EPIX MEDICAL INC
Form 10-K
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2003

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission file number: 0-21863

EPIX 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**
(Address of principal executive offices)	(Zip Code)

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

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

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

Common Stock, $.01 Par Value Per Share
(Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this

Form 10-K or any amendment to this Form 10-K. o

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

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was $242,874,735.

As of February 27, 2004, the registrant had 22,684,562 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on May 26, 2004.

PART I

ITEM 1. BUSINESS

Overview

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

MS-325 is designed to provide visual imaging of the vascular system, through a type of MRI known as magnetic resonance angiography, or MRA. We believe that MS-325-enhanced MRA has the potential to improve the diagnosis of multiple diseases of the vascular system, including vascular disease outside the heart, known as peripheral vascular disease, and diseases that affect the coronary arteries and reduce blood flow to the heart. Our initial target indication for MS-325 is for use in magnetic resonance angiographic imaging of peripheral vascular disease.

We believe that MS-325 will significantly enhance the quality of MRI and provide physicians with a minimally-invasive and cost-effective method for diagnosing vascular disease. We also believe that MS-325-enhanced MRA has the potential to simplify the diagnosis of vascular disease and to replace a significant portion of X-ray angiographic procedures, a highly invasive and expensive catheter-based method most frequently used for the detection of vascular disease. In 2002, approximately 7.5 million angiographic procedures were performed in the U.S. for the diagnosis of diseases of the vascular system, of which 4.6 million procedures were by way of X-ray angiography. We believe that MRA will be a less invasive method of imaging a patient's vascular anatomy for the evaluation of disease.

The NDA we submitted for MS-325 is based on a 780-patient Phase III clinical trial program designed to test the safety and efficacy of MS-325 for the imaging of peripheral vascular disease. Four Phase III trials were conducted to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the lower abdomen and pelvic regions, in the renal arteries of the kidneys and in the pedal arteries of the feet. All four trials in the Phase III program for MS-325 met their primary endpoints. In collaboration with Schering Aktiengesellschaft, or Schering AG, we expect to make analogous regulatory filings in Europe in 2004.

The use of MRI has grown steadily over the past 10 years due to reduced cost and improved imaging capabilities. MRI provides an effective method for diagnosing a broad range of diseases. MRI manufacturers have improved both the hardware and software used in their systems, reducing the procedure time and significantly enhancing image resolution. While MRI is currently used extensively to image many organs and tissues in the body, its use in imaging the vascular system has been limited. Currently available MRI contrast agents for MRA are not optimal for the diagnosis of vascular disease in many vascular beds due to the rapid leakage of the injectable contrast agent from the vascular

system into the surrounding tissue, usually within 30 to 60 seconds. As a result of this leakage, the time available to image blood vessels with these contrast agents is too short to obtain the high resolution images necessary for broad clinical application. In addition, performance of MRA using currently approved contrast agents generally requires specialized equipment and specially trained staff. None of the currently available MRI contrast agents are approved by the FDA for use in MRA. In 2002, approximately 2.2 million MRAs were performed in the U.S., an increase of 36% over 2001.

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

We are developing a second targeted contrast agent, EP-2104R, which is designed to illuminate and identify blood clots using MRI. Finding blood clots is of critical medical significance in the evaluation and diagnosis of patients with stroke, chest pain, heart attack, irregular heartbeat and clots in the lungs and legs. We designed EP-2104R to bind reversibly to fibrin, the dominant protein found in clots. In preclinical studies, EP-2104R has been shown to enhance the ability of MRI to image clots. We plan to commence human trials of EP-2104R in 2004.

We have established collaborations with large pharmaceutical companies to enhance our internal development capabilities and to offset a substantial portion of the financial risk of developing our product candidates. At the same time, we maintain substantial rights to product candidates covered by these collaborations, which provide us the opportunity to participate in a significant portion of the potential economic benefit from successful development and commercialization. Our most significant collaborations involve Schering AG for the development and commercialization of MS-325, EP2104R and for the discovery of other MRI contrast agents. We have also formed collaborations with the three leading MRI scanner manufacturers, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems, to develop advanced imaging techniques and tools designed to facilitate the use of MS-325-enhanced MRA.

Our objective is to become a worldwide leader in MRI contrast agents by developing and commercializing products using our proprietary technology platform. We intend to pursue this strategy through internal product development efforts, collaborations with strategic partners and by acquiring the rights to complementary technologies. We also intend to expand the potential applications for our current product candidates. In addition to developing MS-325 for peripheral vascular disease, we are developing the product for imaging the coronary arteries and the heart. We believe we can build on our leadership in developing targeted contrast agents for MRI through further research and development programs in cardiovascular imaging and therapeutics. In addition, we intend to consider other opportunities to expand beyond MRI.

Cardiovascular Disease

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

Atherosclerosis is one of the most common forms of cardiovascular disease. This condition refers to the accumulation of fatty plaques in the inner lining of blood vessels, resulting in a thickening or hardening of affected vessels. As the disease progresses, the arteries can become weakened or

increasingly narrowed, thereby reducing blood flow to vital organs, including the heart and brain. This condition is often characterized by the vascular region in which it is diagnosed. Coronary artery disease, for example, refers to disease in the arteries in the heart, while peripheral vascular disease refers to disease in the major vessels outside the heart: vessels of the head and neck, the aorta, arteries supplying blood to the kidneys and other organs, and the large vessels of the pelvis, legs, feet and arms. Recent research in cardiovascular disease has begun to highlight the systemic nature of this condition. Because the major risk factors tend to affect all vascular regions, many patients have multiple

clinical symptoms of cardiovascular disease. Therefore, patients diagnosed with cardiovascular disease in one vascular region are at high risk of having disease in other vascular regions.

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

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

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

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

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

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

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

Diagnosing Cardiovascular Disease

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

Screening for Vascular Disease

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

Screening for Coronary Artery Disease

Typically, a patient enters the diagnostic pathway for coronary artery disease after experiencing chest pain or shortness of breath. If the patient cannot be ruled out for this condition after the initial work-up that includes a physical exam, patient history, electrocardiogram and exercise stress test, a cardiologist will often perform a stress echocardiogram and/or a nuclear stress perfusion study.

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

Nuclear Stress Perfusion Studies. Nuclear stress perfusion studies measure the flow of blood to cardiac tissue, and can be used either as the critical diagnostic test prior to conventional X-ray angiography or to confirm the impact on blood flow of an intermediate blockage identified through conventional X-ray angiography. Nuclear stress perfusion tests are non-invasive and use small quantities of radiation. A patient is injected with a radioactive agent and then a radiation sensitive camera is used to detect uptake of the agent in the heart muscle. A deficiency in blood flow to particular regions of the heart is shown in the resulting images. While the test can identify the effects of coronary artery disease, it provides no information about the anatomy of

the coronary arteries and it cannot determine the location of blockages. We estimate that over 5.8 million nuclear stress perfusion studies were conducted in the U.S. in 2002.

Definitive Diagnosis of Atherosclerotic Disease

X-ray Angiography

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

Invasiveness of procedure requires extended recovery time;

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

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

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

Separate exams necessary to view both arteries and veins;

Separate exams necessary for each vascular region;

Provides only two-dimensional images;

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

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

Inability to distinguish atherosclerotic plaques.

Computed Tomography

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

MRI

MRI has been established as the imaging technology of choice for a broad range of applications, including brain tumors, knee injuries and disorders of the head, neck and spine. MRI is performed by placing a portion of the patient's body in a magnetic field and applying safe, low-energy radio waves. The different organs and tissues in the body respond uniquely to the electromagnetic field within the MRI scanner, and these responses can be captured and converted into high-resolution three-dimensional images. When a contrast agent is used, it is injected into a vein in the patient's arm prior to an MRI exam to amplify the signal from the desired anatomical structure. It is estimated that contrast agents are used in 26% of all MRI exams performed in the U.S. MRI scanners are characterized by the strength of the magnetic field they generate. Typical MRI scanners-those most commonly found in hospitals-generate a relatively strong magnetic field and therefore require significant infrastructure for installation. Low-field scanners, whose magnetic fields are less than one-third the strength of traditional scanners, are often found in out-patient settings due to their relatively low cost and infrastructure requirements. The trade-off for low-field MRI scanners is that a decrease in the strength of the magnetic field results in a decrease in the MRI signal detected, which typically results in reduced image quality.

While the use of MRA is expanding among experts, it has not made a significant impact on the diagnosis of cardiovascular disease to date, with the exception of arterial studies of the head and neck. Non-contrast MRA exams of the vascular system, which image blood flow, are often ineffective when used in patients with cardiovascular disease, because of the minimal blood flow or turbulent blood flow associated with this condition. Even for the imaging of carotid arteries in the neck, where flow-based MRA has had some clinical impact, the lack of direct anatomic data limits the ability of MRA to provide a quantitative measurement of stenosis required for accurate diagnosis. MRA exams using existing general use contrast agents are limited by the rapid diffusion of the agents out of the vascular system, which reduces the time during which an

image can be acquired. Consequently, many experts believe MRI contrast agents that remain in the bloodstream for extended periods of time will be necessary to attain widespread use of MRI to image the vascular system. Of the 2.2 million MRAs performed in the U.S. in 2002, approximately 77% were for imaging cerebral and carotid arteries where MRA is less technically challenging than in other regions of the body. We believe that MS-325, by providing a longer imaging window, allowing visualization of multiple arterial beds and making MRA easier to perform, has the potential to become the contrast agent used in a significant portion of MRAs currently performed with general use contrast agents.

Plaque Characterization

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

Summary

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

Our Approach to Cardiovascular MRI

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

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

MS-325-Enhanced Angiography

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

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

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

Multiple Vascular Bed Imaging. Whereas X-ray angiography captures data over a limited vascular region, we expect MS-325-enhanced MRA to provide clinicians with the ability to capture images of many vascular areas in a single exam. We

believe that a multiple vascular bed MR angiogram with a single injection of MS-325 will be particularly well suited for the diagnosis of cardiovascular disease, given the systemic nature of this condition.

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

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

Patient Monitoring. After a therapeutic intervention for cardiovascular disease, such as angioplasty or bypass graft, optimal patient management often includes follow-up exams to look

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

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

Low-Field MR Angiography

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

Integrated Cardiac Exam

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

Other Cardiovascular Applications

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

Beyond Cardiovascular

MRI Additional Applications

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

Technology Platform

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

Targeting

We develop metal complexes that are engineered to bind to particular proteins in the body. This binding causes increased concentration and retention of the contrast agent in the specific tissues and fluids that contain the targeted molecules. Our objectives in designing such agents are to choose the best target the protein or cell type that most precisely characterizes the relevant disease state and to identify a chemical structure that binds to that target without binding to other molecules in the body. The chemical structure of MS-325, for example, is designed to bind selectively to albumin, the most common blood protein, which keeps the agent localized within the bloodstream. In designing EP-2104R for use in imaging blood clots, we have used combinatorial chemistry to select a family of highly specific peptides that bind to fibrin, the dominant protein inside clots, without binding to fibrinogen, a similar, but far less clot-specific protein in blood. We have considerable expertise in peptide synthesis and in labeling the peptides with strongly enhancing clusters of gadolinium.

MRI Signal Generation

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

Image Acquisition and 3-D Visualization

We have also developed significant expertise in the translation of raw MRI data into clinically useful three-dimensional images. MRI is the most flexible of the major medical imaging technologies. The hardware and software of most MRI scanners allow an enormous range of data acquisition

methods and, increasingly, methods for displaying and interpreting the resulting medical images. Through our research and development, extensive academic collaborations and industrial partnerships, we have built a deep understanding of the relationships between the contrast agent biophysics, scanner engineering and medical practice. Our expertise allows us not only to create the best images for our agents in development,

but is critical for optimizing the clinical usefulness of future MRI agents.

Our Products and Development Programs

MS-325

Our lead product candidate, MS-325, is a targeted intravascular contrast agent intended for use with MRI. MS-325 is a small molecule, which produces an MRI signal because of the presence of gadolinium, a magnetically active element favored by clinicians for enhancing MR images. MS-325 is designed with our proprietary technology to bind reversibly to albumin, the most common blood protein. Using standard MRI techniques, MS-325 enhanced MRA produces a strong magnetic signal, resulting in bright images of the blood against the dark background of surrounding tissue. Because of its affinity for albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam providing the extended image acquisition time and signal strength required to obtain a high resolution image of multiple regions of the vascular system. Like most currently available general use contrast agents, MS-325 is designed to be safely eliminated through the kidneys over time.

Lead Indication MRA of Peripheral Vascular Disease

In December 2003, we submitted an NDA to the FDA for MS-325. In February 2004, we were notified by the FDA that the NDA for MS-325 has been accepted for filing and has been designated for a standard review cycle. The target date for the first FDA action in the standard review cycle is ten months from the date of submission. In the context of our collaboration, we expect that Schering will make analogous regulatory filings in Europe in 2004. The NDA is based on a four-part Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease. All four trials in the Phase III program for MS-325 met their primary endpoints.

In September 2001, we completed enrollment in the first of two Phase III trials designed to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease, a common form of vascular disease in the lower abdomen and pelvic regions. We reported preliminary results of this trial in March 2002 at the American College of Cardiology conference. The trial met its primary clinical endpoint, which was an improvement in accuracy of MS-325-enhanced MRA versus that of non-contrast MRA, with each of three blinded radiologist readers showing improvement in accuracy with a p-value less than 0.001. In our Phase III studies, as in many other such studies, the statistical significance of clinical results is determined by a widely used statistical method that establishes the p-value of clinical results. A p-value less than 0.001 means that the likelihood of the improvement in accuracy occurring by chance is less than one in one thousand. The trial demonstrated that MS-325-enhanced MRA compared favorably to conventional X-ray angiography, the current reference standard, achieving 88% accuracy in identifying clinically significant arterial narrowing or stenoses caused by atherosclerotic disease. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 90%.

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

the current reference standard, achieving 84% accuracy in identifying clinically significant stenoses caused by atherosclerotic disease. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 90%.

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

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

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

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

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

In November 2003, we announced results of MS-325 Phase II clinical trials in renally-compromised patients. Based on these studies, MS-325 appeared safe and well tolerated in patients with varying degrees of renal impairment, including those requiring dialysis and MS-325 had no adverse effect on renal function.

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

angiography, in identifying clinically significant stenoses caused by atherosclerotic disease. The results indicated that MS-325 was safe and well-tolerated by patients in this study.

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

Coronary Artery Disease

We have conducted a Phase II feasibility trial in 106 patients to test the safety and preliminary efficacy of MS-325-enhanced MRA for the evaluation of coronary artery disease. As with the completed first two Phase III aortoiliac trials, our coronary trial compares MS-325-enhanced MRA to X-ray angiography, the current reference standard, to determine the location and degree of plaque blockages. Clinical use of MRA for imaging the coronary arteries is more difficult than in other arteries due to the problem of cardiac motion that results from both the beating of the heart and breathing. We have joined with several leading MRI manufacturers, academic centers and other research organizations to develop hardware and software solutions to the problem of cardiac motion. We received promising early images from this study indicating that MS-325 may be useful in assessing coronary artery blockages. We plan to reinitiate studies of the use of MS-325 in coronary imaging and myocardial perfusion imaging in 2004.

Potential Additional Applications

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

Breast Cancer

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

Female Sexual Arousal Dysfunction

In March 2001, we completed enrollment in a Phase II feasibility trial in 25 patients, which we conducted in collaboration with Pfizer to explore the efficacy of MS-325-enhanced MRI in the diagnosis of female sexual arousal dysfunction. Preliminary results from this trial indicate that MS-325-enhanced MRI is able to measure changes in pelvic blood volume and organ volume during

sexual arousal. We believe that this technique may be useful in assessing how different diseases affect sexual response in women as well as examining the effects of potential treatments in restoring impaired sexual response. Commencement of additional clinical studies for this application is contingent upon future outlook and development of the market.

EP-2104R for Thrombus Imaging

Background: Imaging Blood Clots

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

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

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

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

EP-2104R Development Program

We are developing a second targeted contrast agent, EP-2104R, that would enable MRI to illuminate blood clots. This agent could potentially change the diagnostic work-up for many of the conditions associated with thromboembolic disease, including patients with clots in the heart and brain

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

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

Our Business Strategy

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

Obtain regulatory approval and support the commercialization of MS-325 for our lead cardiovascular imaging indication of peripheral vascular disease. As previously discussed in the section "Our Product and Development Programs Lead Indications MRA of Peripheral Vascular Disease," we have announced preliminary results of our four-part Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease. We have submitted our NDA for MS-325 to the FDA and expect to support Schering AG's European regulatory submission for MS-325 in 2004, which we expect Schering AG to make in the context of our collaboration.

