EPIX MEDICAL INC
Form S-3/A
December 20, 2002

REGISTRATION NO. 333-84566
AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON DECEMBER 20, 2002

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

AMENDMENT NO. 3 TO

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933
EPIX MEDICAL, INC.
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE	04-3030815
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

71 ROGERS STREET
CAMBRIDGE, MASSACHUSETTS 02142
TELEPHONE: (617) 250-6000

(ADDRESS, INCLUDING ZIP CODE, AND TELEPHONE NUMBER, INCLUDING AREA CODE, OF REGISTRANT'S PRINCIPAL EXECUTIVE OFFICES)

MICHAEL D. WEBB
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APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC: As soon as practical after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. [ ]

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. [X]

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. [ ]

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. [ ]

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. [ ]

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. A Registration Statement relating to these securities has been filed with the Securities and Exchange Commission. No one may sell these securities nor may offers to buy be accepted until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer, solicitation or sale is not permitted.

SUBJECT TO COMPLETION, DATED DECEMBER 20, 2002

PROSPECTUS

5,000,000 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 December 18, 2002, the last reported sale price of our common stock on the Nasdaq National Market was $7.05 per share.

INVESTING IN OUR SECURITIES INVOLVES RISKS.
SEE "RISK FACTORS" ON PAGE 4.

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 December , 2002

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ABOUT THIS PROSPECTUS

The following is only a summary. We urge you to read the entire prospectus, including the more detailed financial statements, notes to the financial statements and other information incorporated by reference from our other filings with the Securities and Exchange Commission, or SEC. Investing in our common stock involves risk. Therefore, carefully consider the information provided under the heading "Risk Factors" beginning on page 4.

BUSINESS

We are a leading developer of targeted contrast agents, which are substances injected into blood vessels to improve the visual images produced by magnetic

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

The use of MRI has grown steadily over the past 10 years due to reduced cost and improved imaging capabilities. MRI now provides an effective method of diagnosis for a broad range of applications. MRI manufacturers have improved both their hardware and software, reducing the time per procedure dramatically, while significantly enhancing image resolution. While MRI is currently used extensively to image many organs and tissues in the body, its use in imaging the vascular system has been limited. Prior attempts to employ contrast agents to make such vascular MRI more useful as a diagnostic tool have had limited success. Unlike most currently available non-specific MRI contrast agents, MS-325 is specifically designed to

enhance the quality of magnetic resonance images of the arteries and veins and provide physicians with a superior method for diagnosing diseases in these vessels. MS-325 is a small molecule, which produces an MRI signal because of the presence of gadolinium, a magnetically active element favored by clinicians for enhancing magnetic resonance images. This molecule is designed with our proprietary technology to bind to albumin, the most common protein in the blood. In MS-325-enhanced images generated with standard MRI techniques, the blood produces a strong magnetic signal and appears bright against the dark background of surrounding tissue. Because of its attraction to albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam and therefore provides the extended image time and signal strength required to obtain a high contrast, high resolution image of the vascular system. Like most currently available non-specific contrast agents, MS-325 is designed to be excreted safely through the kidneys over time.

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

formed collaborations with the three leading MRI scanner manufacturers, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems to develop advanced imaging techniques and tools designed to facilitate the use of MS-325-enhanced magnetic resonance angiography.

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

As noted above, and as part of our thrombus program, we are seeking to develop a targeted contrast agent in addition to MS-325 that would enable MRI to illuminate blood clots. Such a product could potentially change the method of diagnosis for many of the conditions associated with the formation of blood clots in the arteries and veins. The most common form of these conditions is deep vein thrombosis, which is characterized by the presence of blood clots in the deep veins of the leg and calf. The most severe consequences of deep vein thrombosis is pulmonary embolism, which tends to occur when a blood clot dislodges from the vessel wall to obstruct the arteries in the lung. We believe that the illumination of blood clots by a targeted contrast agent used in conjunction with MRI could lead to better medical outcomes due to earlier and more definitive diagnosis. Early diagnosis is especially important for clots in the thigh, pelvis and vena cava, which can be fatal because of their increased likelihood of migrating to the lungs. We believe that such a contrast agent could eliminate the need for procedures that require the use of large quantities of X-ray contrast dye and expose patients to radiation, diagnostic tests that use radioactive drugs and ultra sound, which are all currently used to identify blood clots in the veins and arteries. We further believe that our proprietary technology could enable MRI to differentiate old and new clot formation, thereby potentially identifying those clots that

pose the most risk to patients. In November 1999, we announced that our prototype agent, EP-862, had been shown in pre-clinical testing to detect sub-millimeter blood clots in animals. Although we are unlikely to develop EP-862 as a thrombus agent, we have continued to advance the thrombus program by identifying several other improved prototype agents. We expect to continue to apply resources to the thrombus program in the future and hope to file an Investigational New Drug application, or IND, with the FDA, which, if approved, will allow us to begin human safety trials.

