.S. patents which broadly cover RIME technology, albumin binding with metal chelates, and liver targeting metal chelates, have been issued a patent in Europe similar to those United States patents, and have received notice of allowance for a similar patent application in Japan. These two United States patents were involved in an interference proceeding with an application owned by Mallinckrodt, but the interference was terminated in our favor. Our Japanese patent application has been opposed by several parties. The sole issue in these proceedings is whether the Japanese Patent Office should have granted and/or allowed patents to us. The Japanese Patent Office has issued a final rejection of the Japanese patent application. A Notice of Appeal was filed in the Japanese Patent Office on May 9, 1999, but the case has not yet been assigned to an Examiner.

In addition, third parties have sought, in an Italian court, a declaration of non-infringement of our European patent. Those third parties seek transborder application of a non-infringement declaration in those European countries where our European patent is in force. The third parties also seek to invalidate the Italian portion of the patent. The complaint was filed on February 23, 1999 in the Court of Milan, Italy. There is no potential liability, other than court costs, to us in this suit. This case is in the early pretrial stage. The parties had previously sued the General Hospital Corporation (hereinafter "the Hospital"), the assignee of the patent, in Italy seeking to invalidate the Italian portion of the same patent. The complaint was filed on October 20, 1998 in the Court of Milan, Italy. The sole issue in this case is whether the Italian

portion of the patent is valid. This case was consolidated with the second Italian action, discussed above. The same parties have also sued the Hospital in the United Kingdom (Patents Court, London) seeking a declaration of invalidity of the UK portion of the Hospital's patent. The appeals court in the United Kingdom has affirmed a stay of the proceedings pending the final outcome of the Opposition Proceedings in the European Patent Office. There is no potential liability to us, except court and legal costs in this case. On May 9, 2000, the European Patent Office maintained the validity of the European patent in a slightly amended form. On May 7, 2000, we granted to Schering AG, one of the opposing parties, a worldwide, royalty-bearing license to the European patent. The remaining opposing parties can elect to appeal the May 9, 2000 decision. In addition, we and the Hospital have continued two patent infringement actions in Europe. In these actions, in France and Germany, we and the Hospital seek to enforce the European patent against the same parties seeking non-infringement and invalidity judgments. We, together with the Hospital, seek both injunctive relief and damages in these actions. In Germany, the case is stayed pending a decision on jurisdiction in Italy. In France, the case is in the early pretrial stage. These oppositions, appeals relating thereto and the European proceedings, will likely take several years to finally resolve.

While we believe that we will prevail in these proceedings, there can be no assurance as to the scope of the claims that will be maintained, if any, or the ultimate benefit, if any, of those claims to us in protecting our products.

We have exclusively licensed five additional patents in the United States. These patents have counterpart patent applications pending in Japan and Europe. We have also received an additional United States patent covering novel metal chelates and have a counterpart parent application pending

in Japan. Finally, we have patent applications pending in the United States, Japan and Europe covering various aspects of our RIME technology. We have received a patent in the United States covering the process by which MS-325 is manufactured (U.S. Patent Number 5,919,967; granted July 6, 1999; expires June 11, 2017). Our patent protection for MS-325 currently extends to 2006 in the United States and Europe. If the currently pending patent applications issue, this protection will be extended until 2015. Protection for the manufacturing process in the United States is already extended until 2017, and will be extended until 2016 in Europe and Japan if the currently pending patent applications issue. In addition, during 1999 and early 2000 we filed four new patent applications for additional products and processes involving compounds, compositions, and methods for imaging.

An issued patent grants to the owner the right to exclude others from practicing inventions claimed therein. In the United States, 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 from June 8, 1995 expire 20 years from the deemed date. The General Agreement on Tariffs and Trade provides that patents whose applications were filed on or after June 8, 1995 are effective for 20 years from filing. This new rule is generally 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 United States and abroad. If any third-party patents are upheld as valid and enforceable in any 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 would 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, including actions brought to challenge or invalidate our own patent rights. At the same time, we are aware of certain products under development by others which we believe may infringe certain of our exclusively licensed patents. We have commenced and/or expect to commence litigation in various European countries against other third parties for infringing our European patent. These litigations will likely take several years to finally resolve. We are pursuing license or cross-license arrangements with or, if necessary and appropriate, are continuing infringement proceedings against, these parties. In this regard, on May 7, 2000, we granted to Schering AG a worldwide royalty-bearing license to our patents covering Schering AG's development project, eovist injection, an MRI contrast agent for imaging the liver. Also on May 7, 2000, Schering AG granted us a non-exclusive royalty-bearing license to its Japanese patents, 1,932,626,

1,968,413 and its Japanese Application, WO99/16474. We have agreed to withdraw our invalidation claim of Shering AG's Japanese patent, 1,932,626 in the Japanese Patent Office pursuant to this license agreement. While we believe that we will prevail in these litigations, there can be no assurance as to the outcome or the scope of any injunctive or monetary relief we may recover. We also intend to pursue license or cross-license arrangements with or, if necessary and appropriate, infringement proceedings against, these parties upon their seeking final regulatory approval for the marketing and sale of any such products.