Establish the clinical utility of MS-325 in other cardiovascular imaging indications. We plan to study the safety and efficacy of MS-325-enhanced MRA for the evaluation of coronary artery disease and myocardial perfusion. In a Phase II trial in 106 patients, we compared MS-325-enhanced MRA to conventional X-ray angiography, the current reference standard. In addition, we are currently evaluating the results of preclinical trials for such applications as myocardial perfusion imaging. We plan to reinitiate clinical trials for coronary imaging in 2004.

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

Maximize the value of strategic alliances. We have established collaborations with Schering AG, Tyco/Mallinckrodt, General Electric Medical Systems, Philips Medical Systems, Siemens Medical Systems and Pfizer. We entered into these alliances, and will seek to enter into future strategic alliances with pharmaceutical, imaging agent and MRI equipment industry leaders, in order to obtain access to resources and infrastructure to leverage our strengths. See "Strategic Alliances and Collaborations."

Maximize the value of our proprietary technology platform. We plan to build on our leadership in developing targeted contrast agents for MRI through further research and development programs in cardiovascular imaging and therapeutics. We have established a collaboration for MRI research with Schering AG in which we and Schering AG are exclusively combining our research programs in the field of MRI to discover novel MRI product candidates for clinical

development. We are initiating exploratory research programs utilizing our skills and intellectual property to discover product candidates for the treatment or prevention of cardiovascular disease. We intend to consider other opportunities to expand beyond MRI.

Strategic Alliances and Collaborations

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

Co-Development, Sales & Marketing

Schering AG

In June 2000, we entered into a strategic collaboration agreement for MS-325 pursuant to which we granted Schering AG an exclusive license to co-develop and market MS-325 worldwide, exclusive of Japan. In December 2000, we amended this strategic collaboration agreement to grant to Schering AG the exclusive rights to develop and market MS-325 in Japan. Generally, each party to the agreement will share equally in MS-325 costs and profits. Under the agreement, we will assume responsibility for completing clinical trials and filing for FDA approval in the U.S. Schering AG will lead clinical and regulatory activities for the product outside the U.S. In addition, we granted Schering AG an exclusive option to develop and market an unspecified cardiovascular MRI blood pool agent from our product pipeline. In connection with this strategic collaboration and the amendment to our strategic collaboration agreement with Tyco /Mallinckrodt, as further described below, Schering AG paid us an up-front fee of $10.0 million, which we then paid to Tyco/Mallinckrodt. Under the agreement, Schering AG also paid us $20.0 million in exchange for shares of our common stock through its affiliate, Schering Berlin Venture Corporation, or Schering BV. We may receive up to an additional $18.75 million in milestone payments under the strategic collaboration agreement, of which $2.5 million was earned upon NDA filing in February 2004 and up to $1.25 million will be earned upon product approval. Under the terms of the December 2000 amendment, Schering AG paid us an up-front fee of $3.0 million and may be required to pay us an additional $7.0 million upon our achievement of certain milestones. Following commercial launch of MS-325, we will also be entitled to receive a royalty on products sold outside the U.S. and a percentage of Schering AG's operating profit margin on products sold in the U.S.

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

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

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

Under the terms of the EP-2104R agreement, we are responsible for execution of a clinical feasibility program in humans. At the end of the feasibility program, Schering AG may exercise an option to develop and commercialize EP-2104R under which Schering AG will receive an exclusive, worldwide license for EP-2104R and become responsible for all further development, manufacturing, marketing and sales. Schering AG will make fixed payments to us totaling approximately $9.0 million over two years to cover our expenditures in the feasibility program. In addition, if Schering AG exercises its option to develop and commercialize EP-2104R, Schering AG will pay us up to $15.0 million in additional

payments upon the occurrence of certain development and commercial events, as well as royalties on sales attributable to the EP-2104R development effort. The royalty rate will depend on the level of annual net sales. In addition to funding for our feasibility program and milestone and base royalty payments, we have the right to increase our royalty rate by paying to Schering AG a portion of the costs of clinical development.

Under the terms of the MRI three-year joint research agreement, we and Schering AG are exclusively combining our existing research programs in the field of diagnosing human disease using MRI to discover novel MRI product candidates for clinical development. Schering AG will fund a portion of our related personnel costs and third party research costs of up to $2.0 million per annum and has made available to us a loan facility of up to $15.0 million with principal repayment beginning in 2007. The loan facility carries a variable, market-based interest rate. $7.5 million of the $15.0 million loan facility available from Schering AG was outstanding as of December 31, 2003. The remaining $7.5 million of the Schering AG loan facility may be available starting May 2004 subject to specified covenants and conditions contained in the loan agreement. Also under the MRI research agreement, Schering AG has the first option to obtain exclusive, worldwide rights for the product candidates and, upon exercising the option, would become responsible for all future development, manufacturing, marketing and sales. We would receive a base royalty on net sales with the option to increase the royalty by participating in development funding. If Schering AG does not exercise its option, we may license the product, and Schering AG would receive a base royalty on net sales and milestone payments.

On May 8, 2000, we granted to Schering AG a worldwide, royalty-bearing license to patents covering Schering AG's development project, Eovist injection, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 8, 2000, Schering AG granted us a non-exclusive, royalty-bearing license to certain of its Japanese patents. We agreed to withdraw our invalidation claim of Schering AG's Japanese patent 1,932,626 in the Japanese Patent Office pursuant to this license agreement. See "Patents and Proprietary Rights." Schering AG had been an opposing party in our European patent case prior to the licensing agreement. On May 9, 2000, the Opposition Division of the European Patent Office maintained our European patent in a slightly amended form. The patent is owned by MGH and is exclusively licensed to us. The remaining opposing parties initially elected to appeal the May 9, 2000 decision. However, in September 2001, we settled this patent dispute with the opposing parties by entering into a non-exclusive royalty bearing license agreement with Bracco. See "Patents and Proprietary Rights" for further discussion of this settlement.

Tyco/Mallinckrodt

In June 2000, in connection with the exclusive license that we granted to Schering AG, we amended our strategic collaboration with Tyco/Mallinckrodt to grant Tyco/Mallinckrodt a non-exclusive, worldwide license to manufacture MS-325 for clinical development and commercial use in accordance with a manufacturing agreement entered into in June 2000 between Tyco/Mallinckrodt and Schering AG, and to enable us to enter into the strategic collaboration agreement with Schering AG described above. In connection with this amendment, we paid Tyco/Mallinckrodt an up-front fee of $10.0 million and are obligated to pay up to an additional $5.0 million in milestone payments, of which $2.5 million is due following NDA filing in February 2004 and $2.5 million will be paid upon product approval. We will also pay Tyco/Mallinckrodt a share of our MS-325 operating profit margins in the U.S. and a percentage of the royalty that we receive from Schering on MS-325 gross profits outside the U.S.

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

Daiichi

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

MRI Equipment Manufacturers

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

General Electric Medical Systems

In January 1998, we announced the formation of a collaboration with General Electric Medical Systems to accelerate the development of cardiovascular MRI. In particular, the collaboration focuses on reducing the effects of cardiac motion on MR images, providing user-friendly computer tools as a means of visualizing arteries and veins in three-dimensional space and optimizing MRI, for intravascular MRI contrast agents, including MS-325. Under the terms of this non-exclusive agreement,

research is performed at several centers in addition to our facilities, including General Electric's corporate research facility in Schenectady, NY, General Electric Medical Research in Milwaukee, WI, and several academic centers.

Philips Medical Systems

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

Siemens Medical Systems

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

Potential New Applications

Pfizer

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

Competition

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

We have many competitors, including pharmaceutical, biotechnology and chemical companies. A number of competitors, including two of our strategic partners, are actively developing and marketing product candidates that, if commercialized, would compete with our product candidates. Many of these competitors have substantially greater capital and other resources than we do and may represent significant competition for us. Such companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. Such companies may be more successful than us in developing, manufacturing and marketing products. Furthermore, there are several well-established medical imaging modalities that currently compete, and will continue to compete, with MRI, including X-ray angiography, CT, nuclear medicine and ultrasound. Other companies are actively developing the capabilities of the competing modalities to enhance their effectiveness in cardiovascular system imaging. For example, we are aware of at least one radiopharmaceutical agent, Schering AG's AcuTect®, which has been approved for imaging acute venous thrombosis. Other nuclear medicine agents, including Draxis Health's FibrImage®, are in clinical testing for DVT and other clot imaging applications. In addition, several ultrasound contrast agents, including Dupont's Definity®, Amersham's Optison® and Alliance Pharmaceutical's Imagent® are approved in the U.S. and may be used for myocardial perfusion imaging. Several other ultrasound contrast agents are undergoing clinical testing for myocardial perfusion imaging including Amersham's Sonazoid®, Point Biomedical's PB-127 and Acusphere's AI-700. We cannot guarantee that we will be able to compete successfully in the future or that developments by others will not render MS-325 or our future product candidates obsolete or non-competitive or that our collaborators or customers will not choose to use competing technologies or products.

Patents and Proprietary Rights

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

We own or have exclusively licensed patents and patent applications related to our core technologies. Our patents and patent applications relating to our technology consist of the following:

Two U.S. patents exclusively licensed from MGH (U.S. Patents 4,899,755 and 4,880,008) as well as their cognate patents in certain foreign countries, including EPO 222,886. These patents broadly cover RIME technology, albumin binding with metal chelates and liver targeting metal chelates.

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

U.S. Patent 5,582,814, "Contrast Agents for Diagnostic Imaging" (granted December 10, 1996; expires April 15, 2014)

U.S Patent 5,919,967, "Process for Synthesizing Phosphodiesters" (granted July 6, 1999; expires April 11, 2017)

U.S. Patent 6,548,044, "Imaging Sexual Response" (granted April 15, 2003; expires November 21, 2020)

U.S. Patent 6,549,798, "Magnetic Resonance Angiography Data" (granted April 15, 2003; expires February 7, 2021)

U.S. Patent 6,652,835, "Targeting Multimeric Imaging Agents Through Multilocus Binding" (granted November 25, 2003; expires July 28, 2020)

U.S. Patent 6,676,929, "Diagnostic Imaging Contrast Agents With Extended Blood Retention" (granted January 13, 2004; the 20 year term expires February 1, 2015; however, the USPTO has indicated that the patent is entitled to 114 days of patent term adjustment)

Sixteen U.S. utility applications in prosecution, one international patent application filed under the Patent Cooperation Treaty and thirteen provisional utility applications as well as their cognate applications in certain foreign countries. Some of these relate to MS-325 and methods of use, and others to EP-2104R and methods of use.

Some of our patents related to MS-325 will expire in 2006 in the United States and Europe. Other patents related to MS-325 will not expire until 2015. Protection for MS-325 manufacturing processes in the U.S. will not expire until 2017. Patents related to methods of using MS-325 will not expire until 2021. We plan to apply for patent term extension under the Hatch/Waxman provisions, which may extend the term of our patent protection.

If our pending patent applications issue, patent protection for EP-2104R will not expire until 2022.

Legal proceedings between Bracco, Schering AG and others against us and MGH involving national patents derived from European Patent No. 222,886, the European patent referred to above, have been terminated. A Settlement and Release Agreement as to litigation between the parties and a License Agreement from us to Bracco for European Patent No. 222,886 and its worldwide counterparts was executed on September 25, 2001. We received various payments, including royalties on a quarterly basis pursuant to the license with Bracco. Previously, on May 8, 2000, we granted to Schering AG a worldwide royalty-bearing license to our patents covering Schering AG's development project, Eovist, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 8, 2000, Schering AG granted us a non-exclusive royalty-bearing license to its Japanese Patent Nos. 1,932,626 and 1,968,413, and its Japanese Application corresponding to PCT Intl. Pub. No. WO99/16474. We have agreed to withdraw our invalidation claim of Schering AG's Japanese Patent No. 1,932,626 in the Japanese Patent Office pursuant to this license agreement. As a result of the Settlement and License Agreements with Bracco and Schering AG, we are not aware of any legal actions involving this patent family.

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

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

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

administrative proceeding or failure to obtain necessary licenses could prevent us from manufacturing and selling our products, which may have a material adverse effect on our business, financial condition and results of operations.

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

Many of our competitors are continuing to actively pursue patent protection for activities and discoveries similar to ours. There can be no assurance that these competitors, many of which have substantially greater resources than us and have made substantial investments in competing technologies, will not in the future seek to assert that our products or chemical processes infringe their existing patents and/or will not seek new patents that claim to cover aspects of our technology. Furthermore, patent applications in the U.S. and in foreign countries are

maintained in secrecy for a specified period after filing. Publication of discoveries in the scientific or patent literature tends to lag behind actual discoveries and the filing of related patent applications. In addition, patents issued and patent applications filed relating to biopharmaceuticals are numerous. Therefore, there can be no assurance that we are aware of all competitive patents, either pending or issued, that relate to products or processes used or proposed to be used by us.

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

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

In November 2003, we entered into an Intellectual Property Agreement with Dr. Martin R. Prince, an early innovator in the field of MRA relating to "dynamic" MRA, which involves capturing MRA images during the limited time, typically 30 to 60 seconds, available for imaging with extracellular agents. Under the terms of the Intellectual Property Agreement, Dr. Prince made certain covenants and agreements, and granted us certain discharges, licenses and releases, in connection with the use of MS-325. In consideration of Dr. Prince entering into this Agreement, we agreed to pay him an upfront fee and royalties on sales of MS-325 consistent with a non-exclusive early stage academic license and agreed to deliver to him 132,000 shares of EPIX common stock and certain quantities of MS-325.

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

We also rely upon trade secrets, technical know-how, and continuing technological innovation to develop and maintain our competitive position. We typically require our employees, consultants, and advisors to execute confidentiality and assignment of invention agreements in connection with their employment, consulting or advisory relationships with us. These agreements require disclosure and assignment to us of ideas, developments, discoveries and inventions made by employees, consultants and advisors. There can be no assurance, however, that these agreements will not be breached or that we will have adequate remedies for any breach. Furthermore, no assurance can be given that competitors will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our proprietary technology, or that we can meaningfully protect our rights in unpatented proprietary technology. We intend to vigorously protect and defend our intellectual property. Costly and time-consuming litigation brought by us may be necessary to enforce our issued patents, to protect our trade secrets or know-how owned by us, or to determine the enforceability, scope, and validity of the proprietary rights of others.

Manufacturing

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

Government Regulation

The manufacture and commercial distribution of pharmaceuticals are subject to extensive governmental regulation in the U.S. and other countries. Pharmaceuticals, including contrast-imaging agents for use with MRI, are regulated in the U.S. by the FDA under the Food, Drug and Cosmetic Act, or FD&C Act, and require FDA approval prior to commercial distribution. Pursuant to the FD&C Act, pharmaceutical

manufacturers and distributors must be registered with the FDA and are subject to ongoing FDA regulation, including periodic FDA inspection of their facilities and review of their operating procedures. Noncompliance with applicable requirements can result in failure to receive approval, withdrawal of approval, total or partial suspension of production, fines, injunctions, civil penalties, recalls or seizure of products and criminal prosecution, each of which would have a material adverse effect on our business, financial conditions and results of operations.

In order to undertake clinical trials and market pharmaceutical products for diagnostic or therapeutic use in humans, the procedures and safety standards established by the FDA and comparable agencies in foreign countries must be followed. In the U.S., a company seeking approval to

market a new pharmaceutical must obtain FDA approval of a new drug application, or NDA. Before a NDA may be filed, however, a certain procedure is typically followed. This includes:

- performance of preclinical laboratory and animal studies;
- submission to the FDA of an application for an IND, which must become effective before human clinical trials may commence;
- completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the pharmaceutical for its intended use;
- submission to the FDA of a NDA; and
- approval of the NDA by the FDA prior to any commercial sale or shipment of the agent.

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

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

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

The process of completing clinical testing and obtaining FDA approval for a new product is likely to take a number of years. When the study for a particular indication as described in the IND is complete, and assuming that the results support the safety and efficacy of the product for that indication, we intend to submit a NDA to the FDA. The NDA approval process can be expensive, uncertain and lengthy. Although the FDA is supposed to complete its review of a NDA within ten months of the date that it is submitted, the review time may be extended by the FDA or additional time may be required for us to respond to an FDA action letter and for FDA review, all of which may require more information or clarification of information already provided in the NDA. During the review period, an FDA advisory committee may be asked to review and evaluate the application and provide recommendations to the FDA about approval of the pharmaceutical. In addition, the FDA will inspect the facility at which the pharmaceutical is manufactured to ensure compliance with GMP and other applicable regulations. Failure of a

manufacturer to comply or come into compliance with GMP requirements could significantly delay FDA approval of the NDA. The FDA may grant an unconditional approval of an agent for a particular indication or may grant approval conditioned on further post-marketing testing and/or surveillance programs to monitor the agent's efficacy and side effects. Results of these post-marketing programs may prevent or limit the further marketing of the

agent. In addition, further studies and a supplement to the initially approved NDA will be required to gain approval for the use of an approved product in indications other than those for which the NDA was approved initially.