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

RISK FACTORS

AN INVESTMENT IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY CONSIDER THE FOLLOWING RISK FACTORS, OTHER INFORMATION INCLUDED IN THIS PROSPECTUS, ANY SUPPLEMENT TO THIS PROSPECTUS AND INFORMATION IN OUR PERIODIC REPORTS FILED WITH THE SEC. IF ANY OF THE FOLLOWING RISKS ACTUALLY OCCUR, OUR BUSINESS, FINANCIAL CONDITION OR RESULTS OF OPERATIONS COULD BE MATERIALLY AND ADVERSELY AFFECTED, AND YOU MAY LOSE SOME OR ALL OF YOUR INVESTMENT.

WE HAVE NEVER GENERATED REVENUES FROM COMMERCIAL SALES OF OUR PRODUCTS AND, IF MS-325 DOES NOT RECEIVE APPROVAL FROM THE FOOD AND DRUG ADMINISTRATION, WE WILL HAVE NO PRODUCTS TO MARKET IN THE FORESEEABLE FUTURE.

We currently have no products for sale, and we cannot guarantee that we will ever have marketable products. MS-325 is currently our only product candidate in human clinical trials, and we cannot be certain that any of our other development projects will yield a product candidate suitable for entry into clinical trials. As a result, our initial revenues and profits from commercial sales of our products, if any, will be derived from sales of MS-325. If MS-325 fails to achieve regulatory approval and market acceptance, and if we do not succeed in bringing any of our other product candidates to human clinical trials and achieve regulatory approval and market acceptance for them, our business will fail and as a result, you may lose all or part of your investment.

To date, we have received revenues from payments made under licensing, royalty arrangements, product development and marketing agreements with strategic collaborators. In particular, our revenue for the year ended December 31, 2001 was $9.6 million, and consisted of $5.7 million from the product development portion of our strategic collaboration agreement with Schering AG, $2.1 million from a patent licensing and royalty agreement entered into with Bracco Imaging, S. p. A. and $1.8 million of license fee revenue related to the strategic collaboration agreements for the development and marketing of MS-325 with Schering AG and Tyco/Mallinckrodt. In addition to these sources of revenue, we have financed our operations to date through public stock offerings, private sales of equity securities and equipment lease financings.

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

- successfully complete our product development efforts;

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

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

- successfully market any approved products.

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

WE ANTICIPATE FUTURE LOSSES AND MAY NEVER BECOME PROFITABLE.

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of September 30, 2002 were approximately $109 million. These losses have primarily resulted from expenses associated with our research and development activities, including preclinical and clinical trials, and general and administrative expenses. We anticipate that our research and development expenses will increase significantly in the future, and we expect to incur substantial losses over at least the next several years as we expand our research and development efforts, pre-clinical testing and clinical trials and we implement manufacturing, marketing and sales programs. As a result, we cannot predict when we will become profitable, if at all, and if we do, we may not remain profitable for any substantial period of time. If we fail to achieve profitability within the time frame expected by investors, the market price of our common stock may decline and consequently our business may not be sustainable.

IF THE MARKET DOES NOT ACCEPT OUR TECHNOLOGY AND PRODUCTS, WE MAY NOT GENERATE SUFFICIENT REVENUES TO ACHIEVE OR MAINTAIN PROFITABILITY.

The commercial success of MS-325 and our other product candidates, when and if approved for marketing by the FDA and corresponding foreign agencies, depends on their acceptance by the medical community and third party payors as clinically useful, cost-effective and safe. While contrast agents are currently used in an estimated 25% to 30% of all MRI exams, there are no FDA approved targeted vascular agents in use. Furthermore, clinical use of MRI for vascular imaging has been limited and use of MRI for peripheral vascular disease imaging has occurred mainly in research. Market acceptance, and thus sales of our product candidates, will depend on several factors, including:

- safety;

- price;

- ease of administration;

- effectiveness; and

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

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

IF WE DO NOT RAISE ADDITIONAL FUNDS NECESSARY TO FUND OUR OPERATIONS, WE MAY NOT BE ABLE TO IMPLEMENT OUR BUSINESS PLAN.

Since inception, we have funded our operations primarily through our public offerings of common stock, private sales of equity securities, equipment lease financings and royalty and license payments from our strategic partners. We believe that we will need to raise substantial additional funds for research, development and other expenses, through equity or debt financings, strategic alliances or otherwise, prior to commercialization of any of our product candidates. Our future liquidity and capital requirements will depend upon numerous factors, including the following:

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

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

WE HAVE A LIMITED MANUFACTURING CAPABILITY AND WE INTEND TO RELY ON OUTSOURCED MANUFACTURING TO PRODUCE MS-325.

