EPIX Pharmaceuticals, Inc.
Form 10-K
March 11, 2005

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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, 2004

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 PHARMACEUTICALS, 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.)
161 First 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 $483,121,720.

As of February 25, 2005, the registrant had 23,227,132 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 June 2, 2005.

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 lead product under development, to the U. S. Food and Drug Administration, or FDA. In January 2005 we received an approvable letter from the FDA for MS-325 in which the FDA requested additional clinical studies to demonstrate efficacy prior to approval. In June 2004, Schering AG, our worldwide sales, marketing and development partner, submitted MS-325 for marketing approval in the European Union.

Our lead product under development, MS-325, is designed to provide visual imaging of the vascular system through a type of MRI known as magnetic resonance angiography, or MRA. We believe that MS-325-enhanced MRA has the potential to improve the diagnosis of multiple diseases of the vascular system, including vascular disease outside the heart and diseases that affect the coronary arteries and reduce blood flow to the heart. Our initial target indication for MS-325 is for use in MRA imaging of non-coronary vascular disease. In 2004 we initiated and are currently conducting a clinical study, known as OPTIMUM, of MS-325 for high resolution vascular MRA in non-coronary vascular disease. We are also developing MS-325 for imaging coronary arteries and perfusion of the heart and are currently conducting a Phase II clinical trial of the use of MS-325 in this application.

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

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 as specified in the clinical trial protocols. We believe that an important feature of MS-325 is that it yielded a minimal number of uninterpretable MRA images in the Phase III trials, while non-contrast MRA produced a significantly higher rate of uninterpretable images. In its approvable letter of the NDA for MS-325, the FDA indicated that its principal questions surrounding the efficacy of MS-325 relate to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. The MS-325 Phase III clinical trial protocol required investigators to use their institutional standard medical imaging practice for acquiring non-contrast MRA comparator scans at each site. The FDA expressed concern that a uniform non-contrast MRA imaging method was not used by all sites. The FDA requested and received a series of analyses showing alternative statistical treatment of uninterpretable scans in the calculation of the sensitivity and

specificity of both non-contrast and MS-325 MRA imaging methods in the Phase III trials. Eliminating the effects of uninterpretable scans completely from the sensitivity and specificity statistical calculation reduces the resultant efficacy improvements for MS-325 over non-contrast MRA reported in the Phase III trials. We are continuing our active dialogue with the FDA in order to determine the next steps we will need to take in the regulatory pathway for MS-325.

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 are not optimal imaging vascular disease in many vascular beds due to the rapid leakage of the injectable contrast agent from the vascular system into the surrounding tissue, allowing only approximately 30 to 60 seconds for imaging a targeted vascular area. 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 desired 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 2003, approximately 2.7 million MRAs were performed in the U. S., an increase of 22% over 2002.

MS-325 is specifically designed to improve the quality of magnetic resonance images of the arteries and veins and to provide physicians with a high resolution 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 an MRI exam, providing the extended, approximately 60-minutes, of imaging time and signal strength required to obtain a high resolution image of multiple regions of the vascular system. Like most currently available general use MRI contrast agents, MS-325 is designed to be safely eliminated from the body through the kidneys over time. In clinical studies of renally-compromised patients, MS-325 appeared safe and well tolerated, a potentially important feature given the inherent risks of X-ray angiography to the kidneys.

We are developing a second targeted contrast agent, EP-2104R, which is designed to illuminate and identify blood clots using MRI. Finding blood clots is of critical medical significance in the evaluation and diagnosis of patients with stroke, chest pain, heart attack, irregular heartbeat and clots in the lungs and legs. We designed EP-2104R to bind reversibly to fibrin, the dominant protein found in clots. In pre-clinical studies, EP-2104R has been shown to enhance the ability of MRI to image clots throughout the vascular system. In 2004, we completed Phase I clinical trials of EP-2104R in which the drug was well-tolerated in healthy volunteers. We plan to initiate Phase II clinical trials to study the feasibility of blood clot imaging using EP-2104R in patients in 2005.

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 and commercializing 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 of our product candidates. Our most significant collaborations involve Schering AG for the development and commercialization of MS-325, EP-2104R and for the discovery of other MRI contrast agents. We have also formed collaborations with the three leading MRI scanner manufacturers, General Electric Medical Systems (also known as GE Healthcare), Philips Medical Systems and

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

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

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 930,000 fatalities each year. One out of every 2.6 deaths in the U.S. is attributed to cardiovascular disease and it is estimated that over 70 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 sixty-five 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 to 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 to 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 evaluation 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 evaluation 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 2.5 million stress echocardiograms were performed in the U.S. in 2003.

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 can be 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 6.3 million nuclear stress perfusion studies were conducted in the U.S. in 2003.

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 2003, of which approximately 2.6 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 used as a 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 1.2 million CTA procedures were performed in the U.S. in 2003, the majority of which were performed for pulmonary angiography of the lungs.

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 anatomical structure that is being imaged. It is estimated that contrast agents are used in 27% 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 non-hospital 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 2.7 million MRAs performed in the U.S. in 2003, approximately 74% 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 preferred contrast agent for a significant portion of MRAs currently performed with general use contrast agents.

Intravascular Ultrasound

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, which is 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. U. S. imaging procedures (millions) for the definitive diagnosis of vascular disease in 2003 are summarized by major vascular region in the following table:

Imaging procedures	Cerebral & carotid	Abdominal, peripheral & other	Coronary	Total
X-ray angiography	0.5	1.5	2.6	**4.6**
MRA	2.0	0.7		**2.7**
CT angiography	0.2	1.0		**1.2**
Total	**2.7**	**3.2**	**2.6**	**8.5**

We 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 MR Angiography

We believe that MS-325-enhanced MRA will be used in the diagnosis of 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 in 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.

Lower-Field MR Angiography

We believe that the extended blood residence time of MS-325 will prove particularly beneficial in facilitating the use of lower-field MRI scanners for diagnosing cardiovascular disease. These scanners, which in 2002 accounted for approximately 28% 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 Disease

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 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 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 phage display 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 gadolinium complexes.

MRI Signal Generation

A key part of our biophysical technology platform is exclusively licensed by us under patents held by MGH. The binding of a contrast 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, binding to albumin results 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 signal-enhancing 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 Non-Coronary 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 had been accepted for filing and had been designated for a standard 10-month review cycle. In October 2004 we were notified by the FDA that they had extended the MS-325 NDA action date by three months to January 2005. In January 2005 we received an approvable letter from the FDA for MS-325 in which the Agency requested additional clinical studies to demonstrate efficacy prior to approval. In June 2004, Schering submitted MS-325 for marketing approval in the European Union. Schering has also submitted MS-325 for marketing approval in Canada and Australia. The NDA and the European regulatory submission are 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 non-coronary vascular disease. All four trials in the Phase III program for MS-325 met their primary endpoints as specified in the clinical trial protocols.

Phase III Trials. The Phase III trials were designed to compare the sensitivity, specificity and accuracy of MS-325-enhanced MRA to non-contrast MRA, where the basis of comparison in the trials was conventional X-ray angiography. The four Phase III trials investigated the use of MS-325 in three vascular regions representative of different types of blood flow. Patients in the four Phase III trials received a non-contrast MR angiogram, an MS-325 enhanced MR angiogram and an X-ray angiogram at 84 geographically dispersed clinical sites using a variety of MRI and X-ray equipment. The MS-325 Phase III clinical trial protocols required investigators to use their institutional standard medical imaging practice for acquiring non-contrast MRA comparator scans at each site and specified the method for acquiring MS-325-enhanced MR angiograms. In each trial, once the angiographic data were acquired, three radiologists, blinded to the acquisition method and patient history, analyzed each patient's MRA images to determine the presence or absence of clinically significant arterial blockage, or stenosis, for both MS-325-enhanced MRA and non-contrast MRA. In each trial, two additional blinded radiologists analyzed all of the X-ray angiograms to provide a basis of comparison of MRA results against X-ray angiography. When the two X-ray readers disagreed, a third blinded radiologist provided a deciding opinion on the reading.

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 results of this trial in March 2002 at the American College of Cardiology conference. The trial met its pre-specified 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 non-contrast MRA, achieving an average of 88% accuracy in identifying clinically significant arterial narrowing or stenoses caused by atherosclerotic disease versus an average of 75% for non-contrast MRA. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 90%. MS-325 significantly increased the number of patients whose images were clinically interpretable. Less than 1% of MS-325-enhanced MRA images were uninterpretable, while approximately 8% of the X-ray angiograms and 14% of the images obtained with non-contrast MRA were uninterpretable.

In October 2002, we completed enrollment in the second of the two Phase III trials for the detection of aortoiliac occlusive disease. We reported results of this trial in March 2003 at the European Congress of Radiology. The trial met its pre-specified 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 non-contrast MRA, achieving an average of 84% accuracy in identifying clinically significant stenoses caused by atherosclerotic disease versus an average of 72% for non-contrast MRA. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 90%. MS-325 significantly increased the number of patients whose images were clinically interpretable. Less than 2% of MS-325-enhanced MRA images were uninterpretable, while approximately 3% of the X-ray angiograms and 17% of the images obtained with non-contrast MRA were uninterpretable.

In September 2001, we expanded our Phase III clinical trial program for MS-325 in order to broaden our target lead indication to non-coronary vascular disease from the previous target 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 expanded our Phase III clinical trial program to respond to the FDA's request and to 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 results of the final two Phase III trials.

The Phase III trial in the renal arteries in the kidney met its pre-specified 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 non-contrast MRA, achieving an average of 77% accuracy in identifying clinically significant arterial narrowing or stenoses caused by atherosclerotic disease versus an average of 50% for non-contrast MRA. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 84%. MS-325 significantly increased the number of patients whose images were clinically interpretable. Less than 1% of MS-325-enhanced MRA images were uninterpretable, while approximately 7% of the X-ray angiograms and 33% of the images obtained with non-contrast MRA were uninterpretable.

The Phase III trial in the pedal arteries in the feet met its pre-specified 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 non-contrast MRA, achieving an average of 76% accuracy in identifying clinically significant stenoses caused by atherosclerotic disease versus an average of 63% for non-contrast MRA. In determining the reference standard in the trial, the X-ray inter-reader accuracy agreement was 79%. MS-325 significantly increased the number of patients whose images were clinically interpretable. Approximately 2% of MS-325-enhanced MRA images were uninterpretable, while approximately 8% of the X-ray angiograms and 16% of the images obtained with non-contrast MRA were uninterpretable.

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 its January 2005 approvable letter for our MS-325 NDA, the FDA identified no safety or manufacturing deficiencies in the NDA, but did request additional clinical studies to demonstrate efficacy prior to approval. The FDA approvable letter indicated that its principal questions surrounding the efficacy of MS-325 relate to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. The MS-325 Phase III clinical trial protocol required investigators to use their institutional standard medical imaging practice for acquiring non-contrast MRA comparator scans at each site. The FDA expressed concern that a uniform non-contrast imaging method was not used at all sites. The FDA has questioned the statistical treatment of uninterpretable scans in the efficacy analysis in our NDA. Our Phase III clinical trial protocols and statistical plans specified that uninterpretable MRA scans would be treated as incorrect in the primary efficacy analysis of MS-325. The FDA has requested and received a series of analyses showing alternative statistical treatment of uninterpretable scans in the calculation of the sensitivity and specificity of the MRA imaging methods in the Phase III trials. Eliminating the effects of uninterpretable scans completely from the sensitivity and specificity statistical calculation reduces the resultant efficacy improvements for MS-325 reported in the Phase III trials. We are continuing our active dialogue with the FDA in order to determine the next steps we will need to take in the regulatory pathway for MS-325.