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

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

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

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

Reimbursement

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

In 2001, the Centers for Medicare and Medicaid Services, or CMS, formerly HCFA, created additional payment codes for contrast-enhanced MRA procedures performed in outpatient settings, where we expect the majority of MRA procedures to occur, improving the reimbursement situation for

such agents. Certain new contrast agents may also be eligible for additional pass-through payments in the outpatient environment. In 2003, CMS expanded its coverage of MRA procedures to include imaging the renal and aortoiliac arteries separate from abdominal aortic aneurysm or aortic dissection, and when clinically warranted and supported by medical necessity, contrast angiography may be performed as an adjunct imaging modality to MRA. CMS previously covered MRA for head and neck, peripheral arteries of the lower extremities, chest, abdomen and pelvis with limitations.

For inpatients, Medicare pays hospitals a prospectively determined amount for the entire patient stay based on a Medicare beneficiary's discharge diagnosis related group, or DRG. This payment usually includes payment for any procedure, including MRI, that is performed while a beneficiary is in the hospital. No additional payment has been made for contrast agents used during the procedure. Other third-party payors may pay a hospital an additional amount for an MRI procedure performed on an in-patient according to another methodology such as a fee schedule or a percentage of charge. Such payment may or may not include a payment for a contrast-imaging agent.

Third-party payors carefully review and increasingly challenge the prices charged for procedures and medical products. In the past few years, the amounts paid for radiology procedures in particular have come under careful scrutiny and have been subject to decreasing reimbursement rates. In addition, an increasing percentage of insured individuals are receiving their medical care through MCOs which monitor and often require preapproval of the services that a member will receive. Many MCOs are paying their providers on a capitated basis, which puts the providers at financial risk for the services provided to their patients by paying them a predetermined payment per member per month. The percentage of individuals, including Medicare beneficiaries, covered by MCOs is expected to grow in the U.S. over the next decade. We believe that the managed care approach to healthcare and the growth in capitated arrangements and other arrangements under which the providers are at financial risk for the services that are provided to their patients may facilitate the market acceptance of our products, as we believe that the use of our products will significantly lower the overall costs and improve the effectiveness of managing patient populations. We cannot assure you, however, that our products will be available, will lower costs of care for any patients or will be utilized by providers, or if reimbursement, will be available.

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

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

Employees

As of December 31, 2003, we employed 86 persons on a full-time basis. Thirty-two of our employees hold Ph.D. or M.D. degrees. We believe that our relations are good with our employees. None of our employees are a party to a collective bargaining agreement.

Research and Development

During the years ended December 31, 2003, 2002 and 2001, we incurred research and development expenses of $28,023,522, $29,084,469 and $22,903,780, respectively.

Available Information

We incorporated in Delaware in 1988 and commenced operations in 1992. Our principal executive offices are located at 71 Rogers Street, Cambridge, Massachusetts 02142-1118 and our telephone number is (617) 250-6000. Our website is located at *http://www.epixmed.com*. Our Corporate Code of Conduct and Ethics as well as our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and all amendments to these reports, which have been filed with the Securities and Exchange Commission, are available to you free of

charge through the Investor Relations section on our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the Commission. We do not intend for the other information contained in our website to be considered a part of this Form 10-K.

Risk Factors

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

We have never generated revenues from commercial sales of our products and, if MS-325 does not receive approval from the Food and Drug Administration, 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 that has undergone human clinical trials and we cannot be certain that any of our other development projects will yield a product candidate suitable for substantial human clinical testing. As a result, our initial revenues and profits from commercial sales of our products, if any, will be derived from sales of MS-325. 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, 2003 was $13.5 million, and consisted of $9.5 million from the product development portion of our collaboration agreements with Schering AG, or Schering for MS-325, EP-2104R and MRI research, and Pfizer, Inc., or Pfizer, $2.8 million from a patent licensing and royalty agreement with Bracco Imaging, S.p.A., or Bracco, and $1.2 million of license fee revenue related to the strategic collaboration agreements for the development, manufacturing and marketing of MS-325 with Schering AG and Tyco/Mallinckrodt. In addition to these sources of revenue, we have financed our operations to date through public stock offerings, private sales of equity securities, debt financing and equipment lease financings.

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

successfully complete our product development efforts;

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

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

successfully market any approved products.

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

We anticipate future losses and may never become profitable.

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of December 31, 2003 were approximately $135.0 million. These losses have primarily resulted from expenses associated with our research and development activities, including preclinical and clinical trials, and general and administrative expenses. We anticipate that our research and development expenses will remain significant in the future, and we expect to incur substantial losses over at least

the next several years as we continue our research and development efforts, pre-clinical testing and clinical trials and as we implement manufacturing, marketing and sales programs. As a result, we cannot predict when we will become profitable, if at all, and if we do, we may not remain profitable for any substantial period of time. If we fail to achieve profitability within the time frame expected by investors, the market price of our common stock may decline and consequently our business may not be sustainable.

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

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

safety;

cost-effectiveness relative to alternative vascular imaging methods;

availability of third party reimbursement;

ease of administration;

clinical efficacy; and

availability of competitive products.

Market acceptance will also depend on our ability and that of our strategic partners to educate the medical community and third party payors about the benefits of diagnostic imaging with MRA

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

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

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

the progress and scope of clinical trials;

the timing and costs of filing future regulatory submissions;

the timing and costs required to receive both U.S. and foreign governmental approvals;

the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;

the extent to which our products gain market acceptance;

the timing and costs of product introductions;

the extent of our ongoing and any new research and development programs;

the costs of training physicians to become proficient with the use of our products; and

the costs of developing marketing and distribution capabilities.

Based on our current plans, expense rates, targeted timelines and our view regarding acceptance of MS-325 in the marketplace, we estimate that cash, cash equivalents and marketable securities on hand as of December 31, 2003 will be sufficient to fund our operations until we turn cash flow positive. As of December 31, 2003, we had outstanding $7.5 million of our $15.0 million loan facility available from Schering as part of our MRI research collaboration. We repaid the $7.5 million loan, plus accrued interest, in January 2004, but expect to redraw the $7.5 million loan as needed. We expect to be able to draw the remaining $7.5 million from the $15.0 million Schering loan facility in May 2004, but could be unable to draw under the terms of the loan if we fail to meet certain covenants or conditions precedent in the loan.

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

We do not have, nor do we currently have plans to develop, full-scale manufacturing capability for MS-325. While we have manufactured small amounts of MS-325 for research and development efforts, we rely on Tyco/Mallinckrodt as the primary manufacturer of MS-325 for any future human clinical trials and commercial use. In the event that Tyco/Mallinckrodt fails to fulfill its manufacturing responsibilities satisfactorily, Schering 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 itself in a timely manner.

If we experience a delay in manufacturing, it could result in a delay in the approval or commercialization of MS-325 and have a material adverse effect on our business, financial condition and results of operations.

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

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

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

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

significant competition for us. These companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. In addition, these companies may be more successful than we are in developing, manufacturing and marketing products.

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

	Advantages	**Disadvantages**
MRI	Three-dimensional images Minimally-invasive Favorable safety profile High quality images	Requires high level of training Inadvisable for patients with cardiac pacemakers Less widely available
CT Angiography	Rapid and easy data acquisition	Radiation Varying levels of toxicity Calcium and bone artifacts Time consuming post-processing
DSA (X-ray angiography)	Significant clinical experience Opportunity to treat in same procedure Highest resolution	Invasive Radiation Varying levels of toxicity Significant safety risks Two-dimensional images Expensive Patient recuperation time
Ultrasound	Low cost Fast Widely available Non-invasive	Operator dependent Lack of anatomic detail Bone precludes use in many vascular beds Inability to visualize small vessels

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

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

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

We depend on strategic collaborators for support in product development and the regulatory approval process as well as a variety of other activities including manufacturing, marketing and distribution of our products in the U.S. and abroad, when, and if, the FDA and corresponding foreign agencies approve our product candidates for marketing. To date, we have entered into strategic alliances and collaborations with Schering AG, Tyco/Mallinckrodt, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems. Four of our key agreements include three collaboration agreements with Schering, to perform joint research and to develop and commercialize MS-325, EP-2104R and other MRI vascular agents worldwide, and an agreement with Tyco/Mallinckrodt, granting Tyco/Mallinckrodt rights to enter into an agreement with Schering to manufacture MS-325 for clinical development and commercial use. We may not receive milestone payments from these alliances should MS-325 or EP-2104R fail to meet certain performance targets in

development and commercialization. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development, and commence marketing of MS-325, EP-2104R or other products in their respective territories, or they may not successfully market MS-325, EP-2104R or other products. In addition, Schering AG and Tyco/Mallinckrodt currently manufacture imaging agents for other technologies that will compete against MS-325 and Schering will be responsible for setting the price of the product worldwide. However, Schering AG may not set prices in a manner that maximizes revenues for us. We are currently in compliance with the terms of these agreements, and although we have completed 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.

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

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

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

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

The protection of our proprietary technologies is material to our business prospects. We pursue patents for our product candidates in the United States and in other countries where we believe that

significant market opportunities exist. We own or have an exclusive license to patents and patent applications on aspects of our core technology as well as many specific applications of this technology. Specifically, patents and patent applications related to our core technology consist of two U.S. patents that are exclusively licensed to us from MGH, as well as their counterpart patents and applications in foreign countries; six U.S. patents and their counterpart patents and applications in certain foreign countries that we own; 16 U.S. patent applications, one international patent application filed under the Patent Cooperation Treaty, and 13 U.S. provisional patent applications as well as their counterpart patents and applications in certain foreign countries. One of our issued patents covers aspects of the process by which MS-325 is manufactured. Another issued patent covers the MS-325 composition of matter. Two of our patents cover methods of imaging with MS-325. We have five patent applications relating to EP-2104R, fibrin binding peptides and methods of imaging. Even though we hold these patents and have made these patent applications, because the patent positions of pharmaceutical and biopharmaceutical firms, including ours, generally include complex legal and factual questions, our patent position remains uncertain. For example, because most patent applications are maintained in secrecy for a period after filing, we cannot be certain that the named applicants or inventors of the subject matter covered by our patent applications or patents, whether directly owned or licensed to us, were the first to invent or the first to file patent applications for such inventions. Third parties may oppose, challenge, infringe upon, circumvent or seek to invalidate existing or future patents owned by or licensed to us. A court or other agency with jurisdiction may find our patents invalid, not infringed or unenforceable and we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future. Even if we have valid patents, these patents still may not provide sufficient protection against competing products or processes. If we are unable to successfully protect our proprietary methods and technologies, or, if our patent applications do not result in issued patents, we may not be able to prevent other companies from practicing our technology and, as a result, our competitive position may be harmed.

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

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

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

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

the agreements may be breached;

we may have inadequate remedies for any breach;

proprietary information could be disclosed to our competitors; or

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

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

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

Our commercial success will depend, to a significant degree, on our ability to operate without infringing upon the patents of others in the U.S. and abroad. There may be pending or issued patents, held by parties not affiliated with us, relating to technologies we use in the development or use of certain of our contrast agents. For example, in November 2003, we entered into an Intellectual Property Agreement with Dr. Martin R. Prince, an early innovator in the field of MRA relating to "dynamic" MRA, which involves capturing MRA images during the limited time, typically 30 to 60 seconds, available for imaging with extracellular agents. Although we are not aware of any other similar patent claims in the field of MRA, they may exist.

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

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

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

Specifically, MS-325 is regulated by the FDA as a pharmaceutical product. The FDA has established substantial requirements for the research, development, manufacture and marketing of pharmaceutical products. The process required by the FDA before MS-325 and our other product candidates may be marketed in the U.S. typically involves the performance of preclinical laboratory and

animal tests; submission of an investigational new drug application or IND; completion of human clinical trials; submission of a NDA to the FDA; and FDA approval of the NDA.

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

Furthermore, we, the FDA or other regulatory authorities may alter, suspend or terminate clinical trials at any time. For example, in September 2001, after discussions with the FDA, we expanded our initial target indication for MS-325 from one specific body region, the aortoiliac region, to a broader indication that includes the entire body's non-coronary vascular system, except for the heart. This expansion

required us to add two new clinical trials to our then existing Phase III clinical trial program, one to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the renal arteries, and another to determine the efficacy of MS-325 enhanced MRA for the detection of vascular disease in the pedal arteries. Although providing us with greater market potential for the sale of MS-325 upon approval, this change to our Phase III clinical trial program, and the associated delay in the start up of new clinical centers, resulted in an approximate fifteen month delay in our NDA submission and an increase in costs associated with the program. If we do not successfully complete clinical trials for our product candidates, we will not be able to market these product candidates.

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

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

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

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

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

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

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

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

also depend in significant part upon our ability to attract and retain qualified management, operational and technical personnel. Competition for personnel is intense, and we may not be successful in attracting or retaining such personnel. If we were to lose these employees to our competitors, we could spend a significant amount of time and resources to replace them, which would impair our research and development or commercialization efforts.

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

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

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

During the year ended December 31, 2003, the closing price of our common stock ranged from $20.16 to $6.36. The last reported closing price for our common stock on December 31, 2003 was $16.28. 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.

ITEM 2. PROPERTIES

We lease a total of 22,950 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 leases at 71 Rogers Street and adjacent locations and at 161 First Street expire on December 31, 2007. We believe that our current facilities are adequate to meet our needs until the expiration of the leases.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material pending legal proceedings.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

No matters were submitted to a vote of our security holders during the quarter ended December 31, 2003.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Our Common Stock commenced trading on the NASDAQ Stock Market on January 30, 1997 under the symbol "EPIX", and is listed on NASDAQ's National Market. The following table sets forth, for the periods indicated, the range of the high and low bid prices for our Common Stock:

	High	Low
2002		
First Quarter	$ 16.20	$ 11.48
Second Quarter	15.50	8.25
Third Quarter	10.72	3.55
Fourth Quarter	9.95	4.25
2003		

	High	Low
First Quarter	$ 8.90	$ 6.21
Second Quarter	14.32	7.83
Third Quarter	20.65	13.55
Fourth Quarter	20.10	15.50

The above quotations reflect inter-dealer prices without retail mark-up, markdown or commission and may not necessarily represent actual transactions.

On February 27, 2004, the last reported bid price for the Common Stock was $21.07 per share. As of February 27, 2004, there were approximately 85 holders of record of our Common Stock. To date, we have neither declared nor paid any cash dividends on shares of our Common Stock and do not anticipate doing so for the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data are derived from our audited financial statements and should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations," the Financial Statements, related Notes and other financial information included elsewhere herein.

	Year Ended December 31,				
	2003	2002	2001	2000	1999
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenues	$ 13,525	$ 12,270	$ 9,569	$ 6,924	$ 1,144
Operating loss	(21,083)	(22,816)	(18,841)	(23,745)	(17,935)
Loss before provision for income taxes	(20,714)	(22,098)	(18,156)	(22,957)	(16,983)
Provision for income taxes	80	94	1,092		
Loss before cumulative effect of change in accounting principle	(20,795)	(22,191)	(19,248)	(22,957)	(16,983)
Cumulative effect of change in accounting principle (1)				(4,363)	
Net loss	$ (20,795)	$ (22,191)	$ (19,248)	$ (27,320)	$ (16,983)
Weighted average common shares outstanding:					
Basic and diluted	19,056	16,878	14,007	12,445	11,556
Loss per share:					
Loss before cumulative effect of change in accounting principle	$ (1.09)	$ (1.31)	$ (1.38)	$ (1.85)	$ (1.47)
Cumulative effect of change in accounting principle				$ (0.35)	
Net loss, basic and diluted	$ (1.09)	$ (1.31)	$ (1.38)	$ (2.20)	$ (1.47)
Pro forma amounts assuming the accounting change is applied retroactively (1):					
Net loss				$ (22,957)	$ (15,892)
Net loss per share, basic and diluted				$ (1.85)	$ (1.38)

	December 31,

	December 31,				
	2003	2002	2001	2000	1999
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 79,958	$ 28,112	$ 24,966	$ 24,713	$ 14,140
Working capital	57,011	12,364	8,277	15,020	10,514
Total assets	81,875	30,155	26,911	29,681	17,886
Long-term liabilities	4,331	7,829	12,844	10,050	2,281
Total stockholders' equity (deficit)	54,157	5,887	(3,210)	6,566	10,764

(1) The cumulative effect of change in accounting principle is a one-time, non-cash charge relating to our adoption of SEC Staff Accounting Bulletin No. 101, *Revenue Recognition* ("SAB 101"). SAB 101 was issued by the Securities and Exchange Commission (SEC) in December 1999 and provides guidance related to revenue recognition policies based on interpretations and practices followed by the SEC. The impact of our adoption of SAB 101 was to defer revenue recognition for certain portions of the revenue previously recognized by us under our strategic alliances into future accounting periods.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We develop targeted contrast agents designed to improve the diagnostic quality of images produced by MRI. Since commencing operations in 1992, we have been principally engaged in research and development activities related to our product candidates, as well as seeking various regulatory clearances and patent protection. We have had no revenues from sales of our products and have incurred cumulative losses since inception through December 31, 2003 aggregating approximately $135.0 million. Most of our revenues to date have come from license fees and product development revenues from collaboration agreements for our product candidates.