We do not have, nor do we currently have plans to develop,

full-scale manufacturing capability for MS-325. While we do manufacture small amounts of MS-325 for research and

development efforts, we intend to rely on Tyco/Mallinckrodt as the primary manufacturer of MS-325 for Phase III clinical trials, as well as for any future human clinical trials and commercial use. In the event that Tyco/Mallinckrodt fails to fulfill its manufacturing responsibilities satisfactorily, Schering AG has the right to purchase MS-325 from a third party or to manufacture the compound itself. However, either course of action could materially delay the manufacture and development of MS-325. Schering AG may not be able to find an alternative manufacturer. In addition, Schering AG may not be able to manufacture MS-325 itself in a timely manner. If we experience a delay in manufacturing, it could result in a delay in the approval or commercialization of MS-325 and have a material adverse effect on our business, financial condition and results of operations.

IF MRI MANUFACTURERS ARE NOT ABLE TO ENHANCE THEIR HARDWARE AND SOFTWARE, WE WILL NOT BE ABLE TO COMPLETE DEVELOPMENT OF OUR CONTRAST AGENT FOR THE EVALUATION OF CARDIAC INDICATIONS.

Although magnetic resonance imaging hardware and software is sufficient for the evaluation of peripheral vascular disease, which is our primary target indication, we believe that the technology is not as advanced for cardiac applications, which will be our next target indication. Our initial NDA filing for MS-325 will be related to peripheral vascular disease. Peripheral vascular disease, as it relates to our primary target indication, occurs in areas of the body where imaging sequences on scanners currently allow for the use of MS-325-enhanced magnetic resonance angiography for diagnostic purposes, which covers the entire body's vascular system, except for the heart. Based on feasibility studies we have conducted, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, is not developed to the point where there is clear visualization of the cardiac region, due to the effects of motion from the beating of the heart. Although not our primary focus, we plan to continue to conduct feasibility studies for cardiac indications using available software and hardware that can be adopted for coronary and cardiac perfusion data acquisition. We have entered into research collaborations with General Electric Medical Systems and Phillips Medical Systems that include development and optimization of cardiac imaging sequences with contrast agents like MS-325. We have also collaborated with a number of leading academic institutions to help optimize cardiac imaging with MS-325. While significant progress has been made in developing these clinical applications for cardiac imaging, we do not know when, or if, these techniques will enable MS-325 to provide clinically relevant images in cardiac indications. If MRI product manufacturers are not able to enhance their scanners to perform cardiac indications, we will not be able to complete our development activities of MS-325 for that application, thereby reducing the potential market for a product in this area.

OUR COMPETITORS MAY HAVE GREATER FINANCIAL RESOURCES, SUPERIOR PRODUCTS OR PRODUCT CANDIDATES, MANUFACTURING CAPABILITIES AND/OR MARKETING EXPERTISE, AND WE MAY NOT BE ABLE TO COMPETE WITH THEM SUCCESSFULLY.

Medical technology is subject to intense competition and rapid technological change. We have many competitors, including pharmaceutical, biotechnology and chemical companies, a number of which, including our strategic partners, are actively developing and marketing products that could compete with our product candidates. Specifically, although there are no FDA-approved targeted vascular contrasts agents for use with MRI, there are a number of non-specific MRI agents approved for marketing in the United States and certain foreign markets that are likely to compete with MS-325 if MS-325 is approved for Magnetic Resonance Angiography or MRA. Collectively, these non-specific agents are referred to as "extracellular" agents, and include: Magnevist(R) by Schering AG, Dotarem(R) by Guerbet, S.A., Omniscan(R) by Amersham Health, ProHance(R) by Bracco Imaging S.p.A. and OptiMark(R) by Tyco/Mallinckrodt. Extracellular agents are broadly-accepted in the market as general purpose

MRI agents. None of these agents is currently approved by the FDA for MRA, but their use in applications outside of the primary indication described in the product labeling is increasing and could present significant adoption hurdles for MS-325 if such use becomes entrenched in the marketplace. Additionally, we believe that some of these general purpose agents are in clinical trials for an MRA indication. However, these general purpose agents are not specifically designed for vascular imaging and because they "leak" out of the vessels into the extracellular space, they do not provide the extended imaging window associated with MS-325. In addition, we are aware of five agents under clinical development, specifically for use with MRA: Schering AG's Gadomer-17 and SHU555C, Guerbet's P792 (Vistarem), Bracco's B-22956/1 and Advanced Magnetic's Code 7228. Public information on the status of clinical development and performance characteristics for these agents is limited. However, many of these competitors have substantially greater capital and other resources than we do and may represent significant competition for us. These companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. In addition, these companies may be more successful than we are in developing, manufacturing and marketing products.