Phase II Trials. 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. The renally-impaired patient population is approximately 13.1 million people in the U.S., with an additional six million people at risk for renal impairment, and this population is significantly more likely to require diagnosis and treatment for cardiovascular disease. Renal safety is a particularly important consideration when imaging renally-compromised patients, as one of the risks associated with the use of traditional X-ray angiography in those patients is renal failure.

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.

Potential Additional Applications

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

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, including coronary imaging and myocardial perfusion imaging. 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 believe that MS-325 may be useful in assessing coronary artery blockages. We are currently conducting a Phase II trial of the use of MS-325 in coronary imaging and myocardial perfusion imaging.

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. We are evaluating the outlook and potential development programs for possible cancer imaging applications for MS-325. The design of development plans and the commencement of additional clinical studies in the area of cancer imaging are contingent on this evaluation.

EP-2104R

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 600,000 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 3.7 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 800,000 such exams were performed in the U.S. in 2003. 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. In 2004, we completed Phase I clinical trials of EP-2104R in which the drug was well-tolerated in healthy volunteers. We plan to initiate Phase II clinical trials to study the feasibility of blood clot imaging using EP-2104R in patients in 2005.

Our Business Strategy

Our objective is to become a worldwide leader in MRI contrast agents by developing and commercializing products using 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 non-coronary vascular disease. As previously discussed in the section "Our Product and Development Programs Lead Indications MRA of Peripheral Vascular Disease," we have announced 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 received an approvable letter from the FDA for our NDA for MS-325 in which the Agency has requested additional clinical studies to demonstrate efficacy prior to approval. We are continuing our active dialogue with the FDA in order to determine the next steps we will need to take in the regulatory pathway for MS-325. We are actively supporting Schering AG's European

regulatory submission for MS-325 and are working with the Schering AG marketing teams to support launch planning for MS-325 in major markets.

Establish the clinical utility of MS-325 in other imaging indications. We are studying 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. We are also evaluating the potential application of MS-325 to cancer imaging. In a Phase II feasibility trial in 45 female patients, we tested the safety and preliminary efficacy of MS-325-enhanced MRI for evaluating breast cancer.

Develop EP-2104R for thromboembolic disease imaging. In our thrombus program, we are developing EP-2104R as an MRI contrast agent for imaging clots. In 2004, we completed Phase I clinical trials of EP-2104R in which the drug was well-tolerated in healthy volunteers. We plan to initiate Phase II clinical trials to study the feasibility of blood clot imaging using EP-2104R in patients in 2005.

Maximize the value of strategic alliances. We have established collaborations with Schering AG, Tyco/Mallinckrodt, GE Medical Systems, Philips Medical Systems and Siemens Medical Systems. 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 and our drug development capabilities. 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, GE Medical Systems, Philips Medical Systems and Siemens Medical Systems.

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 may be earned upon U.S. 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. 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 option, we will enter into a definitive agreement with Schering AG with respect to Gadomer, 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, other thrombus imaging agents 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, unless the joint research agreement is extended. The loan facility carries a variable, market-based interest rate. $15.0 million of the $15.0 million loan facility available from Schering AG was outstanding as of December 31, 2004. The loan facility is 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, Primovist, an MRI contrast agent for imaging the liver, approved in the EU in 2004. 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 was paid following NDA filing in February 2004 and $2.5 million will be paid upon U.S. 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, GE 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.

GE Medical Systems. In January 1998, we announced the formation of a collaboration with GE 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 has been performed at several centers in addition to our facilities, including General Electric's corporate research facility in Schenectady, NY, GE 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 have combined 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 has been 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 has also focused 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 has been carried out at our facilities and at Siemens' Iselin, NJ facilities.

Competition

The healthcare industry is characterized by extensive research efforts and rapid technological change and there are several 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 used or developed for MR angiography or myocardial perfusion imaging, are likely to compete with MS-325. Such products include Magnevist and Gadovist by Schering AG, Dotarem by Guerbet, S.A., Omniscan by GE Healthcare, ProHance and MultiHance by Bracco and OptiMARK by Tyco/Mallinckrodt. We are aware of five agents under clinical development: Schering AG's Gadomer 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 generally relate to MRI signal generation technology, albumin binding with metal chelates and liver targeting metal chelates.

Seven 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)

U.S. Patent 6,709,646, "Bioactivated Diagnostic Imaging Contrast Agents" (granted March 23, 2004; expires March 25, 2017; however, the USPTO has indicated that the patent is entitled to 99 days of patent term adjustment)

Twenty U.S. utility applications in prosecution as well as their cognate applications in certain foreign countries and five provisional utility applications. Some of these relate to MRI, MS-325 and methods of use, EP-2104R and methods of use, and other to therapeutics 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 certain methods of using MS-325 will not expire until 2021. We plan to apply for patent term extension on one or more of the patents and patent applications described above 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 may 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 have received various payments, including royalties on a quarterly basis pursuant to the license with Bracco. In December 2004, we learned from Bracco that Bracco is asserting that it had overstated non-US royalties to us for the period 2001 to 2004 and that it would offset the amount of the overstatement against its royalty payments to us, including those triggered by FDA approval of MultiHance® in the United States. We have challenged Bracco's underpayment, their right to recalculate previous royalties under our License Agreement and the substance of their restatements and are in discussions with Bracco regarding the resolution of this dispute. Previously, on May 8, 2000, we granted to Schering AG a worldwide royalty-bearing license to our patents covering Schering AG's development project, Primovist, an MRI contrast agent for imaging the liver, approved in the EU in 2004. 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, apart from our royalty dispute with Bracco, 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, absent any patent term adjustment or patent term extension. 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 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 or later on any sublicense if the MGH patents related to that sublicense are extended. 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 and two further collaboration and license agreements in November 2004 with Dyax Corp., or Dyax, for research relating to our thrombus program and other research programs. Under the terms of these agreements, we share rights to certain inventions with Dyax in return for specified research related payments, milestone payments and royalty rights upon commercialization of certain products arising from the these programs.

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 manufacturing arrangements for MS-325 for commercial use, including the transfer of manufacturing to Schering AG. 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 pre-clinical 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.

Pre-clinical 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 pre-clinical 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 regulations 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, 2004, we employed 90 persons on a full-time basis. Thirty-five 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, 2004, 2003 and 2002, we incurred research and development expenses of $21,873,991, 28,023,522 and $29,084,469, respectively.

Available Information

We incorporated in Delaware in 1988 and commenced operations in 1992. Our principal executive offices are located at 161 First Street, Cambridge, Massachusetts 02142-1118 and our telephone number is (617) 250-6000. Our website is located at *http://www.epixpharma.com*. Our Corporate Code of Conduct and Ethics as well as our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and all amendments to these reports, which have been filed with the Securities and Exchange Commission, or 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 (FDA), we will have no products to market in the foreseeable future.

We currently have no products for sale and we cannot guarantee that we will ever have marketable products. MS-325 and EP2104R are currently our only product candidates that have undergone human clinical trials and we cannot be certain that any of our other development projects will yield a product candidate suitable for substantial human clinical testing. As a result, our initial revenues and profits from commercial sales of our products, if any, will be derived from sales of MS-325. In January 2005, we received an approvable letter from the FDA for MS-325 in which the FDA requested additional

clinical studies to demonstrate efficacy prior to approval. In its approvable letter, the FDA indicated that its principal questions relate to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. We are continuing our active dialogue with the FDA in order to determine the next steps we will need to take in the regulatory pathway for MS-325. Although we remain confident in the safety and efficacy profile of MS-325, the approval, timeliness of approval or labeling of MS-325 are subject to significant uncertainties related to a number of factors including the process of reaching agreement with the FDA on the clinical data and on any clinical trial protocol required for regulatory approval of MS-325, the timing and process of conducting any clinical studies required, obtaining the desired outcomes of any required clinical trials and the FDA's review process and conclusions regarding any additional MS-325 regulatory submissions. We cannot assume that we will be able to reach agreement with the FDA on the design or clinical endpoints required for additional clinical studies. Further, we cannot assume that any such agreed upon clinical trials will be feasible for us to conduct or whether such trials will be completed in a commercially reasonable timeframe, if at all. Any further clinical trials that are required could take several years to complete. If MS-325 fails to achieve regulatory approval and market acceptance, and if we do not succeed in bringing any of our other product candidates to human clinical trials and achieve regulatory approval and market acceptance for them, our business will fail, and as a result, you may lose all or part of your investment.

To date, we have received revenues from payments made under licensing, royalty arrangements, and product development and marketing agreements with strategic collaborators. In particular, our revenue for the year ended December 31, 2004 was $12.3 million and consisted of $7.6 million from the product development portion of our collaboration agreements with Schering AG for MS-325, EP-2104R and MRI research, $4.0 million from a patent licensing and royalty agreement with Bracco and $617,000 of license fee revenue related to the strategic collaboration agreements for the development, manufacturing and marketing of MS-325 with Schering AG and Tyco/Mallinckrodt. In addition to these sources of revenue, we have financed our operations to date through public stock offerings, private sales of equity securities, debt financing and equipment lease financings.

Although we are currently in compliance with the terms of our collaboration agreements, the revenues derived from them are subject to fluctuation in timing and amount. We may not receive anticipated revenue under our existing collaboration or licensing agreements, these agreements may be subject to disputes 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, 2004 were approximately $155.3 million. These losses have primarily resulted from expenses associated with our research and development activities, including pre-clinical and clinical trials, and general and administrative expenses. We anticipate that our research and development expenses will remain

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

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

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

safety;

cost-effectiveness relative to alternative vascular imaging methods;

availability of third party reimbursement;

ease of administration;

clinical efficacy; and

availability of competitive products.

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

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

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

the progress and scope of clinical trials;

the timing and costs of filing future regulatory submissions;

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

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

the extent to which our products gain market acceptance;

the timing and costs of product introductions;

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

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

the costs of developing marketing and distribution capabilities.

Based on our current plans, expense rates, targeted timelines and our view regarding acceptance of MS-325 in the marketplace, we estimate that cash, cash equivalents and marketable securities on hand as of December 31, 2004 will be sufficient to fund our operations until we turn cash flow positive. If we consider other opportunities or change our planned activities, we may require additional funding. As of December 31, 2004, we had outstanding the entire $15.0 million loan facility available from Schering AG as part of our MRI research collaboration. We repaid the $15.0 million loan, plus accrued interest, in January 2005. We expect to redraw the $15.0 million loan as needed, but could be unable to draw under the terms of the loan if we fail to meet certain covenants or conditions precedent in the loan.

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

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

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

Although MRI hardware and software is sufficient for the evaluation of non-coronary vascular disease, which is our initial target indication, we believe that the technology is not as advanced for cardiac applications, which may be our next clinical development target. Our initial NDA filing for MS-325 is related to non-coronary vascular disease. Imaging sequences on scanners currently allow for the use of MS-325-enhanced MRA for diagnosing non-coronary vascular disease, our lead indication. Based on feasibility studies we completed in 2001, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, was not developed to the point where there was clear visualization of the cardiac region due to the effects of motion from breathing and from the beating of the heart. In 2004, we initiated Phase II feasibility studies for cardiac indications using available software and hardware that can be adapted for coronary and cardiac perfusion data acquisition. We have entered into research collaborations with GE Healthcare, Siemens Medical Systems and Philips Medical Systems that include development and optimization of cardiac imaging sequences with contrast agents like MS-325. We have also collaborated with a number of leading academic institutions to help optimize cardiac imaging with MS-325. While significant progress has been made in developing these clinical applications for cardiac imaging, we do not know when, or

if, these techniques will enable MS-325 to provide clinically relevant images in cardiac indications. If MRI device manufacturers are not able to enhance their scanners to perform clinically useful cardiac imaging, we will not be able to complete our development activities of MS-325 for that application, thereby reducing the potential market for a product in this area.