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

We expect continued operating losses for at least the next two years as we incur expenses to support research and development efforts and to support commercialization of our initial product candidate, MS-325.

Our financial results have been affected significantly by the scope and speed of our clinical trial program and by our interaction with the FDA related to an appropriate clinical trial program for regulatory approval. To date, all of our clinical trial activity has been undertaken to study MS-325. MS-325 is an injectable contrast agent specifically designed for vascular imaging using magnetic resonance angiography, or MRA. We filed an investigational new drug (IND) application for MS-325 in July 1996. We initiated a Phase I clinical trial in 1996 and a Phase I dose escalation study in 1997, both of which have been completed. We completed a Phase II clinical trial in June 1998 to test the safety and preliminary efficacy of MS-325-enhanced MRA, for the evaluation of non-coronary vascular disease and also completed a Phase II trial in June 2001 that was designed to compare the diagnostic accuracy of five different doses of MS-325-enhanced MRA with that of X-ray angiography in the aortoiliac arteries. In 2001, we completed enrollment in the first study of a two-arm Phase III clinical trial, which was initiated in June 1999, and was designed to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease. We announced the results of this trial in March 2002. In October 2002, we announced that we had completed patient enrollment in the second of the two trials designed to detect peripheral vascular disease in the aortoiliac arteries. We announced results of this trial in March 2003. In September 2001, after discussions with the FDA, we expanded our initial target indication for MS-325 beyond aortoiliac occlusive disease to a broad peripheral vascular disease indication, which we expect will include the entire vasculature, except for the heart. As a result of this expansion, we added two new trials to our Phase III MRA clinical trial program, one in the renal arteries and the other in the pedal arteries. In February 2003, we announced that we had completed patient enrollment in these studies. We announced the results of these two trials in July 2003. We submitted a New Drug Application, or NDA, to the Food and Drug Administration, or FDA, in December 2003 and received a

letter from the FDA accepting our NDA as fileable in February 2004. We are co-developing MS-325 with Schering Aktiengesellschaft, Schering AG.

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

We are collaborating with Schering AG on the development of our second product candidate, EP-2104R, for detecting human thrombus, or blood clots, using MRI. We have also established a research collaboration with Schering AG for the discovery of novel drugs for use with MRI.

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

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect our reported assets and liabilities, revenues and expenses, and other financial information. Actual results may differ significantly from the estimates under different assumptions and conditions.

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

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

Revenue Recognition

We recognize revenues from non-refundable license fees and milestone payments not specifically tied to a separate earning process ratably over the period during which we have substantial continuing obligations to perform services under the contract. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed. When the period of deferral cannot be specifically identified from the contract, we estimate the period of deferral based upon our obligations under the contract. We continually review these estimates and, if any of these estimates change, an adjustment is recorded in the period in which they become reasonably estimable. These adjustments could have a material effect on our results of operations. In 2002 and 2003, we have increased the estimated time period over which we will provide services under our agreement with Mallinckrodt, Inc., a subsidiary of Tyco International Ltd., which we refer to as Tyco/Mallinckrodt, from an original estimate of 89 months to a

current estimate of 99 months, resulting in a reduction in revenue of approximately $417,000 for the year ended December 31, 2003. In 2003, we increased the estimated time period for obtaining approval for MS-325 in Japan from an original estimate of 60 months to a current estimate of 117 months, resulting in a reduction in revenue of approximately $102,000 for the year ended December 31, 2003. We will continue to review these estimates and make appropriate adjustments as information becomes available.

Under the MS-325 program, we recognize revenue at the time we perform research and development activities for which Schering AG, and other collaborators are obligated to reimburse us. Product development revenues from Schering AG are recorded net of the Company's portion of Schering AG's actual or most recent estimate of their MS-325 research and development costs.

We recognize reimbursement from Schering AG, for the EP-2104R feasibility program, as revenue proportionate to actual cost incurred relative to expected total program costs. Total estimated costs of the feasibility program are based on management's assessment of costs to complete the feasibility program, which include an evaluation of the portion of the program completed, the costs incurred to date and the expected future costs of the program. Adjustments to revenue will be recorded if estimated costs to complete change. To the extent that our estimated costs change materially, our revenues recorded under this activity could materially be affected and such change could have a material adverse effect on our operations in the future periods. In December 2003, management increased its EP-2104R estimate to complete the feasibility program, resulting in reduction in revenue of $819,000 in the fourth quarter of 2003.

Revenue under our research collaboration with Schering AG to discover novel compounds for diagnosing human disease using MRI is recognized as services are provided for which Schering AG is obligated to reimburse us.

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

Research and Development

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

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

Employee Stock Compensation

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

If we are unable to or decide not to continue to account for stock options under APB 25, our financial results would be materially adversely affected to the extent of the additional compensation expense that we would have to recognize, which could change significantly from period to period based on several factors including the number of stock options granted and fluctuations in our stock price and/or interest rates. See Note 2 to the Financial Statements.

Results of Operations

Years ended December 31, 2003 and 2002

Revenues

Revenues for the years ended December 31, 2003 and 2002 were $13.5 million and $12.3 million, respectively. Revenues for 2003 consisted of $9.5 million of product development revenue from Schering AG, $2.8 million of royalty and license fee revenue related to the Bracco agreement and $1.2 million of license fee revenue related to the Schering AG and Tyco/Mallinckrodt strategic collaboration agreements for the development and marketing of MS-325. The increase in revenues of $1.2 million for the year ended December 31, 2003 compared to the same period last year primarily related to product development revenue from the collaboration agreements signed in 2003 with Schering AG for EP-2104R and MRI joint research of $4.0 million, and to increased royalties from Bracco of $837,000, partly offset by lower product development revenues from MS-325 of $3.2 million and lower license fee revenue related to the Schering AG and Tyco/Mallinckrodt strategic collaboration agreements of $400,000. Product development revenue from EP-2104R was reduced by approximately $819,000 in the fourth quarter of 2003 as a result of an increase in management's estimate of the costs to complete the fixed reimbursement agreement with Schering AG. License fee revenue related to the Schering AG and Tyco/Mallinckrodt agreements were also reduced by approximately $519,000 in 2003 compared to 2002 as a result of the increase in the estimated time frame for obtaining approval for MS-325 in the United States and Japan.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2003 were $28.0 million as compared to $29.1 million for the same period in 2002. The decrease of $1.1 million was primarily attributable to decreased costs related to the completion of the Phase III clinical trial program for MS-325 and to lower spending on our EP-2104R program, partly offset by higher spending on our MRI joint research program.

We are currently performing research and development activities for three projects: MS-325, for which we have completed Phase III clinical trials and for which we submitted an NDA to the FDA in December 2003, our feasibility program for EP-2104R, which is in the preclinical stage and our MRI joint research program.

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. We have completed our Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of non-coronary vascular disease and submitted our NDA for MS-325 to the

FDA in December 2003. In February 2004, we were notified by the FDA that the NDA for MS-325 has been accepted for filing and has been designated for a standard review cycle. The target date for the first FDA action in the standard review cycle is ten months from the date of submission. If approved by the FDA, our partner, Schering AG, will have primary responsibility for the product launch and marketing of MS-325. In 2004, we plan to initiate further Phase II clinical studies of MS-325 for use in cardiac imaging and Phase IIIb/IV clinical studies of MS-325.

We plan to initiate human clinical studies for EP-2104R in 2004.

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

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

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

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

product.

The length of time that the FDA or other regulatory authorities takes to review our regulatory submissions and the length of time it takes us to respond to FDA questions can also vary widely. Any delay in that process would result in an increase in costs and a delay in the commercialization or slower sales growth of our product.

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

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

In November 2003, we entered into an Intellectual Property Agreement with Dr. Martin Prince in which Dr. Prince made certain covenants and agreements, and granted to the Company certain discharges and releases in connection with the use of any magnetic resonance imaging drug product containing MS-325. Dr. Prince also granted to the Company a non-exclusive license to make, use, sell or otherwise transfer MS-325. In consideration of Dr. Prince's covenants, discharges, releases and

license, the Company agreed to pay to Dr. Prince an up front fee, to pay certain royalties on sales of MS-325 consistent with a non-exclusive, early stage academic license, to issue 132,000 shares of common stock to Dr. Prince and to deliver certain quantities of MS-325. The upfront fee and the value of the shares were recognized as research and development expense in 2003. Royalties will be expensed as cost of goods sold as MS-325 sales are recognized. The cost of MS-325 made available will be recognized as cost of goods sold as drug is delivered.

In May 2003, we entered into a collaboration agreement with Schering AG for the development and commercialization of EP-2104R. Under terms of the agreement, we will be responsible for execution of a clinical feasibility program in humans. At the end of the feasibility program, Schering AG may exercise an option to develop EP-2104R through which Schering AG will receive an exclusive, worldwide license for EP-2104R and become responsible for all further development, manufacturing, marketing and sales. Under the agreement, Schering AG has made and will continue to make fixed payments to us totaling approximately $9.0 million over two years intended to cover our costs of the feasibility program. The amount of expenditure necessary to execute the feasibility program, currently estimated to be $11.2 million, is subject to numerous uncertainties, which may adversely affect our ability to execute the program for less than the Schering AG payments to us. In addition, we cannot predict whether Schering AG will exercise its option to develop EP-2104R or, if Schering AG does exercise its option, whether we will exercise our option to bear a portion of the development costs in return for an increase in our royalty rate. If Schering AG does not exercise its option, then we would have to bear the additional cost of a clinical program to develop EP-2104R, which may adversely affect our liquidity and capital resources. Consequently, we cannot predict, at this time, the amount of research and development costs that we will incur with regard to the development and commercialization of EP-2104R.

In May 2003, we also entered into an agreement with Schering AG covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. Under terms of the three-year joint research agreement, we and Schering AG are exclusively combining our existing research programs in the field of MRI to discover novel MRI product candidates for clinical development. Under the agreement, Schering AG will fund a portion of our related personnel costs and third party research costs of up to $2.0 million per annum and will make available to us a loan facility of up to $15 million with principal repayment beginning in 2007. The cost to execute our MRI research plan is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources.

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

Time needed for regulatory approval;

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

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

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

We test our potential product candidates in numerous pre-clinical studies to identify disease indications for which they may be product candidates. We may conduct multiple clinical trials to cover a variety of indications for each product candidate. As we obtain results from trials, we may elect to discontinue clinical trials for certain product candidates or for certain indications in order to focus on more promising product candidates or indications.

General and Administrative Expenses

General and administrative expenses, which consist primarily of salaries, benefits, outside professional services and related costs associated with our executive, finance and accounting, business development, marketing, human resources, legal and corporate communications activities, were $6.6 million for the year ended December 31, 2003 as compared to $6.0 million for the year ended December 31, 2002. The increase in 2003 of $583,000 was primarily due to an increase in legal costs related to executing the collaboration and intellectual property agreements discussed under Research and Development Expenses, to higher liability insurance premiums and to MS-325 marketing personnel and related costs. General and administrative expenses also included royalties payable to Massachusetts General Hospital, or MGH, based on sales by Bracco of MultiHance®. Royalty expenses totaled $103,000 and $74,000 for the years ended December 31, 2003 and 2002, respectively.

Interest Income and Interest Expense

Interest income for the year ended December 31, 2003 was $664,000 as compared to $1.1 million for the year ended December 31, 2002. The decrease of approximately $417,000 was primarily due to lower interest rates in 2003 compared to 2002, partly offset by higher average levels of cash, cash equivalents and marketable securities in 2003 compared to 2002. Also contributing to the decrease was the net realized gains recognized on the sale of marketable securities recorded in 2002 of $156,000, which were included in interest income, compared to no realized gains recognized for the year ended December 31, 2003. Interest expense for the year ended December 31, 2003 was $295,000 compared to $362,000 for the year ended December 31, 2002. The decrease in interest expense in 2003 resulted from the reduction in the outstanding balance of interest-bearing prepaid royalties from Bracco and the payment of the promissory note to Tyco/Mallinckrodt in October 2002, which was partly offset by the draw down of the loan facility of $7.5 million for a portion of the year, pursuant to the 2003 Schering AG collaboration agreements.

Provision for Income Taxes

The provision for income taxes, which represents Italian income taxes related to the Bracco agreement, was $80,000 for the year ended December 31, 2003 as compared to $94,000 for the year ended December 31, 2002. Beginning in July 2003, and until the earlier of FDA approval of MultiHance® or December 31, 2005, the portion of Bracco royalty revenue earned that was previously paid to us in cash is primarily being offset against the prepaid FDA approval license fee. As a result, we will be required to withhold a lesser amount of foreign income tax expense until royalty payments are reinstated upon FDA approval of MultiHance®.

Years ended December 31, 2002 and 2001

Revenues

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

Research and Development Expenses

Research and development expenses for the year ended December 31, 2002 were $29.1 million as compared to $22.9 million for 2001. The increase in 2002 of $6.2 million was primarily attributable to increased costs associated with research and development personnel and clinical trials related to the

advancement of MS-325 through Phase III clinical trials and to increased costs for personnel and other resources to support research and development for our potential discovery phase products.

General and Administrative Expenses

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

Interest Income and Interest Expense

Interest income for the year ended December 31, 2002 was $1.1 million as compared to $1.0 million for the year ended December 31, 2001. The increase of approximately $100,000 was primarily due to realized gains from the sale of marketable securities and higher average levels of invested cash, cash equivalents and marketable securities, partly offset by lower interest rates. Net realized gains on marketable securities were $156,000 for the year ended December 31, 2002 as compared to none for year the ended December 31, 2001. Interest expense for the year ended December 31, 2002 was $362,000 as compared to $339,000 for the year ended December 31, 2001. This increase in interest expense in 2002 was the result of a full year of interest paid to Bracco under the Bracco agreement.

Provision for Income Taxes

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

Liquidity and Capital Resources

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities of $80.0 million at December 31, 2003 as compared to $28.1 million at December 31, 2002.

In August 2003, we raised $65.5 million, net of underwriter discounts, commissions and expenses, through the issuance and sale of 4.645 million shares of our common stock pursuant to our effective shelf registration statement, previously filed with the SEC.

We used approximately $24.0 million of net cash to fund operations for the year ended December 31, 2003, which is consistent with our usage of cash from operations in the prior year. A net loss of $20.8 million, combined with a reduction in deferred revenue of $3.2 million and a reduction in accrued reacquisition costs of $2.4 million resulting from the final up-front payment to Daiichi in December 2003, partly offset by an increase in accrued expenses of $1.5 million primarily related to the Intellectual Property Agreement with Dr. Martin Prince, accounted for the net cash used in operations during the year ended December 31, 2003. For the year ended December 31, 2002, net cash used for operating activities was primarily attributable to our net loss of $22.2 million.

Our investing activities resulted in net cash used of $20.6 million for the year ended December 31, 2003 as compared to net cash used of $13.1 million for the same period last year. During 2003, we purchased available-for-sale marketable securities of $43.3 million, using a portion of the proceeds from the $65.5 million common stock offering in August 2003. The purchase of available-for-sale marketable securities was partly offset by the cash generated from the redemption or sale of $23.5 million of

available-for-sale marketable securities. During the same period in 2002, we purchased approximately $42.4 million of available-for-sale marketable securities, with most of the proceeds coming from our January 2002 common stock offering. The purchase of available-for-sale marketable securities was partly offset by the sale or redemption of available-for-sale marketable securities of $30.3 million. Other investing activities included capital expenditures of $759,000 for the year ended December 31, 2003 as compared to $1.1 million for the same period last year. Our capital expenditures primarily consist of purchases of property and equipment, including lab equipment, computer equipment and software. We expect that our capital expenditures may increase in the future as we continue to refurbish our principal laboratory space.

Cash provided by financing activities was $76.7 million for the year ended December 31, 2003. The primary sources of financing during 2003 were the sale and issuance of 4.645 million shares of common stock pursuant to our effective shelf registration statement, previously filed with the SEC, which generated net proceeds of $65.5 million, the $7.5 million of loan proceeds from Schering AG arising from our MRI research collaboration entered into in May 2003 and the proceeds of $3.7 million from stock option exercises and purchases of stock under the Company's Employee Stock Purchase Plan. This compares with net proceeds of approximately $28.0 million for the year ended December 31, 2002. The primary sources of financing during 2002 came from the issuance and sale of 2.575 million shares of our common stock in January 2002 pursuant to our effective shelf registration statement, previously filed with the SEC, which generated net proceeds of $30.1 million, and proceeds of $1.0 million from stock option exercises and purchases of stock under our Employee Stock Purchase Plan, which was partly offset by the repayment of the promissory note to Tyco/Mallinckrodt of $3.0 million and the repayment of capital lease obligations of $79,000.