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

	Advantages	Disadvantages
MRI	o 3-dimensional images o Minimally-invasive o Favorable safety profile	o Requires high level of training o Inadvisable for patients

	o High quality images	with certain conditions (i. pacemakers, etc.) o Less widely available
CT Angiography	o Rapid and easy data acquisition	o Radiation o Varying levels of toxicity o Calcium and bone artifacts o Time consuming post-processing
DSA (X-ray Angiography)	o Significant clinical experience o Opportunity to treat in same procedure o Highest resolution	o Invasive o Radiation o Varying levels of toxicity o Significant safety risks o 2-dimensional images o Expensive o Patient recuperation time
Ultrasound	o Low cost o Fast o Widely available o Non-invasive	o Operator dependent o Lack of anatomic detail o Bone precludes use in many vascular beds o Inability to visualize small vessels

We cannot guarantee that we will be able to compete successfully in the future, or that developments by others will not render MS-325 or our future product candidates obsolete or non-competitive, or that our collaborators or customers will not choose to use competing technologies or products. Any inability to compete successfully on our part will have a materially adverse impact on our operating results.

WE CURRENTLY DEPEND ON OUR STRATEGIC COLLABORATORS FOR SUPPORT IN PRODUCT DEVELOPMENT AND THE REGULATORY APPROVAL PROCESS, AND, IN THE FUTURE, MAY DEPEND ON THEM FOR PRODUCT MARKETING SUPPORT AS WELL. THESE EFFORTS MAY SUFFER IF WE EXPERIENCE PROBLEMS WITH OUR COLLABORATORS.

We depend on strategic collaborators for support in product development and the regulatory approval process as well as a variety of other activities including manufacturing, marketing and distribution of our products in the United States and abroad, when, and if, the FDA and corresponding foreign agencies approve our product candidates for marketing. To date, we have entered into strategic alliances and collaborations with Schering AG, Tyco/Mallinckrodt, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems. Two of our key agreements include a collaboration agreement with Schering AG, to develop and commercialize MS-325 and other MRI vascular agents worldwide, and an agreement with Tyco/Mallinckrodt, granting Tyco/Mallinckrodt rights to enter into an agreement with Schering AG to manufacture MS-325 for clinical development and commercial use. We may not receive milestone payments from these alliances should MS-325 fail to meet certain performance targets in clinical trials. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our

collaborators. Our collaborators may not devote the resources necessary to complete development, and commence marketing, of MS-325 in their respective territories, or they may not successfully market MS-325. In addition, Schering AG and Tyco/Mallinckrodt currently manufacture imaging agents for other technologies that will compete against MS-325 and Schering AG will be responsible for setting the price of the product worldwide. However, Schering AG may not set prices in a manner that maximizes revenues for us. We are currently in compliance with the terms of these agreements, and although we are currently in Phase III clinical trials, our failure to receive future milestone payments, or a reduction or discontinuance of efforts by our partners would have a material adverse effect on our business, financial condition and results of operations.

Furthermore, our collaboration agreement with Schering AG may be terminated early under certain circumstances, including if there is a material breach of the agreement by either of us. In addition, we intend to seek additional collaborations with third parties, who may negotiate provisions that allow them to terminate their agreements with us prior to the expiration of the negotiated term under certain circumstances. If Schering AG or any other third party collaborator

were to terminate its agreement with us or otherwise fail to perform its obligations under our collaboration or to complete them in a timely manner, we could lose significant revenue. If we are unable to enter into future strategic alliances with capable partners on commercially reasonable terms, we may delay the development and commercialization of future product candidates and could possibly postpone them indefinitely.

WE DEPEND ON EXCLUSIVELY LICENSED TECHNOLOGY FROM THE MASSACHUSETTS GENERAL HOSPITAL AND IF WE LOSE THIS LICENSE, IT IS UNLIKELY WE COULD OBTAIN THIS TECHNOLOGY ELSEWHERE, WHICH WOULD HAVE A MATERIAL ADVERSE EFFECT ON OUR BUSINESS.

Under the terms of a license agreement that we have with Massachusetts General Hospital, or MGH, we are the exclusive licensee to certain technology, including patents and patent applications, which relate to our product candidates, including MS-325. The license agreement imposes various commercialization, sublicensing, royalty and other obligations on us. If we fail to comply with these and other requirements our license could convert from exclusive to nonexclusive or terminate entirely. It is unlikely that we would be able to obtain this technology elsewhere. Any such event would mean that we would be unlikely to produce our product candidates, including MS-325, and would therefore have a material adverse effect on our business, financial condition and results of operations. Currently, we are in compliance with the terms of the license agreement, and we do not have any reason to believe that this license may be terminated.

WE DEPEND ON PATENTS AND OTHER PROPRIETARY RIGHTS, AND IF THEY FAIL TO PROTECT OUR BUSINESS, WE MAY NOT BE ABLE TO COMPETE EFFECTIVELY.