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

Medical technology is subject to intense competition and rapid technological change. We have many competitors, including pharmaceutical, biotechnology and chemical companies, a number of which, including our strategic partners, are actively developing and marketing products that could compete with our product candidates. Specifically, although there are no MRI contrast agents that are FDA-approved for vascular imaging, there are a number of general use MRI agents approved for other clinical applications in the U.S. and certain foreign markets that are likely to compete with MS-325, if MS-325 is approved for MRA. Collectively, these general use agents are referred to as "extracellular" agents and include: Magnevist® and Gadovist® by Schering AG, Dotarem® by Guerbet, S.A., Omniscan® by GE Healthcare, 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 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, GE Healthcare, Philips Medical Systems and Siemens Medical Systems. Four of our key agreements include three collaboration agreements with Schering AG, to perform joint research and to develop and commercialize MS-325, EP-2104R and other MRI vascular agents worldwide, and an agreement with Tyco/Mallinckrodt granting Tyco/Mallinckrodt rights to enter into an agreement with Schering AG to manufacture MS-325 for clinical development and commercial use. We may not receive milestone payments from these alliances should MS-325 or EP-2104R fail to meet certain performance targets in development and commercialization. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development and commence marketing of MS-325, EP-2104R or other products in their respective territories, or they may not successfully market MS-325, EP-2104R or other products. In addition, Schering AG and Tyco/Mallinckrodt currently manufacture imaging agents for other technologies that will compete against MS-325 and Schering AG will be responsible for setting the price of the product worldwide. However, Schering AG may not set prices in a manner that maximizes revenues for us. We are currently in compliance with the terms of these agreements, and although we have filed an NDA,

our failure to receive future milestone payments, or a reduction or discontinuance of efforts by our partners would have a material adverse effect on our business, financial condition and results of operations.

Furthermore, our collaboration agreement with Schering AG may be terminated early under certain circumstances, including if there is a material breach of the agreement by either of us. In addition, we intend to seek additional collaborations with third parties who may negotiate provisions that allow them to terminate their agreements with us prior to the expiration of the negotiated term under certain circumstances. If Schering AG or any other third party collaborator were to terminate its agreement with us or otherwise fail to perform its obligations under our collaboration or to complete them in a timely manner, we could lose significant revenue. If we are unable to enter into future strategic alliances with capable partners on commercially reasonable terms, we may delay the development and commercialization of future product candidates and could possibly postpone them indefinitely.

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

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

Under the terms of a license agreement that we have with Massachusetts General Hospital, or MGH, we are the exclusive licensee to certain technology, including patents expiring in 2006, which relate to royalties we receive and to 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 not receive royalties from Bracco for MultiHance or Schering AG for Primovist, and that we or Schering AG could not sell MS-325, and would therefore have a material adverse effect on our business, financial condition and results of operations. Currently, we are in compliance with the terms of the license agreement and we do not have any reason to believe that this license may be terminated.

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

The protection of our proprietary technologies is material to our business prospects. We pursue patents for our product candidates in the U.S. and in other countries where we believe that significant market opportunities exist. We own or have an exclusive license to patents and patent applications on aspects of our core technology as well as many specific applications of this technology. Specifically, patents and patent applications related to our core technology consist of two U.S. patents that are exclusively licensed to us from MGH as well as their counterpart patents and applications in foreign countries; seven U.S. patents and their counterpart patents and applications in certain foreign countries that we own; 20 U.S. patent applications as well as their counterpart patents and applications in certain foreign countries and five U.S. provisional patent applications. One of our issued patents covers aspects of the process by which MS-325 is manufactured. Another issued patent covers the MS-325 composition

of matter. Two of our patents cover certain methods of imaging with MS-325. We have eight patent applications relating to EP-2104R, fibrin binding peptides and methods of imaging. Even though we hold these patents and have made these patent applications, because the patent positions of pharmaceutical and biopharmaceutical firms, including ours, generally include complex legal and factual questions, our patent position remains uncertain. For example, because most patent applications are maintained in secrecy for a period after filing, we cannot be certain that the named applicants or inventors of the subject matter covered by our patent applications or patents, whether directly owned or licensed to us, were the first to invent or the first to file patent applications for such inventions. Third parties may oppose, challenge, infringe upon, circumvent or seek to invalidate existing or future patents owned by or licensed to us. A court or other agency with jurisdiction may find our patents invalid, not infringed or unenforceable and we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future. Even if we have valid patents, these patents still may not provide sufficient protection against competing products or processes. If we are unable to successfully protect our proprietary methods and technologies, or if our patent applications do not result in issued patents, we may not be able to prevent other companies from practicing our technology and, as a result, our competitive position may be harmed.

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

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

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

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

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

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

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

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

Our commercial success will depend, to a significant degree, on our ability to operate without infringing upon the patents of others in the U.S. and abroad. There may be pending or issued patents, held by parties not affiliated with us, relating to technologies we use in the development or use of certain of our contrast agents. For example, in November 2003, we entered into an Intellectual Property Agreement with Dr. Martin R. Prince, an early innovator in the field of MRA relating to "dynamic" MRA, which involves capturing MRA images during the limited time, typically 30 to 60 seconds, available for imaging with extracellular agents. In this Agreement, Dr. Prince made certain covenants and agreements and granted us certain discharges and releases in connection with the use of any magnetic resonance imaging drug product containing MS-325. Dr. Prince also granted to us a non-exclusive license to make, use, sell or otherwise transfer MS-325. Although we are not aware of any other similar patent claims in the field of MRA, they may exist.

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

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

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

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

This regulatory approval process is lengthy and expensive. Although some of our employees have experience in obtaining regulatory approvals, we have only limited experience in filing or pursuing

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

Furthermore, we, the FDA or other regulatory authorities may alter, suspend or terminate clinical trials at any time. For example, in September 2001, after discussions with the FDA, we expanded our initial target indication for MS-325 from one specific body region, the aortoiliac region, to a broader indication that includes the entire body's vascular system, except for the heart. This expansion required us to add two new clinical trials to our then existing Phase III clinical trial program; one to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the renal arteries, and another to determine the efficacy of MS-325-enhanced MRA for the detection of vascular disease in the pedal arteries. Although providing us with greater market potential for the sale of MS-325 upon approval, this change to our Phase III clinical trial program and the associated delay in the start up of new clinical centers resulted in an approximate fifteen month delay in our NDA submission and an increase in costs associated with the program. If we do not successfully complete clinical trials for our product candidates, we will not be able to market these product candidates.

In addition, we may encounter unanticipated delays or significant costs in our efforts to secure necessary approvals. In October 2004, we were notified by the FDA that it had extended the action date for completion of its review of the MS-325 NDA by 90 days, to January 2005. In January 2005, we received an approvable letter from the FDA for MS-325 in which the FDA requested additional clinical studies to demonstrate efficacy prior to approval. In its approvable letter, the FDA indicated that its principal questions related to the non-contrast MRA comparator scans used in the Phase III trials and to the statistical treatment of uninterpretable scans. We are continuing our active dialogue with the FDA in order to determine the next steps we will need to take in the regulatory pathway for MS-325. Although we remain confident in the safety and efficacy profile of MS-325, the approval, timeliness of approval or labeling of MS-325 are subject to significant uncertainties related to a number of factors, including the process of reaching agreement with the FDA on the clinical data and on any clinical trial protocol required for regulatory approval of MS-325, the timing and process of conducting any clinical studies required, obtaining the desired outcomes of any required clinical trials and the FDA's review process and conclusions regarding any additional MS-325 regulatory submissions. We cannot assume that we will be able to reach agreement with the FDA on the design or clinical endpoints required for additional clinical studies. Further, we cannot assume that any such agreed upon clinical trials will be feasible for us to conduct or whether such trials will be completed in a commercially reasonable timeframe, if at all. Any further clinical trials that are required could take several years to complete. We may not obtain regulatory approval, even after the performance of clinical trials and the passage of time and the expenditure of such resources, for MS-325 or any other product candidates that we develop. Our analysis of data obtained from pre-clinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent FDA regulatory approval. In addition, the FDA may require us to modify our future clinical trial plans or to conduct additional clinical trials in ways that we cannot currently anticipate, resulting in delays in our obtaining regulatory approval. Delays in obtaining government regulatory approval could adversely affect our marketing as well as our ability to generate significant revenues from commercial sales.

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

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

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

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

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

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

timely manner, if at all, and failure to receive international reimbursement approvals could have an adverse effect on market acceptance of our products in the international markets in which such approvals are sought.

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

Our future business and operating results depend in significant part upon the continued contributions of our senior management and key technical personnel. If any such personnel were to be hired away from us by a competitor, or if for any reason, they could not continue to work for us, we could have difficulty hiring officers with equivalent skills in general, financial and research management, and our ability to achieve our business objectives or to operate or compete in our industry may be seriously impaired. Although we maintain key life insurance on our Chief Executive Officer, the loss of any key employee, the failure of any key employee to perform in his or her current position, or our inability to attract and retain skilled employees, as needed, could have a material adverse effect on our business, financial condition and results of operations. Our future business and operating results also depend, in significant part, upon our ability to attract and retain qualified management, operational and technical personnel. Competition for personnel is intense and we may not be successful in attracting or retaining such personnel. If we were to lose these employees to our competitors, we could spend a significant amount of time and resources to replace them, which would impair our research and development or commercialization efforts.

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;

the timing of our achievement of regulatory milestones;

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, 2004, the closing price of our common stock ranged from $25.99 to $15.42. The last reported closing price for our common stock on December 31, 2004 was $17.91. 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 could result in substantial costs and a diversion of management's attention and resources. On January 27, 2005, a securities class action was filed in U.S. District Court for the District of Massachusetts against the Company and certain of its officers on behalf of persons who purchased the Company's common stock between July 10, 2003 and January 14, 2005. The complaint alleges that the defendants violated of the Securities Exchange Act of 1934 by issuing a series of materially false and misleading statements to the market throughout the class period, which statements had the effect of artificially inflating the market price of the Company's securities. After this initial complaint was filed, other similar actions were filed against the Company and the same officers in the United States District Court for the District of Massachusetts. One of these later-filed complaints purports to be brought on behalf of persons who purchased the Company's common stock between March 18, 2002 and January 14, 2005.

We intend to vigorously contest these lawsuits and believe that we and the other named defendants have highly meritorious defenses to the allegations made in these lawsuits.

We are not presently able to estimate the potential losses, if any, related to these lawsuits.

We have significantly increased our leverage as a result of the sale of our 3.00% Convertible Senior Notes due 2024.

In connection with the sale of our 3.00% Convertible Senior Notes due 2024, we have incurred new indebtedness of $100 million. The amount of our indebtedness could, among other things:

make it difficult for us to make payments on the notes;

make it difficult for us to obtain financing for working capital, acquisitions or other purposes on favorable terms, if at all;

make us more vulnerable to industry downturns and competitive pressures; and

limit our flexibility in planning for, or reacting to changes in, our business.