We currently receive quarterly cash payments from Schering AG for their share of development costs of MS-325 and EP-2104R and for their share of research costs in our MRI research collaboration. We also receive monthly interest income on our cash, cash equivalents and available-for-sale marketable securities. Prior to July 2003, we received quarterly royalty payments from Bracco for a portion of the royalty revenue actually earned from the sales of MultiHance®. Beginning in July 2003, and until the earlier of FDA approval of MultiHance® or December 31, 2005, a portion of Bracco royalty revenue earned that was previously paid to us in cash is primarily being offset against the prepaid FDA approval license fee. If MultiHance® is approved in the U.S. by the FDA prior to December 31, 2005, Bracco will be obligated to pay us the amount of royalties previously offset against prepaid FDA approval license fee and resume quarterly royalty payments. Other potential cash inflows include: a milestone payment of $2.5 million from Schering AG related to the acceptance of the filing of our NDA with the FDA, which occurred in February 2004, another milestone payment of $1.3 million from Schering AG, which is dependent on the FDA's approval of MS-325, and up to $22.0 million in additional milestone payments from Schering AG as well as our share of the profits earned on sales of MS-325 worldwide. Additional future cash flows from our EP-2104R collaboration with Schering AG depend on the successful completion of the EP-2104R feasibility program, on Schering AG's decision to exercise its development option and on the success of further development, regulatory and commercialization work by Schering AG. Additional future cash flows from our MRI research collaboration with Schering AG depend on the success of the research program and the success of further development, regulatory and commercialization activities with respect to any products generated. We may also receive royalties on sales of Schering AG's Eovist product, if it is approved for sale by the FDA or international regulatory authorities pursuant to a license agreement with Schering AG.

Known outflows, in addition to our ongoing research and development and general and administrative expenses, include the semi-annual royalties that we owe to MGH on sales by Bracco of MultiHance®. Other potential future outflows include: a milestone payment of $2.5 million to Tyco/Mallinckrodt related to the acceptance of our filing of an NDA with the FDA, which occurred in

February 2004, a milestone payment of $2.5 million, which is dependent on the FDA's approval of MS-325, a share of profits due Tyco/Mallinckrodt on sales of MS-325 worldwide, a royalty to Daiichi on sales of MS-325 in Japan and a royalty due MGH on our share of the profits of MS-325 worldwide. We will also be required to repay Bracco any unearned prepaid royalties, equaling $2.0 million at December 31, 2003, upon termination of our license agreement with Bracco, plus an additional $2.4 million if MultiHance® does not receive FDA approval in the U.S by December 2005. In November 2002, Bracco announced that it had received an approvable letter from the FDA for MultiHance®.

Based on our current plans, expense rates, targeted timelines and our view regarding acceptance of MS-325 in the marketplace, we estimate that cash, cash equivalents and marketable securities on hand as of December 31, 2003 will be sufficient to fund our operations until we turn cash flow positive. As of December 31, 2003, we had outstanding $7.5 million of our $15.0 million loan facility available from Schering AG as part of our MRI research collaboration, of which the additional $7.5 million will not be available until May 2004. We repaid the $7.5 million loan, plus accrued interest, in January 2004, but expect to redraw the $7.5 million loan as needed. We expect to be able to draw the remaining $7.5 million from the Schering AG loan facility in May 2004, but could be unable to draw under the terms of the loan if we fail to meet certain covenants or conditions precedent in the loan. Our future liquidity and capital requirements will depend on numerous factors, including the following: the progress and scope of clinical trials; the timing and costs of filing future regulatory submissions; the timing and costs required to receive both U.S. and foreign governmental approvals; the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; the extent to which our products, if any, gain market acceptance; the timing and costs of product introductions; the extent of our ongoing research and development programs; the costs of training physicians to become proficient with the use of our potential

products; and, if necessary, once regulatory approvals are received, the costs of developing marketing and distribution capabilities.

Because of anticipated spending to support new research programs as well as the continued development of MS-325 and EP-2104R, we do not expect positive cash flow from operating activities for any future quarterly or annual period prior to commercialization of MS-325. Our ability to reach positive cash flow subsequent to the commercialization of MS-325 will depend on its market acceptance and successful launch by our partner Schering AG, as well as the ability of our partner Tyco/Mallinckrodt to manufacture sufficient quantities of MS-325 to support Schering AG's sales and marketing activities. We anticipate continued investments in fixed assets, including equipment and facilities expansion to support new and continuing research and development programs. In October 2003, we signed a lease agreement that increased our future lease commitments by $1.3 million and will enable us to utilize our current principal office facilities through December 31, 2007.

Below is a table that represents payments due under our contractual obligations and commercial commitments as of December 31, 2003:

		Payments due by period			
Contractual Obligations	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Short-Term Debt Obligations	$ 7,500,000	$ 7,500,000	$	$	$
Operating Lease Obligations	4,587,201	1,179,506	2,263,351	1,144,344	
Purchase Obligations	7,443,425	7,420,080	23,345		
Deferred Revenue	4,358,340	1,768,049	2,590,291		
Total	$ 23,888,966	$ 17,867,635	$ 4,876,987	$ 1,144,344	$

We have incurred tax losses to date and therefore have not paid significant federal or state income taxes since inception. As of December 31, 2003, we had net operating loss carryforwards of approximately $123.2 million available to offset future taxable income. These amounts expire at various times through 2023. As a result of ownership changes resulting from sales of equity securities, our ability to use the net operating loss carryforwards is subject to limitations as defined in Sections 382 and 383 of the Internal Revenue Code of 1986, or the Code, as amended. We currently estimate that the annual limitation on our use of net operating losses through May 31, 1996 to be approximately $900,000. Pursuant to Sections 382 and 383 of the Code, the change in ownership resulting from public equity offerings in 1997 and any other future ownership changes may further limit utilization of losses and credits in any one year. We also are eligible for research and development tax credits that can be carried forward to offset federal taxable income. The annual limitation and the timing of attaining profitability may result in the expiration of net operating loss and tax credit carryforwards before utilization.

Certain Factors That May Affect Future Results of Operations

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

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

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

decrease in interest rates would result in a decrease in the fair market value of our total portfolio of approximately $67,000, and an increase of approximately $67,000, respectively, at December 31, 2003.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None

ITEM 9A. CONTROLS AND PROCEDURES

(a)

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

(b)

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

PART III

ITEM 10. DIRECTORS AND OFFICERS OF THE REGISTRANT

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our Proxy Statement for the 2004 Annual Meeting of Stockholders to be held on May 26, 2004.

We have adopted a Corporate Code of Conduct and Ethics that applies to all directors and employees, including our principal executive, financial and accounting officers. The Corporate Code of Conduct and Ethics is filed as an Exhibit to this Annual Report on Form 10-K and posted on our website at www.epixmed.com.

ITEM 11. EXECUTIVE COMPENSATION

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Executive Compensation," "Management Committees of the Board of Directors and Meetings," and "Management-Compensation of Directors" in our Proxy Statement for the 2004 Annual Meeting of Stockholders to be held on May 26, 2004.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in our Proxy Statement for the 2004 Annual Meeting of Stockholders to be held on May 26, 2004.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Certain Relationships and Related Transactions" in our Proxy Statement for the 2004 Annual Meeting of Stockholders to be held on May 26, 2004.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Report of the Audit Committee of the Board of Directors" in our Proxy Statement for the 2004 Annual Meeting of the Stockholders to be held on May 26, 2004.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

Item 15(a). The following documents are filed as part of this Annual Report on Form 10-K

Item 15(a) (1) and (2). See "Index to Financial Statements" at Item 8 to this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

Item 15(a) (3). Exhibits. The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description
3.1@	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.
3.2@	Certificate of Amendment of Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.2 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 (File No. 000-21863) and incorporated herein by reference.
3.3@	Form of 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.
4.1@	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333- 17581) and incorporated herein by reference.

Exhibit Number	Description
10.1@+	Amended and Restated License Agreement between the Company and The General Hospital Corporation dated July 10, 1995. Filed as Exhibit 10.14 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.2@#	Amended and Restated 1992 Equity Incentive Plan. Filed as Appendix A to the Company's 2003 Definitive Proxy Statement on Schedule 14A (File No. 000-21863) and incorporated herein by reference.

10.3@#	Form of Incentive Stock Option Certificate. Filed as Exhibit 10.29 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.4@	Form of Nonstatutory Stock Option Certificate. Filed as Exhibit 10.30 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.5@#	Amended and Restated 1996 Director Stock Option Plan. Filed as Appendix B to the Company's 2003 Definitive Proxy Statement on Schedule 14A (File No. 000-21863) and incorporated herein by reference.
10.6@#	Amended and Restated 1996 Employee Stock Purchase Plan. Filed as Appendix C to the Company's 2003 Definitive Proxy Statement on Schedule 14A (File No. 000-21863) and incorporated herein by reference.
10.7@	Short Form Lease from Trustees of the Cambridge Trust to the Company with a commencement date of January 1, 1998. Filed as Exhibit 10.39 to the Company's Registration Statement on Form S-1 (File No. 333-38399) and incorporated herein by reference.
10.8@	First Amendment dated February 8, 1999 to the Short Form Lease dated as of July 7, 1998 with a commencement date as of January 1, 1998 between the Company and the Trustees of The Cambridge East Trust. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 1999 (File No. 000-21863) and incorporated herein by reference.
10.9@	Second Amendment dated June 30, 2000 to the Short Form Lease dated as of July 7, 1998 with a commencement date as of January 1, 1998 between the Company and the Trustees of The Cambridge East Trust. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2000 and incorporated herein by reference.
10.10@++	Amended and Restated Strategic Collaboration Agreement dated June 9, 2000, among the Company, Tyco/Mallinckrodt Inc. (a Delaware corporation) and Tyco/Mallinckrodt Inc. (a New York corporation). Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 29, 2000 (File No. 000-21863) and incorporated herein by reference.
10.11@++	Strategic Collaboration Agreement dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated June 29, 2000 (File No. 000-21863) and incorporated herein by reference.
10.12@	Stock Purchase Agreement, dated as of June 9, 2000, between the Company and Schering Berlin Venture Corporation. Filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated June 29, 2000 (File No. 000-21863) and incorporated herein by reference.
10.13@	Standstill Agreement, dated as of June 9, 2000, between the Company and Schering Berlin Venture Corporation. Filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated June 29, 2000 (File No. 000-21863) and incorporated herein by reference.
10.14@++	Reacquisition Agreement dated December 22, 2000 between the Company and Daiichi Radioisotope Laboratories, Ltd. Filed as Exhibit 10.32 to the Company's Annual Report on Form 10-K for the period ended December 31, 2000 (File No. 000-21863) and incorporated herein by reference.

10.15@	Amendment No. 1 dated as of December 22, 2000 to the Strategic Collaboration agreement, dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as

	Exhibit 10.33 to the Company's Annual Report on Form 10-K for the period ended December 31, 2000 (File No. 000-21863) and incorporated herein by reference.
10.16@++	Worldwide License Agreement, dated as of September 25, 2001, by and between the Company and Bracco Imaging S.p.A. filed as Exhibit 10.1 to the Company's current report on Form 8-K dated September 25, 2001 (File No. 000-21863) and incorporated herein by reference.
10.17@	Settlement and Release Agreement dated as of September 25, 2001, by and between the Company and Bracco Imaging S.p.A. filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated September 25, 2001 (File No. 000-21863) and incorporated herein by reference.
10.18@	Third Amendment, dated May 21, 2002, to the Short Form Lease dated as July 7, 1998 with a commencement date as of January 1, 1998 between the Company and the Trustees of the Cambridge East Trust. Filed as an Exhibit 10.31 to the Company's Quarterly Report for the period ended June 30, 2002 (File No. 000-21863) and incorporated herein by reference.
10.19@++	Thrombus Development Agreement between the Company and Schering AG, dated as of May 26, 2003. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2003 (File No. 000-21863) and incorporated herein by reference.
10.20@++	Collaborative Research Agreement between the Company and Schering AG, dated as of May 26, 2003. Filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2003 (File No. 000-21863) and incorporated herein by reference.
10.21@++	Loan Agreement by and between the Company and Schering AG, dated as of May 26, 2003. Filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2003 (File No. 000-21863) and incorporated herein by reference.
10.22@*	Lease of premises at 161 First Street, Cambridge, Massachusetts from BHX, LLC, as Trustee of First Binney Realty Trust to EPIX Medical, Inc., dated as of September 30, 2003 and executed on October 10, 2003. Filed herewith.
10.23@++	Intellectual Property Agreement by and between the Company and Dr. Martin R. Prince, dated November 17, 2003. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated November 18, 2003 (File No. 000-21863) and incorporated herein by reference.
10.24@	Stock Purchase Agreement by and between the Company and Dr. Martin R. Prince, dated as of November 17, 3003. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated November 18, 2003 (File No. 000-21863) and incorporated herein by reference.
14.1*	The Company's Code of Conduct and Ethics. Filed herewith.
31.1	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Michael D. Webb.
31.2	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Peyton J. Marshall.
32	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)
23.1*	Consent of Ernst & Young LLP filed herewith.

@ Incorporated by reference as indicated.

* Filed herewith.

Identifies a management contract or compensatory plan or agreement in which an executive officer or director of the Company participates.

+ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

++

Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Item 15(b)

On October 23, 2003, the Company filed a current Report on Form 8-K reporting its financial results for the quarter ended September 30, 2003.

On November 12, 2003, the Company filed a current Report on Form 8-K announcing the results of its MS-325 clinical trials in renally-compromised patients. The Company announced that based on these Phase II studies, MS-325 appears safe and well tolerated in patients with varying degrees of renal impairment, including those requiring dialysis and that MS-325 had no adverse effect on renal function. The Company also announced the departure of Stephen C. Knight, its President and Chief Operating Officer since November 1999.

On November 15, 2003, the Company filed a current Report on Form 8-K announcing that it had entered into an Intellectual Property Agreement with Dr. Martin R. Prince in which Dr. Prince made certain covenants and agreements, and granted to the Company certain discharges and releases, in connection with the use of any magnetic resonance imaging drug product containing MS-325.

On December 17, 2003, the Company filed a current Report on Form 8-K announcing that it had submitted a New Drug Application to the Food and Drug Administration for MS-325, a contrast agent designed specifically for vascular imaging with magnetic resonance angiography.

SIGNATURES

Pursuant to the requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, the Company has duly caused this report to be signed on its behalf by the undersigned, thereto duly authorized.

EPIX MEDICAL, INC.,

March 8, 2004 By: /s/ MICHAEL D. WEBB

Michael D. Webb
Chief Executive Officer and President

Pursuant to the requirements of the Securities Act of 1934, this Report has been signed below by the following persons on behalf of the Company and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ MICHAEL D. WEBB Michael D. Webb	President, Chief Executive Officer and Director (Principal Executive Officer)	March 8, 2004
/s/ PEYTON J. MARSHALL, PH.D. Peyton J. Marshall, Ph.D.	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 8, 2004
/s/ CHRISTOPHER F. O. GABRIELI Christopher F. O. Gabrieli	Chairman of the Board and Director	March 8, 2004
/s/ STANLEY T. CROOKE, M.D., PH.D. Stanley T. Crooke, M.D., Ph.D.	Director	March 8, 2004

Signature	Title	Date
/s/ PETER WIRTH	Director	March 8, 2004
Peter Wirth		

EPIX MEDICAL, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT AUDITORS

Board of Directors and Stockholders
EPIX Medical, Inc.

We have audited the accompanying balance sheets of EPIX Medical, Inc. as of December 31, 2003 and 2002, and the related statements of operations, stockholders' (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2003. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of EPIX Medical, Inc. at December 31, 2003 and 2002, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2003, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 6, 2004

EPIX MEDICAL, INC.

BALANCE SHEETS

	December 31,	
	2003	2002
ASSETS		
Current assets:		
Cash and cash equivalents	$ 36,658,557	$ 4,540,444
Available-for-sale marketable securities	43,299,675	23,571,565
Royalties receivable	46,072	175,132
Prepaid expenses and other assets	393,679	516,199
Total current assets	80,397,983	28,803,340
Property and equipment, net	1,413,346	1,292,802
Other assets	63,401	59,088
Total assets	$ 81,874,730	$ 30,155,230
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,938,365	$ 1,894,561
Accrued expenses	7,858,859	6,403,927
Contract advances	3,172,707	3,132,071
Accrued reacquisition costs		2,400,000
Loan payable to strategic partner	7,500,000	
Deferred revenue	2,917,429	2,609,127
Total current liabilities	23,387,360	16,439,686
Deferred revenue	4,330,798	7,829,029
Stockholders' equity:		
Preferred Stock, $0.01 par value, 1,000,000 shares authorized at December 31, 2003 and 2002, no shares issued and outstanding at December 31, 2003 and 2002, respectively		
Common stock, $.01 par value, 40,000,000 shares authorized at December 31, 2003 and 2002, 22,318,642 and 17,074,034 shares issued and outstanding at December 31, 2003 and 2002, respectively	223,187	170,740
Additional paid-in-capital	188,851,948	119,712,094
Accumulated deficit	(134,952,516)	(114,157,964)
Accumulated other comprehensive income	33,953	161,645
Total stockholders' equity	54,156,572	5,886,515
Total liabilities and stockholders' equity	$ 81,874,730	$ 30,155,230

See accompanying notes.