The protection of our proprietary technologies is material to our business prospects. We pursue a comprehensive patent program for our product candidates in the United States and in other countries where we believe that significant market opportunities exist. We own or have an exclusive license

to patents and patent applications on the critical aspects of our core technology as well as many specific applications of this technology. Specifically, patents and patent applications related to our core technology consist of two U.S. patents that are exclusively licensed to us from MGH, as well as their counterpart patents and applications in foreign countries; two U.S. patents and their counterpart patents and applications in foreign countries that we own; eight patent applications and six provisional patent applications on fourteen different subject matters as well as their counterpart patents and applications in foreign countries. One of our issued patents covers the process by which MS-325 is manufactured. Even though we hold these patents and have made these patent applications, because the patent positions of pharmaceutical and biopharmaceutical firms, including ours, generally include complex legal and factual questions, our patent position remains uncertain. For example, because patent applications in the United States with foreign counterparts and foreign applications are maintained in secrecy until patents are issued or published, and patent applications in foreign countries are maintained in secrecy for a specified period after filing, we cannot be certain that the named applicants or inventors of the subject matter covered by our patent applications or patents, whether directly owned or licensed to us, were the first to invent or the first to file patent applications for such inventions. Third parties may oppose, challenge, infringe upon, circumvent or seek to invalidate existing or future patents owned by or licensed to us. A court or other

agency with jurisdiction may find our patents invalid, not infringed or unenforceable and we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future. Even if we have valid patents, these patents still may not provide sufficient protection against competing products or processes. If we are unable to successfully protect our proprietary methods and technologies, or, if our patent applications do not result in issued patents, we may not be able to prevent other companies from practicing our technology and, as a result, our competitive position would be harmed.

WE MAY NEED TO INITIATE LAWSUITS TO PROTECT OR ENFORCE OUR PATENTS AND OTHER INTELLECTUAL PROPERTY RIGHTS, WHICH COULD INCUR SUBSTANTIAL COSTS, AND WHICH COULD RESULT IN THE FORFEITURE OF THESE RIGHTS.

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

OTHER RIGHTS AND MEASURES THAT WE RELY UPON TO PROTECT OUR INTELLECTUAL PROPERTY MAY NOT BE ADEQUATE TO PROTECT OUR PRODUCTS AND SERVICES AND COULD REDUCE OUR ABILITY TO COMPETE IN THE MARKET.

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

- the agreements may be breached;
- we may have inadequate remedies for any breach;
- proprietary information could be disclosed to our competitors; or
- others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technologies.

If, for any of the above reasons, our intellectual property is disclosed or misappropriated, it would harm our ability to protect our rights and our competitive position. Moreover, several of our management and scientific personnel were formerly associated with other pharmaceutical

and biotechnology companies and academic institutions. In some cases, these individuals are conducting research in similar areas with which they were involved prior to joining us. As a result, we, as well as these individuals, could be subject to claims of violation of trade secrets and similar claims.

OUR SUCCESS WILL DEPEND PARTLY ON OUR ABILITY TO OPERATE WITHOUT INFRINGING THE INTELLECTUAL PROPERTY RIGHTS OF OTHERS, AND IF WE ARE UNABLE TO DO SO, WE MAY NOT BE ABLE TO SELL OUR PRODUCTS.

Our commercial success will depend, to a significant degree, on our ability to operate without infringing upon the patents of others in the United States and abroad. There may be pending or issued patents, held by parties not affiliated with us, relating to technologies we use in the development or use of certain of our contrast agents. If any judicial or administrative proceeding upholds any third party patents as valid and enforceable, we could be prevented from practicing the subject matter claimed in such patents, or would be required to obtain licenses from the owners of each such patent, or to redesign our products or processes to avoid infringement. If we are unable to obtain a required license on acceptable terms, or are unable to design around any third party patent, we may be unable to sell our products, which would have a material adverse effect on our business.

EXTENSIVE GOVERNMENT REGULATION MAY DELAY OR PREVENT US FROM MARKETING MS-325 OR OUR OTHER PRODUCTS UNDER DEVELOPMENT.

We are subject to extensive U.S. and foreign governmental regulatory

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

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

This regulatory approval process is lengthy and expensive. Although some of our employees have experience in obtaining regulatory approvals, we have only limited experience in filing or pursuing applications necessary to gain regulatory approvals. Preclinical testing of our product development candidates is subject to Good Laboratory Practices as prescribed by the FDA and the manufacture of any products developed by us will be subject to Good Manufacturing Practices as prescribed by the FDA. We may not obtain the necessary FDA clearances and subsequent approvals in a timely manner, if at all. We can not be sure as to the length of the clinical trial period or the number of patients that will be required to be tested in the clinical trials in order to establish the safety and efficacy of MS-325 or any of our future product candidates. Our clinical trials may not be successful, and we may not complete them in a timely manner. We could report serious side effects as the clinical trials proceed. Our results from early clinical trials may not predict results that we obtain in large-scale clinical trials, even after promising results in earlier trials. The rate of completion of our clinical trials depends upon, among other things, the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the clinical protocol under which MS-325 is studied, the proximity of the patient to a clinical site and the eligibility criteria for the study. Furthermore, we, the FDA or other regulatory authorities may alter, suspend or terminate clinical trials at any time. For example, in September 2001, after discussions with the FDA, we expanded our initial target indication for MS-325 from one specific body region, the aortoiliac region, to a broader indication that includes the entire body's peripheral vascular system, except for the heart. This expansion required us to add two new clinical trials to our then existing Phase III clinical trial