Our ability to meet our debt service obligations will depend upon our future performance, which will be subject to financial, business and other factors affecting our operations, many of which are beyond our control.

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 are subject to Section 203 of the General Corporate Law of Delaware, which, subject to certain exceptions, restricts certain transactions and business combinations between a corporation and a stockholder owning 15% or more of the corporation's outstanding voting stock for a period of three years from the date the stockholder becomes an interested stockholder. These provisions may have the

effect of delaying or preventing a change in control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

ITEM 2. PROPERTIES

We lease a total of 23,921 square feet of space at 71 Rogers Street and adjacent locations, and 17,737 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

On January 27, 2005, a securities class action was filed in U.S. District Court for the District of Massachusetts against the Company and certain of its officers on behalf of persons who purchased the Company's common stock between July 10, 2003 and January 14, 2005. The complaint alleges that the defendants violated of the Securities Exchange Act of 1934 by issuing a series of materially false and misleading statements to the market throughout the class period, which statements had the effect of artificially inflating the market price of the Company's securities. After this initial complaint was filed, other similar actions were filed against the Company and the same officers in the United States District Court for the District of Massachusetts. One of these later-filed complaints purports to be brought on behalf of persons who purchased the Company's common stock between March 18, 2002 and January 14, 2005.

We intend to vigorously contest these lawsuits and believe that we and the other named defendants have highly meritorious defenses to the allegations made in these lawsuits.

We are not presently able to estimate the potential losses, if any, related to these lawsuits.

We are not a party to any other 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, 2004.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

The Company's Common Stock is traded on The NASDAQ Stock Market 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
2003		
First Quarter	$ 8.90	$ 6.21
Second Quarter	14.32	7.83
Third Quarter	20.65	13.55
Fourth Quarter	20.10	15.50
2004		
First Quarter	$ 23.40	$ 15.94
Second Quarter	26.37	20.34
Third Quarter	22.58	15.80
Fourth Quarter	20.00	15.28

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

On February 25, 2005, the last reported price for the Common Stock was $8.57 per share. As of February 25, 2005, there were approximately 78 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,				
	2004	2003	2002	2001	2000
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenues	$ 12,259	$ 13,525	$ 12,270	$ 9,569	$ 6,924
Operating loss	(20,111)	(21,083)	(22,816)	(18,841)	(23,745)
Loss before provision for income taxes	(20,281)	(20,714)	(22,098)	(18,156)	(22,957)
Provision for income taxes	100	80	94	1,092	
Loss before cumulative effect of change in accounting principle	(20,381)	(20,795)	(22,191)	(19,248)	(22,957)
Cumulative effect of change in accounting principle(1)					(4,363)
Net loss	$ (20,381)	$ (20,795)	$ (22,191)	$ (19,248)	$ (27,320)
Weighted average common shares outstanding:					
Basic and diluted	22,889	19,056	16,878	14,007	12,445
Loss per share:					
Loss before cumulative effect of change in accounting principle	$ (0.89)	$ (1.09)	$ (1.31)	$ (1.38)	$ (1.85)
Cumulative effect of change in accounting principle					$ (0.35)
Net loss, basic and diluted	$ (0.89)	$ (1.09)	$ (1.31)	$ (1.38)	$ (2.20)
Pro forma amounts assuming the accounting change is applied retroactively(1):					
Net loss					$ (22,957)
Net loss per share, basic and diluted					$ (1.85)

	December 31,				
	2004	2003	2002	2001	2000
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 164,440	$ 79,958	$ 28,112	$ 24,966	$ 24,713
Working capital	136,653	57,011	12,364	8,277	15,020
Total assets	171,287	81,875	30,155	26,911	29,681
Long-term liabilities	101,210	4,331	7,829	12,844	10,050
Total stockholders' equity (deficit)	41,382	54,157	5,887	(3,210)	6,566

(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"), superseded by SEC Staff Accounting Bulletin No. 104, *Revenue Recognition*. SAB 104 provides guidance related to revenue recognition policies based on interpretations and practices followed by the SEC. The impact of our adoption of SAB 104 was to defer revenue recognition for certain portions of the revenue previously recognized by us under our strategic alliances into future accounting periods.

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

Overview

We develop innovative pharmaceuticals 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, 2004 aggregating to approximately $155.3 million. Most of our revenues to date have come from license fees and product development revenues from collaboration agreements for our product candidates.

Our primary activities relate to three projects: MS-325, for which we have submitted an NDA to the FDA and received an FDA approvable letter requesting additional clinical studies in January 2005; our feasibility program for EP-2104R, which is in clinical development; and our joint MRI research program with Schering Aktiengesellschaft, or Schering AG.

MS-325 is an injectable intravascular contrast agent intended to enhance the quality of MR images and provide physicians with an improved 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 MR angiography, or 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 had been accepted for filing and had been designated for a standard 10-month review cycle. In October 2004, we were notified by the FDA that it had extended the action date for completion of its review of MS-325 by 90 days to January 2005. In January 2005, we received an approvable letter from the FDA for MS-325 in which the FDA requested additional clinical studies to demonstrate efficacy prior to approval. If our NDA for MS-325 is approved by the FDA, our partner, Schering AG, will have primary responsibility for the product launch and marketing of MS-325. In 2004, we initiated and are conducting the OPTIMUM clinical trial study of MS-325 in high resolution vascular MRA in peripheral disease. We are also developing MS-325 for imaging coronary arteries and the heart and are conducting a Phase II clinical trial of the use of MS-325 for cardiac imaging. In June 2004, Schering AG submitted MS-325 to the European Agency for the Evaluation of Medicinal Product (EMEA) for marketing approval in the European Union. In September 2004, Schering AG initiated Phase I trials in Japanese subjects in support of the Japanese development program for MS-325.

If our MS-325 NDA is approved by the FDA and if MS-325 receives marketing approval from EMEA, in each case, in a timely manner, we believe that we will 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 of commercialization efforts by us and our collaborators and on the success and timing of clinical trials and regulatory approvals for our products. 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.

EP-2104R is an injectable MRI contrast agent that is specifically targeted to fibrin, the dominant protein in blood clots, or thrombi. It is designed to provide a bright MR image of blood clots anywhere in the vascular system and may allow clinicians to identify potential problems early. 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 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 are responsible for the execution of a clinical feasibility program for EP-2104R in humans for which Schering AG is obligated to make fixed payments to us of approximately $9.0 million over a two year period. 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. In 2004, we completed Phase I clinical trials of EP-2104R where the drug was well tolerated in healthy volunteers. We plan to initiate and complete Phase II clinical trials to study the feasibility of blood clots imaging using EP-2104R in patients in 2005.

We are engaged in research activities to discover other pharmaceutical product candidates. In May 2003, we entered into an agreement with Schering AG covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. Under the 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 has agreed to fund a portion of our related personnel costs and third party research costs of up to $2.0 million per year and has made available to us a loan facility of up to $15 million, with principal repayment beginning in 2007.

We expect continued operating losses for at least three years and possibly thereafter 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. We filed an investigational new drug, or IND, application and initiated a Phase I clinical trial for MS-325 in 1996. We completed a Phase II clinical trial in 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 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. We completed two Phase III studies, with results announced in 2002 and 2003, to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease. In 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 expected would 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. These two trials were completed and results announced in 2003. We submitted our NDA to the FDA in December 2003 and our NDA was accepted as fileable by the FDA in February 2004. In October 2004, the Company was notified by the FDA that it had extended the action date for completion of its review of MS-325 by 90 days to January 2005. In January 2005, we received an approvable letter from the FDA for MS-325 in which the FDA requested additional clinical studies to demonstrate efficacy prior to approval. We also completed feasibility trials to test MS-325 in detecting coronary artery disease, in detecting breast cancer and in diagnosing female sexual arousal dysfunction. We are co-developing MS-325 with Schering AG.

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 U.S. The preparation of these financial statements requires us to make estimates and judgments that affect our reported assets and liabilities, revenues and expenses, and other financial information. Actual results may differ significantly from the estimates under different assumptions and conditions.

Our significant accounting policies are more fully described in Note 2 of the Company's Financial Statements for the year ended December 31, 2004. 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 earnings 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 March 2004, we increased the estimated time period over which we will provide services under our agreement with Mallinckrodt, Inc., a subsidiary of Tyco/Mallinckrodt, from 99 months to 101 months because the FDA notified the Company that its NDA for MS-325 had been accepted for filing under a standard review cycle, instead of an accelerated review cycle. In September 2004, we again increased our estimated time period for providing services under the agreement with Tyco/Mallinckrodt to 103 months because of the FDA's notice to extend its review by an additional 90 days. In December 2004, we again increased our estimated time period by 24 months for providing services under the agreement with Tyco/Mallinckrodt to 127 months because of the FDA's January 2005 request for clinical studies to demonstrate efficacy prior to approval. In 2004, the impact of the increase of these estimates resulted in a reduction in revenue of $160,000 compared to the estimates used at the beginning of the year. We will continue to review these estimates and make appropriate adjustments as information becomes available.

Under the MS-325 program, we recognize product development 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 product development revenue from Schering AG for the EP-2104R feasibility program as revenue proportionate to our actual cost incurred relative to our estimate of the total cost of the feasibility program. Total estimated costs of the feasibility program are based on an evaluation of the portion of the program completed, costs incurred to date, planned program activities, anticipated program timelines and the expected future costs of the program. Adjustments to revenue are recorded if estimated costs to complete change materially from previous periods. 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 future periods. During 2004, management increased its EP-2104R estimate to complete the feasibility program,

resulting in a total reduction of revenue of $1.2 million, of which $853,000 was recognized in the fourth quarter of 2004.

Revenue under our research collaboration with Schering AG in 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 Imaging S.p.A, or Bracco. Prior to the fourth quarter of 2004, we recognized royalty revenues based on royalty reports received from Bracco or on Bracco's estimates, historical revenues and trends when royalty reports from Bracco were not available in a timely manner. In December 2004, we learned from Bracco that Bracco is asserting that it had overstated non-U.S. royalties to us for the period 2001 to 2004 and that it would offset the amount of the overstatement against its royalty payments to us, including those triggered by FDA approval of MultiHance® in the United States. Although we are disputing Bracco's position, we have recognized the effects of Bracco's claimed overstatement by reducing 2004 royalty revenues. In addition, we believe that we no longer have a reasonable basis to make royalty estimates and will therefore, effective in the fourth quarter of 2004, recognize future royalties from Bracco in the period in which royalty reports are received.

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 preclinical and clinical trial 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 three types of vendor contracts; time based, patient based or a combination thereof. 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 rendered. 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 under the intrinsic value method, 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, because the exercise price is 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 could 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 Notes to Financial Statements.