EPIX MEDICAL, INC.

STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2003	2002	2001
Revenues:			
Product development revenue	$ 9,534,335	$ 8,715,974	$ 5,720,148
Royalty revenue	2,397,393	1,560,144	2,052,397
License fee revenue	1,593,284	1,993,383	1,796,170
Total revenues	13,525,012	12,269,501	9,568,715
Operating expenses:			
Research and development	28,023,522	29,084,469	22,903,780
General and administrative	6,584,318	6,001,099	5,505,807
Total operating expenses	34,607,840	35,085,568	28,409,587
Operating loss	(21,082,828)	(22,816,067)	(18,840,872)
Interest income	663,519	1,080,561	1,023,659
Interest expense	(295,168)	(362,058)	(339,204)
Loss before provision for income taxes	(20,714,477)	(22,097,564)	(18,156,417)
Provision for income taxes	80,075	93,657	1,091,606
Net loss	$ (20,794,552)	$ (22,191,221)	$ (19,248,023)
Weighted average shares:			
Basic and diluted	19,055,698	16,878,036	14,007,165
Net loss per share, basic and diluted	$ (1.09)	$ (1.31)	$ (1.38)

See accompanying notes.

EPIX MEDICAL, INC.

STATEMENTS OF STOCKHOLDERS' (DEFICIT) EQUITY

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income/(Loss)	Total Stockholders' (Deficit) Equity
	Shares	Amount				
Balance at December 31, 2000	13,203,991	$ 132,040	$ 79,144,912	$ (72,718,720)	$ 7,271	$ 6,565,503
Issuance of common stock upon exercise of options	98,266	983	363,366			364,349
Issuance of common stock under employee stock purchase plan	18,822	188	152,870			153,058
Issuance of common stock	917,008	9,170	8,657,176			8,666,346
Compensatory stock option expense			301,770			301,770
Net loss				(19,248,023)		(19,248,023)
Available-for-sale marketable securities unrealized loss					(13,495)	(13,495)

	Common Stock				Accumulated Other Comprehensive Income/(Loss)	Total Stockholders' (Deficit) Equity
Comprehensive loss						(19,261,518)
Balance at December 31, 2001	14,238,087	142,381	88,620,094	(91,966,743)	(6,224)	(3,210,492)
Issuance of common stock upon exercise of options	230,366	2,304	919,184			921,488
Issuance of common stock under employee stock purchase plan	12,733	127	92,778			92,905
Issuance of common stock for warrants	17,848	178	(178)			
Issuance of common stock	2,575,000	25,750	30,080,216			30,105,966
Net loss				(22,191,221)		(22,191,221)
Available-for-sale marketable securities unrealized gain					167,869	167,869
Comprehensive loss						(22,023,352)
Balance at December 31, 2002	17,074,034	170,740	119,712,094	(114,157,964)	161,645	5,886,515
Issuance of common stock upon exercise of options	573,737	5,738	3,488,632			3,494,370
Issuance of common stock under employee stock purchase plan	25,871	259	207,838			208,097
Issuance of common stock	4,645,000	46,450	65,443,384			65,489,834
Net loss				(20,794,552)		(20,794,552)
Available-for-sale marketable securities unrealized loss					(127,692)	(127,692)
Comprehensive loss						(20,922,244)
Balance at December 31, 2003	22,318,642	$ 223,187	$ 188,851,948	$ (134,952,516)	$ 33,953	$ 54,156,572

See accompanying notes.

EPIX MEDICAL, INC.

STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2003	2002	2001
Operating activities:			
Net loss	$ (20,794,552)	$ (22,191,221)	$ (19,248,023)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	638,282	1,014,106	915,177
Stock compensation expense			301,770
Changes in operating assets and liabilities:			
Due from strategic partner			3,000,000
Royalties receivable	129,060	(78,184)	(96,948)
Prepaid expenses and other current assets	122,520	(24,497)	(120,384)
Other long term assets	(4,313)	53,445	22,419
Accounts payable	43,804	463,548	(369,033)
Accrued expenses	1,454,932	1,422,672	1,303,422
Accrued reacquisition costs	(2,400,000)		(2,800,000)

	Year Ended December 31,		
Contract advances	40,636	(2,037,882)	2,707,613
Deferred revenue	(3,189,929)	(2,617,441)	6,782,870
Net cash used in operating activities	(23,959,560)	(23,995,454)	(7,601,117)
Investing activities:			
Purchases of fixed assets	(758,826)	(1,063,066)	(697,576)
Purchases of marketable securities	(43,344,575)	(42,379,684)	(188,438,532)
Sale or redemption of marketable securities	23,488,773	30,331,773	201,379,505
Net cash provided by (used in) investing activities	(20,614,628)	(13,110,977)	12,243,397
Financing activities:			
Repayment of capital lease obligations		(78,760)	(244,988)
Proceeds from (repayment of) loan payable from strategic partner	7,500,000	(3,004,607)	
Repayment of note payable			(373,783)
Proceeds from Employee Stock Purchase Plan	208,097	92,905	153,058
Proceeds from stock options and warrants	3,494,370	921,488	364,349
Proceeds from sale of common stock	65,489,834	30,105,966	8,666,346
Net cash provided by financing activities	76,692,301	28,036,992	8,564,982
Net increase (decrease) in cash and cash equivalents	32,118,113	(9,069,439)	13,207,262
Cash and cash equivalents at beginning of period	4,540,444	13,609,883	402,621
Cash and cash equivalents at end of period	$ 36,658,557	$ 4,540,444	$ 13,609,883
Supplemental cash flow information:			
Cash paid for interest	$ 329,982	$ 453,135	$ 344,452
Cash paid for taxes	$ 99,655	$ 86,109	$ 1,044,544

See accompanying notes.

EPIX MEDICAL, INC.

NOTES TO FINANCIAL STATEMENTS

December 31, 2003

1. Business

EPIX Medical, Inc. ("EPIX" or the "Company") was formed on November 29, 1988 as a Delaware corporation and commenced operations in 1992. The Company is developing targeted contrast agents both to improve the capability and expand the use of magnetic resonance imaging ("MRI") as a tool for diagnosing human disease. The Company's lead product under development, MS-325, is an injectable contrast agent specifically designed for vascular imaging using magnetic resonance angiography ("MRA") to diagnose atherosclerotic disease, including non-coronary vascular disease and coronary artery disease. In December 2003, the Company submitted a New Drug Application ("NDA") to the U.S. Food and Drug Administration ("FDA") for MS-325. MS-325 is being co-developed by EPIX and Schering AG. The Company is also collaborating with Schering AG on the development of its second drug candidate, EP-2104R, for detecting human thrombus, or blood clots,

using MRI.

2. Significant Accounting Policies

Cash Equivalents

The Company considers investments with an original maturity of three months or less when purchased to be cash equivalents. Cash equivalents consist of money market accounts, commercial paper and federal agency obligations.

Marketable Securities

The Company accounts for marketable securities in accordance with Statement of Financial Accounting Standards No. 115, "*Accounting for Certain Investments in Debt and Equity Securities*" (SFAS 115). SFAS 115 establishes the accounting and reporting requirements for all debt securities and for investments in equity securities that have readily determinable fair values. The Company classifies its marketable securities as available-for-sale and, as such, carries the investments at fair value, with unrealized holding gains and losses included in accumulated other comprehensive income.

Fair Value of Financial Instruments

At December 31, 2003 and 2002, the Company's financial instruments consisted of cash and cash equivalents, available-for-sale marketable securities, a portion of deferred revenue consisting of contract advances and accrued reacquisition costs. The carrying value of cash equivalents approximates fair value due to their short-term maturities. The carrying value of the available-for-sale marketable securities, deferred revenue and loan payable is discussed in Notes 2, 3 and 6, respectively.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and available-for-sale marketable securities. In accordance with the Company's investment policy, marketable securities are principally restricted to United States government issues, high-grade bank obligations, high-grade corporate bonds and certain money market funds. Although the Company had $80.0 million of cash, cash equivalents and available-for-sale marketable securities invested with two financial institutions as of December 31, 2003, the credit risk exposure of its investments was limited because of a diversified portfolio that included debt of various

government-sponsored enterprises, such as Federal National Mortgage Association, Federal Farm Credit Bank and the Federal Home Loan Mortgage Corporation; high-grade corporate bonds and commercial paper; certificates of deposit and money market funds.

Property and Equipment

Property and equipment are recorded at historical cost. Depreciation on laboratory equipment, furniture and fixtures and other equipment is determined using the straight-line method over the estimated useful lives of the related assets, ranging from 3 to 5 years. Leasehold improvements are amortized using the straight-line method over the shorter of the asset life or the remaining life of the lease. Expenditures for maintenance and repairs are charged to expense as incurred; improvements which extend the life or use of equipment, are capitalized. Capital lease obligations and liabilities are recorded at the present value of the future minimum rental payments using interest rates appropriate at the inception of the lease.

Income Taxes

The Company provides for income taxes under Statement of Financial Accounting Standards ("SFAS") No. 109, "*Accounting for Income Taxes*." Under this method, deferred taxes are recognized using the liability method, whereby tax rates are applied to cumulative temporary differences between carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes are based on when and how they are expected to affect the tax return. A valuation allowance is provided to the extent that there is uncertainty as to the Company's ability to generate sufficient taxable income in the future to realize the benefit from its net deferred tax asset.

Segment Information

SFAS No. 131, *"Disclosure about Segments of an Enterprise and Related Information,"* establishes standards for reporting information regarding operating segments and for related disclosures about products and services and geographical areas. The Company operates in one business segment, which is the development of targeted contrast agents.

The Company records license fee and royalty revenue from Bracco Imaging S.p.A. ("Bracco") located in Italy. Total revenue from Bracco for the years ended December 31, 2003 and 2002 was $2.8 million and $2.0 million, or 21% and 16% of total revenue, respectively.

Revenue

For the years ended December 31, 2003, 2002 and 2001, one source represented 74%, 76% and 66%, another source represented 21%, 16% and 23% and a third source represented 5%, 8% and 11% of revenues, respectively.

Product development revenue

In June 2000, the Company entered into a strategic collaboration agreement with Schering AG ("Schering"), whereby each party to the agreement shares equally in MS-325 development costs and U.S. operating profits and the Company will receive royalties related to non-U.S. sales. The Company

recognizes product development revenue at the time it performs research and development activities for which Schering and other collaborators are obligated to reimburse the Company. Product development revenues from Schering are recorded net of the Company's portion of Schering's actual or most recent estimate of their MS-325 research and development costs.

In May 2003, the Company entered into a development agreement with Schering for EP-2104R and a collaboration agreement with Schering for MRI research as described in Note 11. Under the EP-2104R development agreement, Schering will make fixed payments totaling approximately $9.0 million over two years to the Company, which began in the second quarter of 2003, to cover the Company's expenditures in the feasibility program. The Company recognizes reimbursement from Schering AG, for the EP-2104R feasibility program, as revenue proportionate to actual cost incurred relative to expected total program costs. Total estimated costs of the feasibility program are based on management's assessment of costs to complete the program based upon an evaluation of the portion of the program completed, costs incurred to date and expected future costs of the program. To the extent that estimated costs to complete the feasibility program change materially from previous periods, adjustments to revenue will be recorded. In December 2003, management increased its EP-2104R estimate to complete the feasibility program from $9.0 million to $11.2 million, resulting in a reduction in product development revenue of $818,793 in the fourth quarter of 2003. Revenue recognition under the MRI research collaboration is recognized at the time services are provided for which Schering is obligated to reimburse the Company.

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

Royalty revenue

The Company earns royalty revenues pursuant to its sub-license on certain of its patents to Bracco Imaging S.p.A. ("Bracco"). Royalty revenues are recognized based on actual revenues as reported by Bracco to the Company, as available. Otherwise, the Company estimates royalty revenues based on Bracco's estimates, historical revenues and trends. In connection with the execution of the sub-licensing arrangement in September 2001, Bracco made a $4.0 million refundable advance royalty payment to the Company, which is accounted for as deferred revenue. When royalty revenue is earned, a portion of the royalty revenue earned is offset against the $4.0 million refundable advance royalty. Prior to July 2003, the remaining portion of royalty revenue earned was paid to the Company in cash. Beginning in July 2003 and until the earlier of FDA approval of MultiHance® or December 31, 2005, a portion of royalty revenue earned that was previously paid to the Company in cash is primarily offset against the $3.0 million FDA approval license fee, which is discussed under license fee revenue. At December 31, 2003 and December 31, 2002, the remaining balance of the refundable advance royalty was $2.0 million and $3.0 million, respectively.

Massachusetts General Hospital ("MGH") owns the patents and has exclusively licensed those patents to the Company, which have in turn been sub-licensed to Bracco by the Company. The Company owes MGH a percentage of all royalties received from its sub-licenses. Royalties paid to MGH, which totaled $90,453 and $123,851 for the years ended December 31, 2003 and 2002, respectively, are classified as general and administrative expenses in the Statements of Operations.

Royalties paid to MGH in 2002 included a full year of royalties earned by MGH in 2002, plus a catch-up of an additional half year of royalties earned in 2001.

License fee revenue

In 2000, the Company adopted SEC Staff Accounting Bulletin No. 101, *Revenue Recognition* ("SAB 101"), which has been superceded by SAB 104, retroactively to January 1, 2000, changing its method of recognizing certain types of revenue. Pursuant to SAB 101, the Company recognizes revenues from non-refundable license fees and milestone payments, not specifically tied to a separate earnings process, ratably over the period during which the Company has a substantial continuing obligation to perform services under the contract. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed.

In September 2001, the Company sub-licensed certain patents to Bracco and received a $2.0 million license fee from Bracco. This license fee is included in deferred revenue and is being recorded as revenue ratably from the time of the payment until the expiration of MGH's patent in 2006.

The Company also received a $3.0 million license fee from Bracco, which is contingent upon Bracco's principal product, MultiHance®, gaining FDA approval in the United States. This license fee is included in deferred revenue and will be recorded as revenue when FDA approval for MultiHance® is granted. Beginning in July 2003, a portion of royalty revenue earned is offset against the FDA approval license fee. If MultiHance® is approved, Bracco will be obligated to reimburse the Company the amount of royalties previously offset against the license fee. If MultiHance® does not gain FDA approval by December 31, 2005, the Company is obligated to repay the remaining balance of the $3.0 million to the extent such royalties are insufficient to meet the entire obligation. The balance of the original $3.0 million license fee at December 31, 2003 was $2.4 million.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Research and Development Expenses

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

In order to conduct research and development activities and compile regulatory submissions, the Company enters into contracts with vendors who render services over an extended period of time, generally one to three years. Typically, the Company enters into two types of vendor contracts,

time-based or patient-based. Under a time based contract, using critical factors contained within the contract such as the stated duration of the contract and the timing of services provided, the Company records the contractual expense for each service provided ratably over the period during which the Company estimates the service will be performed. Under a patient based contract, the Company first determines an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. The Company then records expense based upon the total number of patients enrolled during the period.

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

In November 2003, the Company entered into an Intellectual Property Agreement with Dr. Martin R. Prince in which Dr. Prince made certain covenants and agreements, and granted to the Company certain discharges and releases in connection with the use of any magnetic resonance imaging drug product containing MS-325. Dr. Prince also granted to the Company a non-exclusive license to make, use, sell or otherwise transfer MS-325. In consideration of Dr. Prince's covenants, discharges, releases and license, the Company agreed to pay to Dr. Prince an up front fee, to pay certain royalties on sales of MS-325 consistent with a non-exclusive, early stage academic license, to issue 132,000 shares of common stock to Dr. Prince and to deliver certain quantities of MS-325. The upfront fee and the value of the shares were recognized as research and development expense in 2003. Royalties will be expensed as cost of goods sold as MS-325 sales are recognized. The cost of MS-325 made available to Dr. Prince will be recognized as cost of goods sold as drug is delivered.

Loss Per Share

The Company computes loss per share in accordance with the provisions of SFAS No. 128, *"Earnings per Share."* Basic net loss per share is based upon the weighted-average number of common shares outstanding and excludes the effect of dilutive common stock issuable upon exercise of stock options. Diluted net loss per share includes the effect of dilutive common stock issuable upon exercise of stock options using the treasury stock method. In computing diluted loss per share, only potential common shares that are dilutive, or those that reduce earnings per share, are included. The exercise of options is not assumed if the result is anti-dilutive, such as when a loss is reported. Accordingly, basic net loss per share and diluted net loss per share are the same for all periods presented.