program, one to determine the efficacy of MS-325 enhanced MRA for the detection of peripheral vascular disease in the renal (kidney) arteries, and another to determine the efficacy of MS-325 enhanced MRA for the detection of peripheral vascular disease in the pedal (feet) arteries. Although providing us with greater market potential for the sale of MS-325 upon approval, we expect that this change to our Phase III clinical trial program, and the associated delay in the start up of new clinical centers, will result in an approximate fifteen month delay to our NDA submission date from our previous forecast, and an increase in costs associated with the program. If we do not successfully complete our Phase III clinical trial program, we will not have a product to market.

In addition, we may encounter unanticipated delays or significant costs in our efforts to secure necessary approvals. We may not obtain regulatory approval, even after the performance of clinical trials and the passage of time and the expenditure of such resources, for MS-325 or any other product candidates that we develop. Our analysis of data obtained from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent FDA regulatory approval. Delays in obtaining government regulatory approval could adversely affect our marketing as well as our ability to generate significant revenues from commercial sales.

Future United States legislative or administrative actions also could prevent or delay regulatory approval of our product candidates. Even if we obtain regulatory approvals, they may include significant limitations on the indicated uses for which we may market a product. A marketed product also is subject to continual FDA and other regulatory agency review and regulation. Later discovery of previously unknown problems or failure to comply with the

applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market, as well as possible civil or criminal sanctions. Further, many academic institutions and companies conducting research and clinical trials in the MRI contrast agent field are using a variety of approaches and technologies. If researchers obtain any adverse results in preclinical studies or clinical trials, it could adversely affect the regulatory environment for MRI contrast agents generally. In addition, if we obtain marketing approval, the FDA may require post marketing testing and surveillance programs to monitor the product's efficacy and side effects. Results of these post-marketing programs may prevent or limit the further marketing of the monitored product. If we cannot successfully market our products, we will not generate sufficient revenues to achieve or maintain profitability.

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

PRODUCT LIABILITY CLAIMS COULD INCREASE OUR COSTS AND ADVERSELY AFFECT OUR RESULTS OF OPERATIONS.

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

IF WE FAIL TO GET ADEQUATE LEVELS OF REIMBURSEMENT FROM THIRD PARTY PAYORS FOR OUR PRODUCT CANDIDATES AFTER THEY ARE APPROVED IN THE U.S. AND ABROAD, WE WILL NOT BE ABLE TO COMMERCIALIZE OUR PRODUCT CANDIDATES.

We could be adversely affected by changes in reimbursement policies of governmental or private healthcare payors, particularly to the extent any such changes affect reimbursement for procedures in which our product candidates would be used. Failure by physicians, hospitals and other users of our products to obtain sufficient reimbursement from third party payors for the procedures in which our products would be used or adverse changes in governmental and private third party payors' policies toward reimbursement for such procedures would have a material adverse effect on our ability to market our products and consequently it would have an adverse effect on our business, financial condition and results of operations. If we obtain the necessary foreign regulatory approvals, market acceptance of our product candidates in international

markets would be dependent, in part, upon the availability of reimbursement within prevailing healthcare payment systems. Reimbursement and healthcare payment systems in international markets vary significantly by country, and include both government sponsored health care and private insurance. We intend to seek international reimbursement approvals, although we cannot assure you that any such approvals will be obtained in a timely manner, if at all, and failure to receive international reimbursement approvals could have an adverse effect on market acceptance of our products in the international markets in which such approvals are sought.

WE DEPEND ON OUR KEY PERSONNEL, THE LOSS OF WHOM WOULD HURT OUR ABILITY TO COMPETE.

Our future business and operating results depend in significant part upon the continued contributions of our senior management and key technical personnel. If any such personnel were to be hired away from us by a competitor, or if for any reason, they could not continue to work for us, we would have difficulty hiring officers with equivalent skills in general, financial and research management and our ability to achieve our business objectives or to operate or compete in our industry may be seriously impaired. Although we maintain key life insurance on the lives of some key officers, the loss of any key employee, the failure of any key employee to perform in his or her current

position, or our inability to attract and retain skilled employees, as needed, could have a material adverse effect on our business, financial condition and results of operations. Our future business and operating results also depend in significant part upon our ability to attract and retain qualified management, operational and technical personnel. Competition for this personnel is intense, and we may not be successful in attracting or retaining such personnel. If we were to lose these employees to our competitors, we could spend a significant amount of time and resources to replace them, which would impair our research and development efforts.

OUR STOCK PRICE IS VOLATILE. IT IS POSSIBLE THAT YOU MAY LOSE ALL OR PART OF YOUR INVESTMENT.