Results of Operations

Years ended December 31, 2004 and 2003

Revenues

Our revenues arise principally from our collaboration agreements with Schering AG for MS-325, EP-2104R and MRI discovery research; from license fee revenues relating to our agreements with Schering AG, Tyco/Mallinckrodt and Bracco; and from royalties related to our agreement with Bracco. Revenues for the years ended December 31, 2004 and 2003 were $12.3 million and $13.5 million, respectively. Revenues for 2004 consisted of $7.6 million of product development revenue from Schering AG, $4.0 million of royalty and license fee revenue related to the Bracco agreement and $617,000 of license fee revenue related to the Schering AG and Tyco /Mallinckrodt strategic collaboration agreements for the development and marketing of MS-325. The decrease in revenues of $1.2 million for the year ended December 31, 2004 compared to the same period last year was the result of reduced product development activities of $1.9 million primarily from MS-325 and lower royalties of $1.8 million from Bracco, partly offset by higher license fee revenue of $2.5 million resulting from the milestone related to Bracco's announcement of FDA's approval of MultiHance in the U.S. The lower royalties were primarily attributed to our decision to recognize the full $1.8 million amount reflected in Bracco's position taken in December 2004 that it had overstated non-U.S. royalties over the previous four year period from 2001 to 2004. We have challenged Bracco's underpayment, Bracco's right to recalculate previous royalties under the License Agreement and the substance of Bracco's position that royalties were overstated. We are in discussions with Bracco regarding the resolution of this dispute.

Research and Development Expenses

Our research and development expenses arise from our development activities for MS-325 and EP-2104R and from our discovery research programs. Research and development expenses for the year ended December 31, 2004 were $21.9 million as compared to $28.0 million for the same period in 2003. The decrease of $6.1 million was primarily attributable to decreased costs related to the completion of the NDA submission for MS-325 and the Intellectual Property Agreement entered into with Dr. Martin Prince in the fourth quarter of 2003, partly offset by higher spending for EP-2104R and other research programs.

Both the time-frame and costs involved in developing MS-325 and EP-2104R, gaining regulatory approval and commercializing the products 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 or to increase patient numbers, we could incur significant additional costs and additional time to complete our clinical trials. This could 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 could 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 take to review our regulatory submissions and the length of time it takes us to respond to the FDA or other regulatory authorities' questions can also vary widely. In January 2005, we received an approvable letter from the FDA for MS-325 in which the FDA requested additional clinical studies to demonstrate efficacy prior to approval. The process of obtaining agreement with the FDA for conducting necessary clinical trial studies is subject to significant uncertainties in terms of timing, costs and success. The additional time and any other delays in the process could result in an increase in a delay in the commercialization or slower sales growth of our product.

Our partner, Schering AG, is responsible for the commercial 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 become 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.

Under our EP-2104R agreement, Schering AG has made fixed payments to us totaling approximately $9.0 million over a two year period intended to cover our costs of the feasibility program. The amount of expenditure necessary to execute the feasibility program, currently estimated to be $13.2 million, is subject to numerous uncertainties, which may adversely affect our cash outlay, net of Schering's reimbursement 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, at this time, we cannot predict the amount of additional research and development costs that we will incur with regard to the development and commercialization of EP-2104R.

The cost to execute our joint research plan with Schering AG 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. In addition, the FDA may require us to modify our future clinical trial plans or to conduct additional clinical trials in ways that we cannot currently anticipate. Such modifications or additional clinical trials could result in an increase in costs of our product development and a delay in the commercialization or slower sales growth of our product.

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 $10.5 million for the year ended December 31, 2004 as compared to $6.6 million for the year ended December 31, 2003. The increase of $3.9 million was primarily attributable to higher spending both by EPIX and by Schering AG for MS-325 marketing, higher business development expenses, higher legal expenses related to patent and intellectual property filings, increased compliance costs due to the internal control review required by the Sarbanes-Oxley Act and to higher liability insurance premiums. General and administrative expenses also include royalties payable to Massachusetts General Hospital, or MGH, based on sales by Bracco of MultiHance®. Royalty expenses totaled $31,000 and $103,000 for the years ended December 31, 2004 and 2003.

Interest Income and Interest Expense

Interest income for the year ended December 31, 2004 was $2.0 million as compared to $664,000 for the year ended December 31, 2003. The increase of approximately $1.3 million was primarily due to higher average levels of invested cash, cash equivalents and marketable securities during the period related to net proceeds from the issuance of $100 million convertible senior notes in June 2004. Interest expense for the years ended December 31, 2004 and 2003 was $2.1 million and $295,000, respectively. The increase in interest expense of $1.8 million during the year ended December 31, 2004 resulted from the issuance of convertible senior notes in June 2004 and the drawdown of the entire $15.0 million loan facility made available to us by Schering AG as part of the joint MRI research collaboration entered into in May 2003, partly offset by the reduction in the outstanding balance of interest-bearing prepaid royalties from Bracco. The entire principal balance of the loan facility, which was $15.0 million as of December 31, 2004, plus accrued interest, was repaid in January 2005.

Provision for Income Taxes

The provision for income taxes, which represents Italian income taxes related to the Bracco agreement, was $100,000 for the year ended December 31, 2004 as compared to $80,000 for the year ended December 31, 2003. Beginning in July 2003 and continuing throughout 2004, a portion of royalty revenue earned was offset against the prepaid FDA approval license fee, thereby reducing both payments to us and the requirement to withhold foreign taxes.

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.

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 upfront 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 will make fixed payments to us totaling approximately $9.0 million over two years intended to cover our costs of the feasibility program. 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.

General and Administrative Expenses

General and administrative expenses 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 continuing up to when MultiHance® was approved in the United States in November 2004, a portion of royalty revenue earned was offset against the prepaid FDA approval license fee, thereby reducing both payments to us and the requirement to withhold foreign taxes.

Liquidity and Capital Resources

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities of $164.4 million at December 31, 2004 as compared to $80.0 million at December 31, 2003. The increase in cash, cash equivalents and available-for-sale marketable securities was primarily attributed to the net proceeds of approximately $96.4 million resulting from the issuance of convertible senior notes in June 2004.

We used approximately $22.5 million of net cash to fund operations for the year ended December 31, 2004, which compares to $24.0 million for the same period last year. A net loss of $20.4 million, combined with a reduction in deferred revenue of $3.7 million, a reduction of accrued expenses of $1.3 million and a reduction of accounts payable of $1.0 million, partly offset by increases in contract advances of $3.0 million accounted for the net cash used in operations during the year

ended December 31, 2004. The reduction in deferred revenue resulted from the recognition of the Bracco's MultiHance® approval by the FDA, plus other license fee revenue recognition related to payments from Schering, Tyco/Mallinckrodt and Bracco, which are being amortized into revenue in accordance with the requirements of SAB 104. The decrease in accrued expenses is due to the completion of preclinical development activity in 2004 and to the issuance of common stock to Dr. Martin Prince in early January 2004 to offset last year's accrual in connection with the Intellectual Property Agreement entered into in November of 2003. The decrease in accounts payable is due to lower year end spending levels compared to the prior year. The increase in contract advances primarily relates to Schering AG's funding of both EPIX's and Schering AG's MS-325 pre-launch activities. Also during 2004, we received a $2.5 million milestone payment from Schering AG related to the acceptance of the filing of the NDA with the FDA for MS-325. Immediately following this receipt, we paid Tyco/Mallinckrodt $2.5 million in recognition of the same milestone. These payments were offset in the Company's Statements of Operations, resulting in no impact on revenues, expenses or net loss. For the year ended December 31, 2003, net cash used for operating activities of $24.0 million was primarily attributable to our net loss of $20.8 million, combined with a reduction in deferred revenue of $3.2 million, resulting from royalty revenues from sales by Bracco of MultiHance ®, and a reduction in reacquisition costs of $2.4 million resulting from a 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.

Our investing activities resulted in net cash used of $50.1 million for the year ended December 31, 2004 as compared to net cash used of $20.6 million for the same period last year. During the year ended December 31, 2004, we purchased available-for-sale marketable securities of $93.7 million that was primarily funded from the convertible debt issuance, partly offset by the cash generated from the redemption or sale of $45.6 million of available-for-sale marketable securities. During the same period in 2003, we redeemed approximately $23.5 million of available-for-sale marketable securities, which was partly offset by the purchase of available-for-sale marketable securities of $43.3 million. Other investing activities included capital expenditures of $2.1 million for the year ended December 31, 2004 as compared to $759,000 for the same period last year. The increase in our capital expenditures was primarily attributed to leasehold improvements and to the acquisition of equipment, including lab equipment, computer equipment and software, related to the refurbishment of our laboratory space.

Cash provided by financing activities was $109.3 million for the year ended December 31, 2004. The primary sources of financing during the year ended December 31, 2004 came from net proceeds of $96.4 million attributable to the issuance of convertible senior notes, the cumulative drawdown of the loan facility of $52.5 million with Schering, of which $15 million was outstanding at December 31, 2004, and proceeds from stock option exercises and employee stock purchases of $5.5 million. Also during this period, we repaid $45.0 million on a cumulative basis against our loan facility with Schering AG, which was outstanding at December 31, 2004. During the year ended December 31, 2003, we received net proceeds of $65.5 million from the sale and issuance of 4.645 million shares of common stock, pursuant to our effective shelf registration statement, previously filed with the Securities and Exchange Commission, and another $3.7 million from stock option exercises and employee stock purchases. In addition, we cumulatively borrowed $15.0 million and repaid $7.5 million during the year ended December 31, 2003 on our loan facility with Schering AG.

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 on our joint MRI research collaboration. We also receive monthly interest income on our cash, cash equivalents and available-for-sale marketable securities. We also receive quarterly royalty payments from Bracco for a portion of the royalty revenue actually earned from the sales of MultiHance®. In December 2004, we learned from Bracco that Bracco is asserting that it had overstated non-U.S. royalties to us for the period 2001 to 2004 and that it would offset the amount of the overstatement against its royalty

payments to us, including those triggered by FDA approval of MultiHance® in the United States. Although we are disputing Bracco's position, we have recognized the effects of Bracco's claimed overstatement by reducing 2004 royalty revenues. Other potential cash inflows include: a 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 of up to $15 million 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 Primovist product, if it is approved for sale by the FDA or international regulatory authorities pursuant to a license agreement with Schering AG. In October 2004, Schering AG announced that Primovist had been approved in 25 countries of the European Union and that Schering AG expects to begin marketing the product in those countries in the first quarter of 2005.

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®; a milestone payment of $2.5 million owed to Tyco/Mallinckrodt, 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, which equals $1.7 million at December 31, 2004, upon termination of our license agreement with Bracco.

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, 2004 will be sufficient to fund our operations until we turn cash flow positive. If we consider other opportunities or change our planned activities, we may require additional funding. As of December 31, 2004, we had outstanding the entire balance of our $15.0 million loan facility available from Schering AG as part of our MRI research collaboration. We repaid the entire $15.0 million loan, plus accrued interest, in January 2005, but expect to redraw the $15.0 million loan as needed. We expect to be able to redraw the $15.0 million from the Schering AG loan facility, of which $7.5 million can be redrawn until May 2007 and the remaining $7.5 million until May 2008, but could be unable to redraw under the terms of the loan if we fail to meet certain covenants or conditions precedent in the loan. As of December 31, 2004, we were in compliance with the covenants of the loan facility. If holders of our convertible senior notes require redemption of the notes, we may be required to repay $100.0 million in June 2011. 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 and new 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.

Below is a table that represents payments due under contractual obligations and commercial commitments as of December 31, 2004:

		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, including interest payments	$ 15,030,833	$ 15,030,833	$	$	$
Long-term debt obligations, including interest payments	119,375,000	3,000,000	6,000,000	6,000,000	104,375,000
Operating lease obligations	3,926,699	1,298,703	2,622,812	5,184	
Purchase obligations	6,330,896	6,245,231	85,665		
Deferred revenue	1,745,352	1,745,352			
Total	$ 146,408,780	$ 27,320,119	$ 8,708,477	$ 6,005,184	$ 104,375,000

We have incurred tax losses to date and therefore have not paid significant federal or state income taxes since inception. As of December 31, 2004, we had federal net operating loss carryforwards of approximately $154.5 million available to offset future taxable income. These amounts expire at various times through 2024. 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 generated 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 government-sponsored enterprises, 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 $129,000, and an increase of approximately $129,000, respectively, at December 31, 2004.