Comprehensive Income (Loss)

Statement of Financial Accounting Standards No. 130, *"Reporting Comprehensive Income"* ("SFAS 130") requires unrealized gains or losses on the Company's available-for-sale marketable securities to be included in other comprehensive income (loss). Total comprehensive loss for the years ended December 31, 2003, 2002 and 2001 amounted to $20.9 million, $22.0 million and $19.3 million, respectively.

Employee Stock Compensation

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

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

	Year Ended December 31,		
	2003	2002	2001
Net loss as reported	$ (20,794,552)	$ (22,191,221)	$ (19,248,023)
Add: employee stock-based compensation included in net loss as reported			301,770
Less: pro forma adjustment for stock-based compensation	(4,040,572)	(4,147,448)	(3,585,962)
Net loss pro forma	$ (24,835,124)	$ (26,338,669)	$ (22,532,215)
Net loss per share, basic and diluted			
As reported	$ (1.09)	$ (1.31)	$ (1.38)
Pro forma	(1.30)	(1.56)	(1.61)
Effect of pro forma adjustment	$ (0.21)	$ (0.25)	$ (0.23)

The weighted-average grant date fair value of stock options granted during 2003, 2002 and 2001 was $6.43, $8.04 and $5.61 per share, respectively, on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Options			ESPP		
	Year Ended December 31,					
	2003	2002	2001	2003	2002	2001
Expected life of option (years)	6.6	6.5	5.0	0.5	0.5	0.5
Expected stock price volatility	0.87	0.87	0.86	0.86	0.87	0.86
Weighted average risk-free interest rate	3.27%	3.52%	4.72%	1.12%	3.65%	4.72%

The effects on 2003, 2002 and 2001 pro forma net loss and net loss per share of expensing the estimated fair value of stock options and common shares issued pursuant to the stock option and stock purchase plans are not necessarily representative of the effects on reported results of operations for future years as options vest over several years.

Recent Accounting Pronouncements

In November 2002, the Emerging Issues Task Force ("EITF") of the FASB issued EITF 00-21, "Revenue Arrangements with Multiple Deliverables," ("EITF 00-21") which addressed certain aspects of the accounting for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets. Under EITF 00-21, revenue arrangements with multiple deliverables should be divided into separate accounting units if the deliverables meet certain criteria, including whether the delivered items have standalone value, as defined and whether there is evidence of fair value of the undelivered items. In addition, the consideration should be allocated among the separate units of accounting based on their fair values, and the applicable revenue recognition criteria should be considered separately for each of the separate units of accounting. EITF 00-21 is effective for revenue arrangements entered into after June 30, 2003. The EITF did not have a material impact on the Company's revenue recognition.

In January 2003, the FASB issued Interpretation No. 46, "Consolidation of Variable Interest Entities, an Interpretation of Accounting Research Bulletin No. 51" ("FIN 46"). FIN 46 provides a new consolidation model which determines control and consolidation based on potential variability in gains and losses. The provisions of FIN 46 are effective for enterprises with variable interests in variable interest entities created after January 31, 2003. For public companies with variable interest in variable interest entities created before February 1, 2003, the provisions of FIN 46 are to be applied no later than the first quarter of 2004. The Company has not invested in any variable interest entities after January 31, 2003. The Company does not anticipate a significant impact on its financial position or results of operations upon adoption of this Statement in the first quarter of 2004.

In May 2003, the FASB issued Statement of Financial Accounting Standards No. 150, "Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity" ("SFAS 150"). SFAS 150 requires certain financial instruments that embody obligations of the issuer and have characteristics of both liabilities and equity to be classified as liabilities. Many of these instruments previously were classified as equity or temporary equity and as such, SFAS 150 represents a significant change in practice in the accounting for a number of financial instruments, including mandatorily redeemable equity instruments and certain equity derivatives that frequently are used in connection with share repurchase programs. SFAS 150 is effective for public companies for all financial instruments created or modified after May 31, 2003, and to other instruments at the beginning of the first interim period beginning after June 15, 2003. The Company has no financial instruments under SFAS 150.

3. Marketable Securities

The estimated fair value of marketable securities is determined based on broker quotes or quoted market prices or rates for the same or similar instruments. The estimated fair value and cost of marketable securities are as follows at December 31:

	2003	2002

	Fair Value	Cost	Fair Value	Cost
Federal agency obligations	$ 22,369,189	$ 22,338,682	$ 23,571,565	$ 23,409,920
Corporate bonds	13,884,177	13,880,813		
Commercial paper	5,041,822	5,041,740		
Certificates of deposit	2,004,487	2,004,487		
	$ 43,299,675	$ 43,265,722	$ 23,571,565	$ 23,409,920

Maturities of marketable securities classified as available-for-sale by contractual maturity are shown below:

	December 31,	
	2003	2002
Due within one year	$ 25,441,206	$ 23,571,565
Due after one year through two years	17,858,469	
	$ 43,299,675	$ 23,571,565

Gross unrealized gains on marketable securities amounted to $37,683 and $161,645 in 2003 and 2002, respectively. Gross unrealized losses on marketable securities amounted to $3,730 and $0 in 2003 and 2002, respectively. The aggregate fair value of investments with unrealized losses was $11.8 million and $0 at December 31, 2003 and 2002, respectively. All such investments have been in an unrealized loss position for less than one year.

There were no realized gains or losses on marketable securities in 2003. Realized gains on marketable securities amounted to $155,901 in 2002 and there were no realized losses on marketable securities in 2002. The net amount of realized gains and losses is classified as interest income in the Statement of Operations. The cost of securities sold is based on the specific identification method.

4. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2003	2002
Leasehold improvements	$ 2,602,577	$ 2,377,562
Laboratory equipment	1,808,116	1,586,495
Furniture, fixtures and other equipment	1,028,611	738,909
Assets under capital lease	1,375,691	1,375,691
	6,814,995	6,078,657
Less accumulated depreciation and amortization	(5,401,649)	(4,785,855)
	$ 1,413,346	$ 1,292,802

Depreciation and amortization expense, which includes amortization of assets recorded under capital leases, was $638,282, $1,014,106 and $915,177 in 2003, 2002 and 2001, respectively.

5. Accrued Expenses

Accrued expenses consist of the following:

	December 31,	
	2003	2002
Accrued product development expenses	$ 3,000,088	$ 4,673,367
Accrued compensation	1,654,702	1,070,856
Accrued intellectual property expenses	2,339,040	
Other accrued expenses	865,029	659,704
	$ 7,858,859	$ 6,403,927

6. Loan Payable to Strategic Partner

In May 2003, the Company entered into a Non-Negotiable Note and Security Agreement (the "Loan Agreement") with Schering AG, under which the Company is eligible to borrow up to a total of $15.0 million. The Loan Agreement carries a variable, market-based interest rate, which was 8.0% at December 31, 2003. Of the $15.0 million Loan Agreement, $7.5 million was available and drawn as of December 31, 2003. The outstanding balance of $7.5 million, plus accrued interest, was repaid to Schering AG in January 2004 and is available to be redrawn by EPIX until May of 2007. The remaining $7.5 million of the Schering AG Loan Agreement is available beginning May 2004, subject to specified conditions and covenants contained in the Loan Agreement, including a commitment to maintain cash and cash equivalents of at least $2.0 million. The outstanding balance of the Loan Agreement is repayable beginning in May 2007 and there is no penalty for prepayment. The Loan Agreement is secured by a first priority security interest in certain of the Company's intellectual property. The carrying value of the loan balance approximated fair value due to its variable interest rate.

In October 1999, the Company entered into a Non-Negotiable Promissory Note and Security Agreement (the "Loan") with Tyco/Mallinckrodt, under which the Company was eligible to borrow its share of development costs up to a total of $9.5 million. In June 2000, pursuant to the amended collaboration agreement with Tyco/Mallinckrodt and a new strategic collaboration with Schering AG, Schering AG assumed the development cost sharing obligation for MS-325 from Tyco/Mallinckrodt as of January 1, 2000. As a result, the Company amended the terms of the Loan to allow funding for the Company's portion of development costs through December 31, 1999. The Loan balance of $3,004,607 at December 31, 2001 represented the Company's share of third and fourth quarter 1999 MS-325 development costs. The Loan balance, along with accrued interest, which was adjustable on a quarterly basis at the Prime Rate published in the Wall Street Journal, was repaid on October 1, 2002. No additional funding is available to the Company under the Loan. The Loan was secured by a first priority security interest in all of the Company's intellectual property, which has been released. The carrying value of the loan approximated fair value due to its variable interest rate.

7. Leases

Assets under capital lease, the majority of which are for laboratory equipment, totaled $1,375,691 and were fully depreciated as of December 31, 2003 and 2002. During the years ended December 31, 2002 and 2001, the Company incurred amortization expense relating to assets under capital leases of $56,438 and $237,933, respectively.

The Company leases office space and certain office equipment under operating lease arrangements. The Company's office space lease at the First Street facility and the office and laboratory space lease at the Rogers Street facility both expire in December 2007.

Future minimum commitments under leases with non-cancelable terms of one or more years are as follows at December 31, 2003:

2004	$ 1,179,506

2005	1,133,237
2006	1,130,114
2007	1,144,344
Total minimum lease payments	$ 4,587,201

Total rental expense amounted to $1,573,643, $1,540,573 and $1,344,440 for 2003, 2002 and 2001, respectively.

8. Stockholders' (Deficit) Equity

In September 2000, the Company entered into an agreement with Acqua Wellington North American Equities Fund Ltd. ("Acqua Wellington") for an equity financing facility covering the sale of up to $45 million of the Company's common stock over a 28 month period. During 2001, the Company received $8,666,346 and in 2000 the Company received $885,397 in net proceeds under this facility. These shares were sold at the Company's discretion at a small discount to the market price of the Company's shares at the time of the sale. The total amount of the investment was dependent, in part, on the Company's stock price, with the Company controlling the amount and timing of the stock sold. This equity financing facility was terminated in January 2002, in accordance with the terms of the equity financing facility agreement, as a result of an underwritten sale of all of the remaining shares available on the Company's then current effective S-3 shelf registration statement. The January 2002 offering raised $30.1 million in net proceeds, and the Company issued 2.575 million shares. Acqua Wellington did not purchase any shares in the January offering. In August 2003, the Company raised $65.5 million, net of underwriter discounts, commissions and expenses, through the issuance and sale of 4.645 million shares of its common stock pursuant to its effective shelf registration statement, previously filed with the SEC.

Warrants

In connection with the issuance of certain notes payable and the sale of Series D preferred stock in 1996, the Company issued warrants to purchase 40,000 shares of Series D preferred stock. Effective with the Company's initial public offering and the conversion of Series D preferred stock into the Company's common stock, the holders of the warrants became entitled to exercise the warrants for an aggregate of 26,665 shares of common stock at a cost equal to $4.50 per common share. In February 2002, the holders of the warrants exercised their warrants requiring the Company to issue 17,848 shares of its common stock. As a result of these warrant exercises, there are no remaining warrants outstanding.

Equity Plans

Equity Incentive Plan

The Company has in place an Amended and Restated 1992 Equity Incentive Plan (the "Equity Plan"), which provides stock awards to purchase shares of Common Stock to be granted to employees and consultants. In May 2003, the Company amended the Equity Plan to increase the number of shares reserved for issuance pursuant to future grants by 500,000. The Equity Plan provides for the grant of stock options (incentive and non-statutory), stock appreciation rights, performance shares, restricted stock or stock units, for the purchase of an aggregate of 6,099,901 shares of Common Stock since the Equity Plan inception, subject to adjustment for stock-splits and similar capital changes. Awards under the Equity Plan may be granted to officers, employees and other individuals as determined by the Compensation Committee. The Compensation Committee also selects the participants and establishes the terms and conditions of each option or other equity right granted under the Equity Plan, including the exercise price, the number of shares subject to options or other equity rights and the time at which such options become exercisable. The stock options have a contractual term of ten years and generally vest over a period of five years. As of December 31, 2003, 4,178,708 shares of Common Stock are reserved for issuance under the Equity Plan.

Stock option information relating to the Equity Plan is as follows:

					Options Exercisable	
	Options Outstanding	Option Price Range Per Share	Weighted Average Exercise Price	Available for Grant	Number	Weighted Average Exercise Price
December 31, 2000	2,384,663	$ 0.42-$22.50	$ 7.69	1,191,083	786,682	$ 5.25
Granted	1,061,532	$ 6.91-$12.13	$ 8.44			

				Options Exercisable		
Exercised	(98,266)	$ 0.42-$11.50	$ 3.67			
Cancelled	(99,453)	$ 5.13-$22.50	$ 10.65			
December 31, 2001	3,248,476	$ 0.42-$21.63	$ 8.00	729,004	1,076,447	$ 6.56
Granted	781,747	$ 4.48-$15.10	$ 10.64			
Exercised	(225,035)	$ 0.42-$14.63	$ 3.89			
Cancelled	(133,454)	$ 4.88-$18.50	$ 10.40			
December 31, 2002	3,671,734	$ 0.42-$21.63	$ 8.64	580,711	1,450,742	$ 7.65
Granted	643,588	$ 6.36-$19.87	$ 8.18			
Exercised	(573,737)	$ 0.42-$15.38	$ 6.09			
Cancelled	(339,086)	$ 5.13-$19.40	$ 9.49			
December 31, 2003	3,402,499	$ 0.45-$21.63	$ 8.90	776,209	1,365,079	$ 8.76

1996 Director Stock Option Plan

The Company has in place an Amended and Restated 1996 Director Stock Option Plan (the "Director Plan"). All of the directors who are not employees of the Company are currently eligible to participate in the Director Plan. In May 2003, the Company amended the Director Plan to increase the number of shares reserved for issuance pursuant to future grants by 100,000 to an aggregate of 300,000 shares. Effective January 1, 2001, the numbers of shares underlying the option granted to each eligible director upon election or re-election was increased from 15,000 to 25,000 shares. Each option becomes exercisable with respect to 8,333 shares on each anniversary date of grant for a period of three years,

provided that the option holder is still a director of the Company at the opening of business on such date. In addition, each eligible director is automatically granted an option to purchase 5,000 shares annually during the years in which such director is not up for reelection. Such options become exercisable in full on the first anniversary date of the grant, provided the option holder is still a director of the Company at the opening of business on such date. The term of each option granted under the Director Plan is ten years from the date of grant. The exercise price for the options is equal to the fair value of the underlying shares at the date of grant. As of December 31, 2003, 294,668 shares of common stock are reserved for issuance under the Director Plan.

Stock option information relating to the Director Plan is as follows:

					Options Exercisable	
	Options Outstanding	Option Price Range Per Share	Weighted Average Exercise Price	Available for Grant	Number	Weighted Average Exercise Price
December 31, 2000	75,000	$ 7.00-$17.75	$ 12.03	25,000	42,333	$ 11.53
Granted	50,000	$ 7.98-$10.00	$ 8.99			
Cancelled	(11,334)	$ 8.50-$17.75	$ 16.66			
December 31, 2001	113,666	$ 7.00-$17.75	$ 10.23	86,334	58,666	$ 11.56
Granted	25,000	$ 9.05	$ 9.05			
Exercised	(5,332)	$ 8.50	$ 8.50			
Cancelled	(13,334)	$ 13.25-$17.75	$ 14.94			
December 31, 2002	120,000	$ 7.00-$13.25	$ 9.54	74,688	61,668	$ 10.03
Granted	35,000	$ 11.64	$ 11.64			

				Options Exercisable	
December 31, 2003	155,000	$ 7.00-$13.25	$ 10.01	139,668	86,668 $ 9.74

Combined Option Information

The following table summarizes information about options under the Equity Plan and the Director Plan outstanding at December 31, 2003:

	Outstanding			Exercisable	
Range of Exercise Price	Options Outstanding at December 31, 2003	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Options Exercisable at December 31, 2003	Weighted Average Exercise Price
$0.45-$6.36	1,032,985	6.72	$ 5.40	366,912	$ 4.34
$6.65-$8.75	1,047,567	6.72	$ 8.13	435,650	$ 8.22
$8.78-$12.40	1,137,255	6.93	$ 10.97	506,138	$ 10.90
$12.51-$21.63	339,692	7.30	$ 15.55	143,047	$ 14.72
	3,557,499			1,451,747	

1996 Employee Stock Purchase Plan

The Company sponsors the Amended and Restated 1996 Employee Stock Purchase Plan (the "Purchase Plan") under which employees may purchase shares of Common Stock at a discount from fair market value at specified dates. In May 2003, the Company amended the Purchase Plan to increase the number of shares of common stock that may be purchased under the Purchase Plan by 50,000 shares to an aggregate of 166,666. Employees purchased 25,871 shares in 2003 at an average price of $8.04 per share and 12,733 shares in 2002 at an average price of $7.30 per share. At December 31, 2003, 51,866 common shares remained available for issuance under the Purchase Plan. The Purchase Plan is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Internal Revenue Code of 1986, as amended (the "Code"). Rights to purchase Common Stock under the Purchase Plan are granted at the discretion of the Compensation Committee, which determines the frequency and duration of individual offerings under the Purchase Plan and the dates when stock may be purchased. Eligible employees participate voluntarily and may withdraw from any offering at any time before stock is purchased. Participation terminates automatically upon termination of employment. The purchase price per share of Common Stock in an offering is 85% of the lesser of its fair market value at the beginning of the offering period or on the applicable exercise date and is paid through payroll deductions. The Purchase Plan terminates in November 2006.