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

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

During 2001, the closing price of our common stock ranged from $14.60 to $6.24. Our common stock reached a high of $15.86 and traded as low as $4.11 during the first three quarters

of 2002. The last reported sales price for our common stock on December 18, 2002 was $7.05. If our stock price declines significantly, we may be unable to raise additional capital. Significant declines in the price of our common stock could also impede our ability to attract and retain qualified employees and reduce the liquidity of our common stock.

In addition, the stock market has from time to time experienced significant price and volume fluctuations that have particularly affected the market prices for the common stock of similarly staged companies. These broad

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

CERTAIN ANTI-TAKEOVER CLAUSES IN OUR CHARTER AND BY-LAW PROVISIONS AND IN DELAWARE LAW MAY MAKE AN ACQUISITION OF US MORE DIFFICULT.

Our Restated Certificate of Incorporation authorizes the Board of Directors to issue, without stockholder approval, up to 1,000,000 shares of preferred stock with voting, conversion and other rights and preferences that could adversely affect the voting power or other rights of the holders of Common Stock. The issuance of Preferred Stock or of rights to purchase Preferred Stock could be used to discourage an unsolicited acquisition proposal. In addition, the possible issuance of Preferred Stock could discourage a proxy contest, make more difficult the acquisition of a substantial block of our Common Stock or limit the price that investors might be willing to pay for shares of our Common Stock. The Restated Certificate provides for staggered terms for the members of the Board of Directors. A staggered Board of Directors and certain provisions of our By-laws and of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us. We, for example, are subject to Section 203 of the General Corporate Law of Delaware, which, subject to certain exceptions, restricts certain transactions and business combinations between a corporation and a stockholder owning 15% or more of the corporation's outstanding voting stock for a period of three years from the date the stockholder becomes an interested stockholder. These provisions may have the effect of delaying or preventing a change of control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These statements can be identified by the use of forward-looking terminology such as "may," "will," "could," "expect," "anticipate," "estimate," "continue" or other similar words. These statements discuss future expectations, contain projections of results of operations or of financial condition or state trends and known uncertainties or other forward-looking information. Examples of forward-looking statements can be found in the discussion set forth under "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" in the Form 10-K for the year ended December 31, 2001 filed with the SEC on March 29, 2002 and incorporated in this prospectus by reference. Such statements are based on current expectations that involve a number of uncertainties. When considering forward-looking statements, you should keep in mind that the risk factors noted above and other factors noted throughout this prospectus or incorporated by reference could cause our actual results to differ significantly from those contained in any forward-looking statement. We do not intend to update any forward-looking statements to conform to actual results unless required by law.

USE OF PROCEEDS

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

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

PLAN OF DISTRIBUTION

We may offer the common stock:

- directly to purchasers;
- to or through underwriters;
- through dealers, agents or institutional investors; or
- through a combination of such methods.

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

- the identity of any underwriters, dealers, agents or investors who purchase the common stock;
- the material terms of the distribution, including the number of shares sold and the consideration paid;
- any over-allotment options under which underwriters may purchase additional securities from us;
- the amount of any compensation, discounts or commissions to be received by the underwriters, dealers or agents;

- any public offering price;
- the terms of any indemnification provisions, including indemnification from liabilities under the federal securities laws; and
- the nature of any transaction by an underwriter, dealer or agent during the offering that is intended to stabilize or maintain the market price of the common stock.

SALE THROUGH AGENTS

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

SALE THROUGH UNDERWRITERS OR DEALERS

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

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

COMPENSATION OF UNDERWRITERS, DEALERS AND AGENTS

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

liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

DIRECT SALES

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

DELAYED DELIVERY CONTRACTS

If we so indicate in a prospectus supplement, we may authorize underwriters, dealers or agents to solicit offers from selected types of institutions to purchase common stock from us at the public offering price under delayed delivery requirements. These contracts would provide for payment and delivery on a specified date in the future. Institutions with which such contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement relating to such contracts will set forth the price to be paid for common stock under the contracts, the commission payable for solicitation of the contracts and the date or dates in the future for delivery of the common stock under the contracts.

STABILIZATION ACTIVITIES

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

PASSIVE MARKET MAKING

Any underwriters who are qualified market makers on the NASDAQ National Market may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of highest independent bid for the security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid then must be lowered when certain purchase limits are exceeded.

LEGAL MATTERS

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

EXPERTS

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

WHERE YOU CAN FIND MORE INFORMATION

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

This prospectus is only part of a Registration Statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933 and therefore omits certain information contained in the Registration Statement. We have also filed exhibits and schedules with the Registration Statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may:

- inspect a copy of the Registration Statement, including the exhibits and schedules, without charge at the public reference room, or
- obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

INCORPORATION OF DOCUMENTS BY REFERENCE

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

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

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

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

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

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

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

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

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

PART II. INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The table sets forth our estimates of our expenses in connection with the issuance and distribution of the common stock being registered.