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 United States are maintained in secrecy until patents issue, and patent applications 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 and MGH have entered into a license agreement 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. We must also pay MGH a percentage of all royalties received from our sublicensees. Accordingly, we will be required to make payments to MGH on profits generated under the Schering collaboration, if any, and on royalties received from Daiichi under our license agreement, 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.

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 United States 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 currently manufacture, as part of our ongoing development efforts, small non-GMP (good manufacturing practices as promulgated by the FDA) batches of MS-325 in our laboratories located in Cambridge, Massachusetts. MS-325 for use in preclinical and Phase I and II clinical trials has been manufactured in accordance with GMP by outside contractors. As part of its strategic alliance with the Company, Mallinckrodt will serve as primary manufacturer for MS-325 thereafter worldwide except for Japan and, possibly, for Japan. If Mallinckrodt is unable to produce MS-325 in adequate amounts and at a reasonable cost or to comply with any applicable regulations, including GMP, it could have a material adverse effect on our business, financial condition and results of operations.

Furthermore, should Mallinckrodt fail to fulfill its manufacturing responsibilities satisfactorily, Schering AG could be forced to manufacture the compound itself, or to find an alternative manufacturer. We can not assure you that Schering AG would be able to find such an alternative manufacturer or 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. We currently procure the raw materials for the various components of MS-325 from a broad variety of vendors and, wherever possible, maintain relationships with multiple vendors for each component. There are a number of components of MS-325 for which the largest suppliers may have significant control over the market price due to controlling market shares. If any one of our suppliers decided to increase prices significantly or reduce quantities of any component of MS-325 available for sale to us, it could have a material adverse effect on our ability to commercialize MS-325 and on our business, financial condition and results of operations. See "--Strategic Alliances."

GOVERNMENT REGULATION

The manufacture and commercial distribution of our product candidates are subject to extensive governmental regulation in the United States and other countries. Pharmaceuticals, including contrast-imaging agents for use with MRI, are regulated in the United States by the FDA under the Food, Drug and Cosmetic Act ("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 United States, a company seeking approval to market a new pharmaceutical must obtain FDA approval of a new drug application ("NDA"). Before an NDA may be filed, however, a certain procedure is typically followed. This includes: (i) performance of preclinical laboratory and animal studies; (ii) submission to the FDA of an application for an investigational new drug application ("IND"), which must become effective before human clinical trials may commence; (iii) completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the pharmaceutical for its intended use; (iv) submission to the FDA of an NDA; and (v) 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 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. 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, an NDA is submitted to the FDA. The NDA approval process can be expensive, uncertain and lengthy. Although the FDA is supposed to complete its review of an 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 the third-party manufacturers 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 an 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 an 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. Failure by us to receive approval of an 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 other 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 United States are subject to regulatory requirements that vary widely from country to country. In the European Union ("EU"), the general trend has been towards coordination of common standards for clinical testing of new agents, leading to changes in various requirements imposed by each EU country. The level of regulation in the

EU and other foreign jurisdictions varies widely. 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.

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. 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.

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 United States 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 will 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 can not assure you, however, that our products will be available, will lower costs of care for any patients or that providers will choose to utilize them even if they do, 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. 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 United States 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 the Company. We can not assure you, in either the United States 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.

PROPERTIES

We lease a total of 17,050 square feet of space at 71 Rogers Street and adjacent locations, and 13,310 square feet at 161 First Street, all in Cambridge, Massachusetts. The current lease at 71 Rogers Street and adjacent locations runs until December 31, 2002, and we have an option to extend the lease for an additional three or five years. During 1999, we extended our lease at 161 First Street through December 31, 2002. We believe that our current facilities and currently available space are adequate to meet our requirements for the foreseeable future.

EMPLOYEES

As of June 30, 2000 we employed 78 persons on a full-time basis, of which 64 were involved in research and development and 14 in administration and general management. Twenty-three of our employees hold Ph.D. or M.D. degrees. We believe that our relations are good with all of our employees. None of our employees are a party to a collective bargaining agreement.

LEGAL PROCEEDINGS

We are not a party to any material legal proceedings.

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

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

The financial statements of EPIX Medical, Inc. included in EPIX Medical, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 1999, 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, 2000 and June 30, 2000;

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 1999;

- Our Form 8-K filed on June 29, 2000;

- Our Definitive Proxy Statement filed on March 31, 2000

You may request a copy of these filings at no cost by writing or telephoning our Chief Executive 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.