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.

Management's Report on Internal Controls

The management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, the Company's principal executive and principal financial officers and effected by the Company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. The Company's internal control over financial reporting includes those policies and procedures that:

pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflects transactions in and dispositions of the assets of the Company;

provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and

provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

The Company's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2004. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on our assessment, management concludes that, as of December 31, 2004, the Company's internal control over financial reporting is effective based on those criteria.

The Company's independent registered public accounting firm has issued an audit report on our assessment of the Company's internal control over financial reporting. This report appears immediately following Management's Report.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders
EPIX Pharmaceuticals, Inc.:

We have audited management's assessment, included in the accompanying Management's Report on Internal Controls, that EPIX Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). EPIX Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management's assessment that EPIX Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, EPIX Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of EPIX Pharmaceuticals, Inc. as of December 31, 2004 and 2003, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2004 of EPIX Pharmaceuticals, Inc. and our report dated March 4, 2005 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 4, 2005

ITEM 9B. OTHER INFORMATION

None

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 2005 Annual Meeting of Stockholders to be held on June 2, 2005.

We have adopted a Corporate Code of Conduct and Ethics that applies to all directors and employees, including our principal executive, and 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.epixpharma.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 2005 Annual Meeting of Stockholders to be held on June 2, 2005.

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 2005 Annual Meeting of Stockholders to be held on June 2, 2005.

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 2005 Annual Meeting of Stockholders to be held on June 2, 2005.

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 2005 Annual Meeting of the Stockholders to be held on June 2, 2005.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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@	Certificate of Amendment of Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2004 (File No. 000-21863) and incorporated herein by reference.
3.4@	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.
4.2@	Indenture dated as of June 7, 2004 between the Company and U.S. Bank National Association as Trustee, relating to 3% Convertible Senior Notes due June 15, 2024. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 7, 2004 (File No. 000-21863) and incorporated herein by reference.
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 Pharmaceuticals, Inc., dated as of September 30, 2003 and executed on October 10, 2003. Filed as Exhibit 10.22 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 File No. 000-21863) and incorporated herein by reference.
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.
10.25++	First Amendment to the Loan Agreement dated as of June 1, 2004 by and between the Company and Schering AG. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2004 (File No. 000-81863) and incorporated herein by reference.
10.26*	First Amendment dated October 8, 2004 to the Short Form Lease dated as of September 30, 2003 with a commencement date as of November 1, 2003 between the Company and the BHX, LLC, as Trustees of First Binney Realty Trust. Filed as Exhibit 10.22 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 (File No. 000-21863). Filed herewith.
10.27*	Director Compensation Arrangements. Filed herewith.
10.28*	Named Executive Officer Compensation Arrangements. Filed herewith.
10.29*	Form of Indemnification Agreement. Filed herewith.
10.30*	Form of Amendment to Stock Option Agreement. Filed herewith.
14.1@	The Company's Code of Conduct and Ethics. Filed as Exhibit 14.1 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2003 (File No. 000-21863) and incorporated herein by reference.
23.1*	Consent of Independent Registered Public Accounting Firm.
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)

@ 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.

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 PHARMACEUTICALS, INC.

March 10, 2005 By: /s/ MICHAEL D. WEBB

Michael D. Webb
Chief Executive Officer

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	Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2005
/s/ PEYTON J. MARSHALL, PH.D Peyton J. Marshall, Ph.D	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 10, 2005
/s/ CHRISTOPHER F. O. GABRIELI Christopher F. O. Gabrieli	Chairman of the Board and Director	March 10, 2005
/s/ STANLEY T. CROOKE, M.D., PH.D Stanley T. Crooke, M.D., Ph.D	Director	March 10, 2005
/s/ PETER WIRTH Peter Wirth	Director	March 10, 2005
/s/ GREGORY D. PHELPS Gregory D. Phelps	Director	March 10, 2005
/s/ MARK LEUCHTENBERGER Mark Leuchtenberger	Director	March 10, 2005

EPIX PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
EPIX Pharmaceuticals, Inc.:

We have audited the accompanying balance sheets of EPIX Pharmaceuticals, Inc. (formerly EPIX Medical, Inc.) as of December 31, 2004 and 2003, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2004. 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 the standards of the Public Company Accounting Oversight Board (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 Pharmaceuticals, Inc. at December 31, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of EPIX Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 4, 2005 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 4, 2005

EPIX PHARMACEUTICALS, INC.

BALANCE SHEETS

	December 31,	
	2004	**2003**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 73,364,538	$ 36,658,557
Available-for-sale marketable securities	91,075,630	43,299,675
Accounts receivable	322,546	46,072
Prepaid expenses and other assets	585,138	393,679
Total current assets	165,347,852	80,397,983
Property and equipment, net	2,490,804	1,413,346
Other assets	3,448,270	63,401
Total assets	$ 171,286,926	$ 81,874,730
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 938,498	$ 1,938,365
Accrued expenses	4,218,834	7,858,859
Contract advances	6,150,013	3,172,707
Loan payable to strategic partner	15,000,000	7,500,000
Deferred revenue	2,387,882	2,917,429
Total current liabilities	28,695,227	23,387,360
Deferred revenue	1,209,725	4,330,798
Convertible debt	100,000,000	
Commitments and Contigencies		
Stockholders' equity:		
Preferred Stock, $0.01 par value, 1,000,000 shares authorized; no shares issued		
Common stock, $.01 par value, 40,000,000 shares authorized; 23,190,154 and 22,318,642 share issued and outstanding at December 31, 2004 and 2003, respectively	231,900	223,187
Additional paid-in-capital	196,730,731	188,851,948
Accumulated deficit	(155,333,774)	(134,952,516)
Accumulated other comprehensive income (loss)	(246,883)	33,953
Total stockholders' equity	41,381,974	54,156,572
Total liabilities and stockholders' equity	$ 171,286,926	$ 81,874,730

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS

	Year ended December 31,		
	2004	**2003**	**2002**
Revenues:			
Product development revenue	$ 7,594,280	$ 9,534,335	$ 8,715,974
Royalty revenue	626,685	2,397,393	1,560,144
License fee revenue	4,037,636	1,593,284	1,993,383
Total revenues	12,258,601	13,525,012	12,269,501
Operating expenses:			
Research and development	21,873,991	28,023,522	29,084,469
General and administrative	10,495,377	6,584,318	6,001,099
Total operating expenses	32,369,368	34,607,840	35,085,568
Operating loss	(20,110,767)	(21,082,828)	(22,816,067)
Interest income	1,958,152	663,519	1,080,561
Interest expense	(2,128,738)	(295,168)	(362,058)
Loss before provision for income taxes	(20,281,353)	(20,714,477)	(22,097,564)
Provision for income taxes	99,905	80,075	93,657
Net loss	$ (20,381,258)	$ (20,794,552)	$ (22,191,221)
Weighted average shares:			
Basic and diluted	22,888,673	19,055,698	16,878,036
Net loss per share, basic and diluted	$ (0.89)	$ (1.09)	$ (1.31)

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income/(Loss)	Total Stockholders' (Deficit) Equity
	Shares	Amount				
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
Issuance of common stock upon exercise of options	723,554	7,234	5,211,805			5,219,039
Issuance of common stock under employee stock purchase plan	15,958	159	231,950			232,109
Issuance of common stock	132,000	1,320	2,337,720			2,339,040
Compensatory stock option expense			97,308			97,308
Net loss				(20,381,258)		(20,381,258)
Available-for-sale marketable securities unrealized loss					(280,836)	(280,836)
Comprehensive loss						(20,662,094)
Balance at December 31, 2004	23,190,154	$ 231,900	$ 196,730,731	$ (155,333,774)	$ (246,883)	$ 41,381,974

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2004	**2003**	**2002**
Operating activities:			
Net loss	$ (20,381,258)	$ (20,794,552)	$ (22,191,221)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,000,101	638,282	1,014,106
Stock compensation expense	97,308		
Amortization of deferred financing costs	260,188		
Changes in operating assets and liabilities:			
Accounts receivable	(276,474)	129,060	(78,184)
Prepaid expenses and other current assets	(191,459)	122,520	(24,497)
Other assets	4,943	(4,313)	53,445
Accounts payable	(999,867)	43,804	463,548
Accrued expenses	(1,300,985)	1,454,932	1,422,672
Accrued reacquisition costs		(2,400,000)	
Contract advances	2,977,306	40,636	(2,037,882)
Deferred revenue	(3,650,620)	(3,189,929)	(2,617,441)
Net cash used in operating activities	(22,460,817)	(23,959,560)	(23,995,454)
Investing activities:			
Purchases of marketable securities	(93,663,936)	(43,344,575)	(42,379,684)
Sale or redemption of marketable securities	45,607,145	23,488,773	30,331,773
Purchases of fixed assets	(2,077,559)	(758,826)	(1,063,066)
Net cash used in investing activities	(50,134,350)	(20,614,628)	(13,110,977)
Financing activities:			
Net proceeds from issuance of convertible debt	96,350,000		
Proceeds from loan payable from strategic partner	52,500,000	15,000,000	
Repayment of loan payable to strategic partner	(45,000,000)	(7,500,000)	(3,004,607)
Proceeds from stock options and warrants	5,219,039	3,494,370	921,488
Proceeds from Employee Stock Purchase Plan	232,109	208,097	92,905
Proceeds from sale of common stock		65,489,834	30,105,966
Repayment of capital lease obligations			(78,760)
Net cash provided by financing activities	109,301,148	76,692,301	28,036,992
Net increase (decrease) in cash and cash equivalents	36,705,981	32,118,113	(9,069,439)
Cash and cash equivalents at beginning of period	36,658,557	4,540,444	13,609,883
Cash and cash equivalents at end of period	$ 73,364,538	$ 36,658,557	$ 4,540,444
Supplemental cash flow information:			
Cash paid for interest	$ 1,747,236	$ 329,982	$ 453,135
Cash paid for taxes	$ 107,889	$ 99,655	$ 86,109
Supplemental disclosure of noncash financing and investing			

	Year Ended December 31,		
activities:			
Issuance of common stock in connection with Intellectual Property Agreement	$ 2,339,040	$	$

See accompanying notes.

EPIX PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS

December 31, 2004

1. Business

EPIX Pharmaceuticals, Inc. ("EPIX" or the "Company"), formerly known as EPIX Medical, Inc., 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. In January 2005, the Company received an approvable letter from the FDA for MS-325 in which the FDA requested additional clinical studies prior to approval. 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. The Company is collaborating with Schering AG in a joint research program for the discovery of novel MRI product candidates for clinical development.

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 or loss.