9. Income Taxes

The Company has reported losses since inception and, due to the degree of uncertainty related to the ultimate use of the net operating loss carry forwards, has fully reserved this tax benefit. The Company has the following deferred tax assets as of December 31, 2003 and 2002:

	December 31,	
	2003	2002
Deferred tax assets:		
Net operating loss carry forwards	$ 47,700,000	$ 39,322,000
Research and development tax credits	6,922,000	4,336,000
Book over tax depreciation and amortization	2,081,000	1,425,000
Deferred revenue	2,685,000	2,914,000
Other	152,000	1,086,000

	December 31,	
Total deferred tax assets	59,540,000	49,083,000
Valuation allowance	(59,540,000)	(49,083,000)
Deferred income taxes, net	$	$

As of December 31, 2003, the Company has net operating loss carry forwards for income tax purposes of approximately $123 million and $97 million for Federal and State purposes, respectively, which expire through the year 2023 and 2008, respectively. The valuation allowance increased by $10.5 million during the year the ended December 31, 2003. The tax net operating loss carry forwards differ from the accumulated deficit principally due to temporary differences in the recognition of certain revenue and expense items for financial and tax reporting purposes.

As a result of ownership changes resulting from sales of equity securities, the Company's ability to use the net operating loss carry forwards is subject to limitations as defined in Sections 382 and 383 of the Code. The Company currently estimates that the annual limitation on its use of net operating losses through May 31, 1996 will be approximately $900,000. Pursuant to Sections 382 and 383 of the Code, the change in ownership resulting from public equity offerings in 1997 and other subsequent ownership changes may further limit utilization of losses and credits in any one year. The Company is also eligible for research and development tax credits, which can be carried forward to offset federal taxable income. The annual limitation and the timing of attaining profitability may result in the expiration of net operating loss and tax credit carry forwards before utilization.

The reconciliation of income tax computed at the U.S. federal statutory rate to income tax expense is as follows:

	Years Ended December 31,		Years Ended December 31,	
	2003	2002	2003	2002
Tax at U.S. statutory rate	$ (7,043,000)	$ (7,513,000)	-34.00%	-34.00%
State taxes, net of federal benefit	(1,243,000)	(1,326,000)	-6.00%	-6.00%
Non-deductible items	447,030	(196,343)	2.16%	-0.88%
Foreign taxes, net of benefit	48,045	56,000	0.23%	0.25%
Tax credits	(2,586,000)	(976,000)	-12.48%	-4.42%
Change in valuation allowance	10,457,000	10,049,000	50.48%	45.48%
Income tax expense	$ 80,075	$ 93,657	0.39%	0.43%

10. Defined Contribution Plan

The Company offers a defined contribution 401(k) plan, which covers substantially all employees. The plan permits participants to make contributions from 1% to 15% of their compensation. Beginning in 1999, the Company began matching up to 3% of employees' contributions. During 2003, 2002 and 2001, the Company's match amounted to $200,801, $207,696, and $173,413, respectively.

11. Strategic Alliances and Collaborations

The Company's business strategy includes entering into alliances with companies primarily in the pharmaceutical industry to facilitate the development, manufacture, marketing, sale and distribution of EPIX products.

Schering AG

In May 2003, the Company announced a broad alliance with Schering AG for the discovery, development and commercialization of molecularly-targeted contrast agents for MRI. The alliance is comprised of two areas of collaboration, with one agreement providing for exclusive development and commercialization collaboration of EP-2104R, the Company's product candidate for the detection of human thrombus (blood clots), and the second agreement covering an exclusive research collaboration to discover novel compounds for MRI. As a

result of the alliance, Schering AG has an option to the

later stage development and worldwide marketing rights for EP-2104R and for all development candidates emerging from the MRI research collaboration.

Under the terms of the EP-2104R agreement, the Company is responsible for execution of a clinical feasibility program in humans. At the end of the feasibility program, Schering AG may exercise an option to develop EP-2104R under which Schering AG will receive an exclusive, worldwide license for EP-2104R and become responsible for all further development, manufacturing, marketing and sales. Schering AG began to make fixed payments in the second quarter of 2003 and will continue to make payments to the Company, totaling approximately $9.0 million, over two years through the first quarter of 2005. The payments are intended to cover the Company's expenditures in the feasibility program. In addition, if Schering AG exercises its option to develop and commercialize EP-2104R, Schering AG will pay the Company up to $15.0 million in additional payments upon the occurrence of certain development and commercial events, as well as royalties on sales attributable to the EP-2104R. The Company has the right to increase its royalty rate through financial participation in clinical development, in which case the Company would earn a higher royalty rate.

Under the terms of the MRI three-year joint research agreement, the Company and Schering AG are exclusively combining their existing research programs in the field of MRI to discover novel MRI product candidates for clinical development. Schering AG will fund a portion of EPIX's related personnel costs and third-party research costs of up to $2.0 million per annum and has made available to the Company a loan facility of up to $15.0 million. The loan facility carries a variable, market-based interest rate. Of the $15.0 million loan facility from Schering AG, $7.5 million was available and drawn as of December 31, 2003. The outstanding balance of $7.5 million, plus accrued interest, was repaid to Schering AG in January 2004 and is available to be redrawn by EPIX until May of 2007. The remaining $7.5 million of the Schering AG loan facility is available beginning May 2004, subject to specified covenants and conditions contained in the loan agreement. The outstanding balance of the loan is repayable beginning in May 2007 and there is no penalty for prepayment. Also under the MRI research agreement, Schering AG has the first option to obtain exclusive, worldwide rights for the product candidates, then becoming responsible for all future development, manufacturing, marketing and sales. The Company would receive a base royalty on sales with the option to increase the royalty by participating in development funding. If Schering AG does not exercise its option, the Company has the right to develop the product and to license the product to a party of its choosing, and Schering AG would receive a base royalty on sales and milestone payments.

In June 2000, the Company entered into a strategic collaboration agreement pursuant to which EPIX granted Schering AG an exclusive license to co-develop and market MS-325 worldwide, exclusive of Japan. In December 2000, the Company amended this strategic collaboration agreement to grant to Schering AG the exclusive rights to develop and market MS-325 in Japan while simultaneously reacquiring the Japanese rights from Daiichi (see Daiichi below). Generally, each party to the agreement shares equally in MS-325 costs and profits. Under the agreement, the Company assumed responsibility for completing clinical trials and filing for FDA approval in the United States, and Schering AG will manage clinical activities for the product outside the United States. In addition, the Company granted Schering AG an exclusive option to develop and market an unspecified cardiovascular MRI blood pool agent from the Company's product pipeline. In connection with this strategic collaboration and the amendment to the Company's strategic collaboration agreement with

Tyco/Mallinckrodt ("Tyco"), Schering AG paid the Company an up-front fee of $10.0 million, which the Company then paid to Tyco (see Tyco below). The Company did not reflect the receipt and the disbursement in its statement of operations on the basis that Schering AG's payment to the Company did not constitute an earnings process, nor did the Company's payment to Tyco represent an expense. Such payments were, however, reflected in the statement of cash flows. Under the agreement, Schering AG also paid the Company $20.0 million in exchange for shares of the Company's common stock through its affiliate, Schering Berlin Venture Corporation, or Schering BV. The Company may receive up to an additional $18.8 million in milestone payments under the strategic collaboration agreement, of which up to $2.5 million will be earned upon acceptance of the NDA filing and $1.3 million will be earned upon FDA approval. The Company in turn will have to pay Tyco (see Tyco below) $2.5 million upon the acceptance of the NDA filing and another $2.5 million upon FDA approval. Under the terms of the December 2000 amendment, Schering AG paid the Company an up-front fee of $3.0 million and may be required to pay the Company an additional $7.0 million upon the Company's achievement of certain milestones.

Under the strategic collaboration agreement, the Company also has options to acquire certain participation rights with respect to two of Schering AG's products currently in clinical trials, SHU 555C and Gadomer-17. The Company is entitled to exercise these options on a region-by-region basis upon the payment of certain fees. The Company is entitled to exercise the SHU 555C option for a period of twelve months after the date the option becomes exercisable. If and when the Company exercises the SHU 555C option, the Company will enter into a

definitive agreement with Schering AG with respect to SHU 555C, pursuant to which Schering AG will be responsible for the conduct of all development, marketing and sales activities in connection with SHU 555C. The Company is entitled to exercise the Gadomer-17 option for a period of 120 days following Schering AG's performance of certain milestones. If and when the Company exercises the Gadomer-17 option, the Company will enter into a definitive agreement with Schering AG with respect to Gadomer-17, pursuant to which the Company will share development costs incurred from the date of the option exercise, as well as profits, equally with Schering AG.

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

On May 8, 2000, the Company granted to Schering AG a worldwide, royalty-bearing license to patents covering Schering AG's development project, Eovist injection, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 8, 2000, Schering AG granted the Company a non-exclusive, royalty-bearing license to certain of its Japanese patents. The Company agreed to withdraw its invalidation claim of Schering AG's Japanese patent number 1,932,626 in the Japanese Patent Office pursuant to this license agreement. As more fully described in the section entitled "Bracco" below, Schering AG had been an opposing party in the Company's European patent case prior to the licensing agreement. On May 9, 2000, the Opposition Division of the European Patent

Office maintained the Company's European patent in a slightly amended form. The patent is owned by MGH and is exclusively licensed to the Company. The remaining opposing parties initially elected to appeal the May 9, 2000 decision. However, in September 2001, the Company settled this patent dispute with such opposing parties by entering into a non-exclusive royalty bearing license agreement with Bracco Imaging S.p.A. See "Bracco" for further discussion of this settlement.

Tyco

In June 2000, in connection with the exclusive license that the Company granted to Schering AG, the Company amended its strategic collaboration with Tyco to grant Tyco a non-exclusive, worldwide license to manufacture MS-325 for clinical development and commercial use in accordance with a manufacturing agreement entered into in June 2000 between Tyco and Schering AG, and to enable the Company to enter into the strategic collaboration agreement with Schering AG described above. In connection with this amendment, and only after receiving the $10.0 million up-front fee from Schering AG, the Company paid Tyco an up-front fee of $10.0 million and may pay up to an additional $5.0 million in milestone payments, of which $2.5 million is due upon acceptance of the NDA filing and $2.5 million is due upon FDA approval. The Company will also pay Tyco a share of its MS-325 operating profit margins in the U.S. and a royalty on MS-325 gross profits outside the U.S., except in Japan where no payments are due Tyco.

In October 1999, the Company entered into a Non-Negotiable Promissory Note and Security Agreement, or the Loan, with Tyco, the Company's strategic partner, under which the Company was eligible to borrow its share of MS-325 development costs, on a quarterly basis, up to a total of $9.5 million. In June 2000, pursuant to the amended strategic collaboration agreement with Tyco and the new strategic collaboration agreement with Schering AG, Schering AG assumed the development cost sharing obligation for MS-325 from Tyco as of January 1, 2000. As a result, the Company amended the terms of the Loan to allow funding for its portion of development costs through December 31, 1999. The balance due under the Loan as of December 31, 2001 was $3,004,607 and represented the Company's share of the third and fourth quarter MS-325 development costs in 1999. No additional funding was available to the Company under the Loan. The Loan bore interest, adjustable on a quarterly basis, at the Prime Rate published in the Wall Street Journal. The loan was secured by a first priority security interest in all of the Company's intellectual property, which has been released. On October 1, 2002, the Company paid Tyco $3,040,580, which consisted of its outstanding loan balance of $3,004,607 plus accrued interest of $35,973, to fully satisfy its obligation under the Loan.

Daiichi

In March 1996, the Company entered into a development and license agreement with Daiichi Radioisotope Laboratories, or Daiichi, pursuant to which EPIX granted Daiichi an exclusive license to develop and commercialize MS-325 in Japan. Under this agreement, Daiichi assumed primary responsibility for clinical development, regulatory approval, marketing and distribution of MS-325 in Japan. The Company retained the right and obligation to manufacture MS-325 for development activities and commercial sale under the agreement. In December 2000, the Company reacquired the rights to develop and commercialize MS-325 in Japan from Daiichi. Under the terms of this reacquisition agreement with Daiichi, the Company agreed to pay Daiichi a total amount of

$5.2 million of which $2.8 million was paid in January 2001 and the remaining $2.4 million was paid in December 2003. Daiichi will also receive a royalty from the Company based on net sales of MS-325 in Japan. Simultaneously with the Company's reacquisition from Daiichi of the MS-325 development and marketing rights in Japan, the Company assigned these rights to Schering AG.

Bracco

In September 2001, pursuant to a Settlement and Release Agreement and Worldwide License Agreement, referred to as the License Agreement, the Company granted Bracco a worldwide, non-exclusive royalty bearing sub-license to certain EPIX patents. The Company received $10.0 million ($9.0 million net of Italian income taxes) in up-front payments pursuant to the License Agreement, which consisted of a $2.0 million license fee, $1.0 million of royalties on past sales of MultiHance®, $4.0 million of prepaid royalties and a $3.0 million contingent license fee based upon FDA approval of MultiHance® in the U.S. In addition, Bracco is obligated to pay EPIX a quarterly royalty on its sales of MultiHance® beginning in January 2001 and ending on the patent expiration date in each country in which MultiHance® is sold, which is currently 2006 in the U.S. and Europe.

Upon the termination of the License Agreement, any remaining balance of the prepaid royalties must be repaid to Bracco. Prepaid royalties were $2.0 million as of December 31, 2003. In addition, if MultiHance® does not gain FDA approval, the Company is obligated to repay the outstanding portion of the contingent license fee, which is $2.4 million at December 31, 2003, first as an offset against royalties due, and then in cash to the extent that such royalty offsets are insufficient to meet the entire obligation. In November 2002, Bracco announced that it had received an approvable letter from the FDA for MultiHance®. The License Agreement may be terminated by either party upon thirty days notice if there is a material breach of the License Agreement or the other party becomes bankrupt.

12. Quarterly Financial Information (unaudited)

	First Quarter Ended March 31, 2003	Second Quarter Ended June 30, 2003	Third Quarter Ended September 30, 2003	Fourth Quarter Ended December 31, 2003
Revenues:				
Product development revenue	$ 2,544,165	$ 2,781,037	$ 2,834,438	$ 1,374,695
Royalty revenue	482,800	617,396	682,116	615,081
License fee revenue	468,701	423,767	401,300	299,516
Total revenues	3,495,666	3,822,200	3,917,854	2,289,292
Operating expenses:				
Research Development	7,391,448	5,890,935	5,618,628	9,122,511
General & administrative	1,606,917	1,558,091	1,677,654	1,741,656
Total operating expenses	8,998,365	7,449,026	7,296,282	10,864,167
Other income, net	81,331	45,904	16,838	224,278
Income taxes	27,194	38,818	2,973	11,090
Net loss	$ (5,448,562)	$ (3,619,740)	$ (3,364,563)	$ (8,361,687)
Weighted average shares, basic and diluted	17,090,243	17,177,677	19,765,976	22,125,758
Net loss per share:				
Basic and diluted	$ (0.32)	$ (0.21)	$ (0.17)	$ (0.39)

	First Quarter Ended March 31, 2002	Second Quarter Ended June 30, 2002	Third Quarter Ended September 30, 2002	Fourth Quarter Ended December 31, 2002
Revenues:				
Product development revenue	$ 1,230,887	$ 2,776,790	$ 1,975,500	$ 2,732,797
Royalty revenue	307,338	432,480	310,970	509,356
License fee revenue	527,990	527,990	468,701	468,702
Total revenues	2,066,215	3,737,260	2,755,171	3,710,855
Operating expenses:				
Research Development	5,411,514	9,002,603	6,966,702	7,703,650
General & administrative	1,378,457	1,670,328	1,453,275	1,499,039
Total operating expenses	6,789,971	10,672,931	8,419,977	9,202,689
Other income, net	152,598	273,003	88,989	203,913
Income taxes	18,489	25,949	18,658	30,561
Net loss	$ (4,589,647)	$ (6,688,617)	$ (5,594,475)	$ (5,318,482)
Weighted average shares, basic and diluted	16,417,407	16,985,677	17,038,125	17,062,091
Net loss per share:				
Basic and diluted	$ (0.28)	$ (0.39)	$ (0.33)	$ (0.31)

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