ITEM	AMOUNT
SEC registration fee	$ 5,999.00
Legal fees and expenses	$ 75,000.00
Accounting fees and expenses	$ 75,000.00
Miscellaneous fees and expenses	$ 10,000.00
Total	$165,999.00

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Section 145(a) of the General Corporation Law of the State of Delaware provides that a Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that he is or was a director, officer, employee or agent of the corporation or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation or enterprise, against expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no cause to believe his conduct was unlawful.

Section 145(b) provides that a Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that such person acted in any of the capacities set forth above, against expenses actually and reasonably incurred by him in connection with the defense or settlement of such action or suit if he acted under similar standards, except that no indemnification may be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the court in which such action or suit was brought shall determine that despite the adjudication of liability, such person is fairly and reasonably entitled to be indemnified for such expenses which the court shall deem proper.

Section 145 further provides that to the extent a director or officer of a corporation has been successful in the defense of any action, suit or proceeding referred to in subsections (a) and (b) or in the defense of any claim, issue or matter therein, he shall be indemnified against expenses actually and reasonably incurred by him in connection therewith; that indemnification provided for by Section 145 shall not be deemed exclusive of any other rights to which the indemnified party may be entitled; and that the corporation may purchase and maintain insurance on behalf of a director or officer of the corporation against any liability asserted against him or incurred by him in any such capacity or arising out of his status as such whether or not the corporation would have the power to indemnify him against such liabilities under such Section 145.

The Certificate of Incorporation, as amended, and By-laws, as amended, of the Company provide for indemnification of the Company's directors and officers to the fullest extent permitted by law. The By-laws also permit the Board of Directors to authorize the Company to purchase and maintain insurance against any liability asserted against any director, officer, employee or agent of the Company arising out of his capacity as such. Insofar as indemnification for liabilities under the Securities Act may be permitted to directors, officers, or controlling persons of the Company pursuant to the Company's Certificate of Incorporation, as amended, its By-laws, as amended, and the Delaware General Corporation Law, the Company has been informed that in the opinion of the Commission such indemnification is against public policy as expressed in such Act and is therefore unenforceable.

As permitted by Section 102(b)(7) of the Delaware General Corporation Law, the Company's Certificate of Incorporation, as amended, provides that directors of the Company shall not be personally liable to the Company or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the Company or

its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the Delaware General Corporation Law, relating to prohibited dividends or distributions or the repurchase or redemption of stock or (iv) for any transaction from which the director derives an improper personal benefit. As a result of this provision, the Company and its stockholders may be unable to obtain monetary damages from a director for breach of his or her duty of care.

ITEM 16. EXHIBITS

EXHIBIT NUMBER	DESCRIPTION
4.1**	Restated Certificate of Incorporation of the Company. (Filed as Exhibit 4.1 to the Company's Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.)
4.2**	Amended and Restated By-laws of the Company. (Filed as Exhibit 4.2 to the Company's Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.)
4.3**	Specimen certificate for shares of Common Stock of the Company. (Filed as Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.)
5.1**	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., with respect to the legality of the securities being registered.
23.1	Consent of Ernst & Young LLP.
23.2**	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1).
24.1**	Power of Attorney (included on signature page).

** Previously filed

ITEM 17. UNDERTAKINGS.

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or any decrease in volume of securities offered (if the total

dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the registration statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(b) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

(c) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(d) The undersigned registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X are not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all the requirements for filing on Form S-3 and has duly caused this Amendment No. 3 to Form S-3 Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Cambridge, Massachusetts on December 20, 2002.

EPIX MEDICAL, INC.

BY: /s/ MICHAEL D. WEBB

Michael D. Webb
Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No. 3 to Registration Statement on Form S-3 has been signed below by the following persons in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ MICHAEL D. WEBB Michael D. Webb	Chief Executive Officer (Principal Executive Officer)	Decembe
/s/ PEYTON J. MARSHALL Peyton J. Marshall	Senior Vice President of Finance and Administration and Chief Financial Officer (Principal Financial and Accounting Officer)	Decembe

*	Chairman of the Board and Director	Decembe
Christopher F. O. Gabrieli		
*	Director	Decembe
Stanley T. Crooke, M.D., Ph.D.		
*	Director	Decembe
Peter Wirth		
*	Director	Decembe
Randall B. Lauffer, Ph.D.		

*By: /s/ Michael D. Webb
Michael D. Webb
Attorney-in-fact

INDEX TO EXHIBITS FILED WITH
FORM S-3 REGISTRATION STATEMENT

EXHIBIT NUMBER	DESCRIPTION
4.1**	Restated Certificate of Incorporation of the Company. (Filed as Exhibit 4.1 to the Company's Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.)
4.2**	Amended and Restated By-laws of the Company. (Filed as Exhibit 4.2 to the Company's Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.)
4.3**	Specimen certificate for shares of Common Stock of the Company. (Filed as Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.)
5.1**	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., with respect to the legality of the securities being registered.
23.1	Consent of Ernst & Young LLP.
23.2**	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1).
24.1**	Power of Attorney (included on signature page).

** Previously filed