Fair Value of Financial Instruments

At December 31, 2004 and 2003, the Company's financial instruments consisted of cash and cash equivalents, available-for-sale marketable securities and a portion of deferred revenue consisting of contract advances and debt. The carrying value of cash equivalents and the loan payable to strategic partner approximates fair value due to their short-term nature. The carrying value of the available-for-sale marketable securities, deferred revenue and convertible debt is discussed in Notes 2, 3 and 7, respectively.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents, available-for-sale marketable securities and accounts receivables. In accordance with the Company's investment policy, marketable securities are principally restricted to

United States government securities, high-grade bank obligations, high-grade corporate bonds, commercial paper and certain money market funds. Although the Company had $164.4 million of cash, cash equivalents and available-for-sale marketable securities invested through two investment advisors as of December 31, 2004, 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 Federal Home Loan Mortgage Corporation and the Federal Home Loan Bank; high-grade corporate bonds and commercial paper; certificates of deposit and money market funds.

The Company performs ongoing credit evaluations of its collaborators' financial condition, but does not require collateral. The Company continuously monitors collections from collaborators. Historically, the Company has not experienced losses related to its accounts receivable. If the financial condition of its collaborators were to deteriorate, resulting in an impairment of their ability to make payments, the establishment of an allowance may be required.

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 2 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.

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"), which is located in Italy. Total revenue from Bracco for the years ended December 31, 2004 and 2003 was $4.0 million and $2.8 million, or 33% and 21% of total revenue, respectively.

Revenue

For the years ended December 31, 2004, 2003 and 2002, one source represented 64%, 74% and 76%, another source represented 33%, 21% and 16% and a third source represented 3%, 5% and 8% 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 12. Under the EP-2104R development agreement, Schering has made 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 2003, management increased its EP-2104R estimate to complete the feasibility program from its original estimate of $9.0 million to $11.2 million, resulting in a reduction in product development revenue of $818,793 in 2003. As of December 2004, management had increased its EP-2104R estimate to complete the feasibility program to $13.2 million, resulting in a further reduction in product development revenue of $1.2 million in 2004, of which $853,138 was recognized in the fourth quarter of 2004. 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. Prior to the fourth quarter of 2004, the Company recognized royalty revenues based on royalty reports received from Bracco or on Bracco's estimates, historical revenues and trends when royalty reports from Bracco were not available in a timely manner. In December 2004, the Company learned from Bracco that Bracco is asserting that it had overstated non-U.S. royalties to the Company for the period 2001 to 2004 and that it would offset the amount of the overstatement against

its royalty payments to the Company, including those triggered by FDA approval of MultiHance® in the United States. Although the Company is disputing Bracco's position, the Company has recognized the effects of Bracco's claimed overstatement by reducing 2004 royalty revenues. In addition, the Company believes that it no longer has a reasonable basis to make royalty estimates and will therefore, effective in the fourth quarter of 2004, recognize future royalties from Bracco in the period in which royalty reports are received. 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. At December 31, 2004 and December 31, 2003, the remaining balance of the refundable advance royalty was $1.7 million and $2.0 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 $128,801 and $90,453 for the years ended December 31, 2004 and 2003, respectively, are classified as general and administrative expenses in the Statements of Operations.

License fee revenue

The Company records license fee revenues in accordance with SEC Staff Accounting Bulletin No. 104, *Revenue Recognition* ("SAB 104"). Pursuant to SAB 104, 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 March 2004, the Company increased the estimated time period over which it will provide services under its agreement with Mallinckrodt, Inc., a subsidiary of Tyco/Mallinckrodt, from 99 months to 101 months because the FDA notified the Company that its NDA for MS-325 had been accepted for filing under a standard review cycle, instead of an accelerated review cycle. In September 2004, the Company again increased its estimated time period for providing services under the agreement with Tyco/Mallinckrodt to 103 months because of the FDA's notice to extend its review by an additional 90 days. In December 2004, the Company again increased its estimated time period by 24 months for providing services under the agreement with Tyco/Mallinckrodt to 127 months because of the FDA's January 2005 request for clinical studies to demonstrate efficacy prior to approval. In 2004, the impact of the increase of these estimates resulted in a reduction in revenue of $160,000 compared to the estimates used at the beginning of the year. The Company will continue to review these estimates and make appropriate adjustments as information becomes available.

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 non-refundable license fee from Bracco as a result of Bracco's principal product under license, MultiHance®, gaining FDA approval in the United States. In November 2004, Bracco announced that it had received FDA approval for MultiHance® in the United States. The license fee, which was previously included in deferred revenue, was recorded as revenue upon FDA approval for MultiHance®. Beginning in July 2003, a portion of royalty revenue that was earned during the period was offset against the prepaid FDA approval license fee. When MultiHance® was approved in November 2004, Bracco was obligated to reimburse the Company the amount of royalties previously offset against the license fee. Instead, Bracco only reimbursed a portion of the royalties previously offset and took the position that the remaining amount was not owed to the Company because Bracco had overstated their non-U.S. MultiHance® royalties to the Company over the period from 2001 to 2004. As noted above, the Company is disputing Bracco's right to do so, but has recorded a reduction in royalty revenue in the fourth quarter of 2004 recognizing Bracco's failure to payback royalties owed.

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.

Reclassifications

Certain amounts in the accompanying financial statements have been reclassified to conform to the current year presentation.

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 three types of vendor contracts; time based, patient based or a combination thereof. 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, the Company records the contractual expense for each service provided under the contract ratably over the period during which it 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 upfront 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. The shares were delivered to Dr. Prince during 2004. Royalties will be expensed as cost of goods sold as revenues arising from 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 and convertible debt. Diluted net loss per share includes the effect of dilutive common stock issuable upon exercise of stock options and convertible debt 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 or convertible debt is not assumed if the result is anti-dilutive, such as when a loss is reported. For the years ended December 31, 2004, 2003 and 2002, 6,919,568, 3,557,499 and 3,791,734 potential common shares, respectively, pursuant to outstanding stock options and convertible debt, were not included in diluted weighted average shares outstanding as they were antidilutive. Accordingly, basic net loss per share and diluted net loss per share are the same for all periods presented.

Comprehensive Income (Loss)

In accordance with Statement of Financial Accounting Standards No. 130, *"Reporting Comprehensive Income"*("SFAS 130"), components of comprehensive income include net income and certain transactions that have generally been reported in the statements of stockholders' equity. Other comprehensive income is comprised of unrealized gains or losses on available-for-sale marketable securities.

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,		
	2004	2003	2002
Net loss as reported	$ (20,381,258)	$ (20,794,552)	$ (22,191,221)
Add: employee stock-based compensation included in net loss as reported	97,308		
Less: pro forma adjustment for stock-based compensation	(6,047,438)	(4,040,572)	(4,147,448)
Net loss pro forma	$ (26,331,388)	$ (24,835,124)	$ (26,338,669)
Net loss per share, basic and diluted			
As reported	$ (0.89)	$ (1.09)	$ (1.31)
Pro forma	(1.15)	(1.30)	(1.56)
Effect of pro form adjustment	$ (0.26)	$ (0.21)	$ (0.25)

The weighted-average grant date fair value of stock options granted during 2004, 2003 and 2002 was $15.66, $6.43 and $8.04 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,					
	2004	2003	2002	2004	2003	2002
Expected life of option (years)	7.3	6.6	6.5	0.5	0.5	0.5
Expected stock price volatility	0.85	0.87	0.87	0.84	0.86	0.87
Weighted average risk-free interest rate	3.25%	3.27%	3.52%	1.40%	1.12%	3.65%

The effects on 2004, 2003 and 2002 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

On December 16, 2004, the Financial Accounting Standards Board (FASB) issued FASB Statement No. 123 (revised 2004), Share-Based Payment, which is a revision of FASB Statement No. 123, Accounting for Stock-Based Compensation. Statement 123(R) supersedes APB Opinion No. 25, Accounting for Stock Issued to Employees, and amends FASB Statement No. 95, Statement of Cash Flows. Generally, the approach in Statement 123(R) is similar to the approach described in Statement 123. However, Statement 123(R) requires all share-based payments to employees, including

grants of employee stock options, to be recognized in the income statement based on their fair values. Pro forma disclosure is no longer an alternative.

Statement 123(R) must be adopted no later than July 1, 2005. Early adoption will be permitted in periods in which financial statements have not yet been issued. The Company expects to adopt Statement 123(R) on July 1, 2005.

Statement 123(R) permits public companies to adopt its requirements using one of two methods:

A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of Statement 123(R) for all share-based payments granted after the effective date and (b) based on the requirements of Statement 123 for all awards granted to employees prior to the effective date of Statement 123(R) that remain unvested on the effective date.

A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under Statement 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

The Company has not yet determined which method it will use.

As permitted by Statement 123, the Company currently accounts for share-based payments to employees using Opinion 25's intrinsic value method and, as such, generally recognizes no compensation cost for employee stock options. Accordingly, the adoption of Statement 123(R)'s fair value method will have a significant impact on the Company's results of operations, although it will have no impact on its overall financial position. The impact of adoption of Statement 123(R) cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, had the Company adopted Statement 123(R) in prior periods, the impact of that standard would have approximated the impact of Statement 123 as described in the disclosure of pro forma net loss and net loss per share discussed above.

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:

	2004		2003	
	Fair Value	Cost	Fair Value	Cost
Government-sponsored agency securities	$ 38,237,366	$ 38,364,954	$ 22,369,189	$ 22,338,682
Corporate bonds	38,506,427	38,625,721	13,884,177	13,880,813
Commercial paper	3,991,800	3,991,800	5,041,822	5,041,740
Certificates of deposit	10,340,037	10,340,037	2,004,487	2,004,487
	$ 91,075,630	$ 91,322,512	$ 43,299,675	$ 43,265,722

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

	December 31,	
	2004	2003
Due within one year	$ 47,193,349	$ 25,441,206
Due after one year through two years	43,882,281	17,858,469
	$ 91,075,630	$ 43,299,675

Gross unrealized gains on marketable securities amounted to $2,799 and $37,683 in 2004 and 2003, respectively. Gross unrealized losses on marketable securities amounted to $249,681 and $3,730 in 2004 and 2003, respectively. The aggregate fair value of investments with unrealized losses was $76.7 million and $11.8 million at December 31, 2004 and 2003, respectively. All such investments have been in an unrealized loss position for less than one year, except for one investment in corporate bonds that has an unrealized loss of $1,764 at December 31, 2004, and matures in February 2005.

There were no realized gains or losses on marketable securities in 2004 and 2003. The net amount of realized gains and losses in 2002 was 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,	
	2004	2003
Leasehold improvements	$ 3,607,588	$ 2,602,577
Laboratory equipment	3,568,169	2,901,687
Furniture, fixtures and other equipment	1,716,801	1,310,731
	8,892,558	6,814,995
Less accumulated depreciation and amortization	(6,401,754)	(5,401,649)
	$ 2,490,804	$ 1,413,346

5. Accrued Expenses

Accrued expenses consist of the following:

	December 31,	
	2004	2003
Accrued contractual product development expenses	$ 2,330,849	$ 3,000,088
Accrued compensation	969,925	1,654,702
Accrued intellectual property expenses		2,339,040
Other accrued expenses	918,060	865,029
	$ 4,218,834	$ 7,858,859

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 9.25% and 8.0% at December 31, 2004 and 2003, respectively. The entire $15.0 million amount under the Loan Agreement was available and drawn as of December 31, 2004. The entire outstanding balance of $15.0 million, plus accrued interest, was repaid to Schering AG in January 2005. Of the $15.0 million available under the Loan Agreement, $7.5 million is available to be redrawn by the Company until May of 2007 and the remaining $7.5 million is available to be redrawn until May 2008, subject to specified conditions and covenants contained in the Loan Agreement, including a commitment to maintain cash and cash equivalents of at least $2.0 million. The Company was in compliance with such covenants at December 31, 2004 and 2003, respectively. Any outstanding balance under 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.

7. Convertible Debt

In June 2004, the Company completed a sale, pursuant to Rule 144A under the Securities Act of 1933, of $100 million of 3% convertible senior notes due 2024 for net proceeds of approximately $96.4 million. Each $1,000 of senior notes is convertible into 33.5909 shares of the Company's common stock representing a conversion price of approximately $29.77 per share if (1) the price of the Company's common stock trades above 120% of the conversion price for a specified time period, (2) the trading price of the senior notes is below a certain threshold, (3) the senior notes have been called for redemption, or (4) specified corporate transactions have occurred. None of these conversion triggers has occurred as of December 31, 2004. Each of the senior notes is also convertible into the Company's common stock in certain other circumstances. The senior notes bear an interest rate of 3%, payable semiannually on June 15 and December 15, beginning on December 15, 2004. An interest payment of $1.6 million was made on December 15, 2004. The senior notes are unsecured and are subordinated to secured debt, including the loan payable to Schering AG.

The Company has the right to redeem the notes on or after June 15, 2009 at an initial redemption price of 100.85%, plus accrued and unpaid interest. Noteholders may require the Company to

repurchase the notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other events, including change of control and termination of trading.

In connection with the issuance of the senior notes, the Company incurred $3.65 million of issuance costs, which primarily consisted of investment banker fees and legal and other professional fees. The costs are being amortized as interest expense using the effective interest method over the term from issuance through the first date that the holders are entitled to require repurchase of the senior notes (June 2011). Amortization of the issuance costs was $260,188 for 2004.

8. Leases

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, 2004:

2005	$	1,298,703
2006		1,303,059
2007		1,319,753
2008		5,184
Total minimum lease payments	$	3,926,699

Total rental expense amounted to $1,194,586, $1,573,643 and $1,540,573 for 2004, 2003 and 2002, respectively.

9. Stockholders' Equity

In January 2002, the Company raised $30.1 million, net of underwriter discounts, commissions and expenses, through the issuance and sale of 2.575 million shares of its common stock pursuant to its effective shelf registration statement, previously filed with the SEC. 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.

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 2004, 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 6,599,901 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, 2004, 3,955,154 shares of Common Stock are reserved for issuance under the Equity Plan. Since the inception of the Equity Plan, options to purchase 2,644,747 shares of Common Stock have been exercised.

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, 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
Granted	944,430	$ 15.50-$25.37	$ 20.02			
Exercised	(723,554)	$ 0.45-$16.50	$ 7.21			
Cancelled	(302,897)	$ 5.13-$21.54	$ 10.94			
December 31, 2004	3,320,478	$ 0.83-$25.37	$ 12.25	634,676	1,273,690	$ 9.76

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. The number of shares underlying the option granted to each eligible director upon election or re-election is 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, 2004, 294,668 shares of common stock are reserved for

issuance under the Director Plan. Since the inception of the Director Plan, options to purchase 5,332 shares of Common Stock have been exercised.

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, 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			
December 31, 2003	155,000	$ 7.00-$13.25	$ 10.01	139,668	86,668	$ 9.74
Granted	85,000	$ 18.92-$24.95	$ 22.05			
December 31, 2004	240,000	$ 7.00-$24.95	$ 14.28	54,668	130,001	$ 9.87

Combined Option Information

The following table summarizes information about options under the Equity Plan and the Director Plan outstanding at December 31, 2004:

	Outstanding			Exercisable	
Range of Exercise Prices	Options Outstanding at December 31, 2004	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Options Exercisable at December 31, 2004	Weighted Average Exercise Price
$ 0.83-$7.10	781,883	6.35	$ 6.09	301,995	$ 5.85
$ 7.13-$10.25	900,144	5.74	$ 8.66	533,679	$ 8.73
$ 10.32-$18.27	936,535	6.13	$ 13.14	562,017	$ 12.76
$ 18.51-$25.37	941,916	9.26	$ 20.42	6,000	$ 19.71
	3,560,478	6.91	$ 12.39	1,403,691	$ 9.77

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. Employees purchased 15,958 shares in 2004 at an average price of $14.55 per share and 25,871 shares in 2003 at an average price of $8.04 per share. At December 31, 2004, 35,908 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.

10. 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 carryforwards, has fully reserved this tax benefit. The Company has the following deferred tax assets as of December 31, 2004 and 2003:

	December 31,	
	2004	2003
Deferred tax assets:		
Net operating loss carryforwards	$ 59,256,000	$ 47,700,000
Research and development tax credits	7,406,000	6,922,000
Book over tax depreciation and amortization	2,272,000	2,081,000
Deferred revenue	1,394,000	2,685,000
Other	198,000	152,000
Total deferred tax assets	70,526,000	59,540,000
Valuation allowance	(70,526,000)	(59,540,000)
Deferred income taxes, net	$	$

As of December 31, 2004, the Company has net operating loss carryforwards for Federal and State income tax purposes of approximately $154.5 million and $112.3 million, respectively, which expire through the year 2024 and 2009, respectively. The valuation allowance increased by $11.0 million during the year the ended December 31, 2004. The tax net operating loss carryforwards 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 carryforwards 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 generated 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 carryforwards 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,		
	2004	2003	2002	2004	2003	2002
Tax at U.S. statutory rate	$ (6,896,000)	$ (7,043,000)	$ (7,513,000)	(34.00)%	(34.00)%	(34.00)%
State taxes, net of federal benefit	(1,217,000)	(1,243,000)	(1,326,000)	(6.00)%	(6.00)%	(6.00)%
Non-deductible items	(2,348,038)	447,030	(196,343)	(11.58)%	2.16 %	(0.88)%
Foreign taxes, net of benefit	59,943	48,045	56,000	0.30%	0.23%	0.25%
Tax credits	(485,000)	(2,586,000)	(976,000)	(2.39)%	(12.48)%	(4.42)%
Change in valuation allowance	10,986,000	10,457,000	10,049,000	54.17%	50.48%	45.48%
Income tax expense	$ 99,905	$ 80,075	$ 93,657	0.50%	0.39%	0.43%

11. 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 2004, 2003 and 2002, the Company's match amounted to $227,994, $200,801, and $207,696, respectively.

12. 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 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, excluding 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 development costs and U.S. profits. In addition, the Company is entitled to receive royalties on non-U.S. gross 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 in 2000 and a milestone payment of $2.5 million for the acceptance of the NDA filing for MS-325 in 2004, which the Company then paid to Tyco (see Tyco below). The Company did not reflect these receipts and the disbursements in its statement of operations on the basis that Schering AG's payments to the Company

did not constitute an earnings process, nor did the Company's payments to Tyco represent an expense. Such payments were reflected in the statement of cash flows in both 2000 and 2004. 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 $16.3 million in milestone payments under the strategic collaboration agreement, of which $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 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. 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 option for a period of 120 days following Schering AG's performance of certain milestones. If and when the Company exercises the Gadomer option, the Company will enter into a definitive agreement with Schering AG with respect to Gadomer, 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. As of December 31, 2004, neither option to acquire participation rights was exercisable.

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.

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, which is expected to occur in 2005, 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 continued to make payments to the Company, totaling approximately $9.0 million, up through the end of 2004. The payments were 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 the Company'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 (see Note 6 for description of loan facility). 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, with Schering AG receiving a base royalty on sales and milestone payments.

On May 8, 2000, the Company granted to Schering AG a worldwide, royalty-bearing license to patents covering Schering AG's development project, Primovist injection, an MRI contrast agent for imaging the liver, which was approved in the EU in 2004. 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 is obligated to pay Tyco up to an

additional $5.0 million in milestone payments, of which $2.5 million was paid in February 2004 when the Company received acceptance of its 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 US and a royalty on MS-325 gross profits outside the US, except in Japan, where no payments are due Tyco.

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, which was net of Italian income taxes) in upfront 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 US. 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 $1.7 million as of December 31, 2004. After June 30, 2003, Bracco had the right to offset against royalties a portion of its $3.0 million FDA contingent license fee until the approval of MultiHance®, at which time the royalty offset became payable. In November 2004, Bracco announced that it had received FDA approval for MultiHance®. In December 2004, Bracco made a partial payment against their obligation to royalty offsets previously withheld by Bracco. In December 2004, the Company learned from Bracco that Bracco is asserting that it had overstated non-U.S. royalties to the Company for the period 2001 to 2004 by a cumulative total of approximately $1.8 million. The Company has challenged Bracco's underpayment, Bracco's right to recalculate previous royalties under the License Agreement and the substance of Bracco's position that royalties were overstated. The Company is in discussions with Bracco regarding the resolution of this dispute. 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.

13. Subsequent Event

On January 27, 2005, a securities class action was filed in U.S. District Court for the District of Massachusetts against the Company and certain of its officers on behalf of persons who purchased the Company's common stock between July 10, 2003 and January 14, 2005. The complaint alleges that the defendants violated of the Securities Exchange Act of 1934 by issuing a series of materially false and misleading statements to the market throughout the class period, which statements had the effect of artificially inflating the market price of the Company's securities. After this initial complaint was filed, other similar actions were filed against the Company and the same officers in the United States District Court for the District of Massachusetts. One of these later-filed complaints purports to be brought on behalf of persons who purchased the Company's common stock between March 18, 2002 and January 14, 2005.

The Company intends to vigorously contest these lawsuits and believes that the Company and the other named defendants have highly meritorious defenses to the allegations made in these lawsuits.

The Company is not presently able to estimate the potential losses, if any, related to these lawsuits.

14. Quarterly Financial Information (unaudited)

	First Quarter Ended March 31, 2004	Second Quarter Ended June 30, 2004	Third Quarter Ended September 30, 2004	Fourth Quarter Ended December 31, 2004	Total Year
Revenues:					
Product development revenue	$ 2,651,925	$ 1,962,067	$ 2,273,957	$ 706,331	$ 7,594,280
Royalty revenue	688,453	1,009,062	700,601	(1,771,431)(1)	626,685
License fee revenue	283,288	275,175	263,585	3,215,588	4,037,636
Total revenues	3,623,666	3,246,304	3,238,143	2,150,488	12,258,601
Operating expenses:					
Research Development	5,513,267	5,073,265	6,508,418	4,779,041	21,873,991
General & administrative	2,171,976	3,119,630	2,878,916	2,324,855	10,495,377
Total operating expenses	7,685,243	8,192,895	9,387,334	7,103,896	32,369,368
Other income, net	203,017	8,576	(246,645)	(135,534)	(170,586)
Income taxes	8,719	20,947	16,676	53,563	99,905
Net loss	$ (3,867,279)	$ (4,958,962)	$ (6,412,512)	$ (5,142,505)	$ (20,381,258)
Weighted average shares, basic and diluted	22,622,249	22,818,822	22,987,878	23,122,088	22,888,673
Net loss per share:					
Basic and diluted	$ (0.17)	$ (0.22)	$ (0.28)	$ (0.22)	$ (0.89)

(1) reflects the Company's decision to recognize the full $1.8 million of Bracco's assertion that it had overstated non-U.S. royalties to us during the period 2001 to 2004. In addition, the Company believes that it no longer has a reasonable basis to make royalty estimates and will therefore, effective in the fourth quarter of 2004, recognize future royalties from Bracco in the period in which royalty reports are received.

	First Quarter Ended March 31, 2003	Second Quarter Ended June 30, 2003	Third Quarter Ended September 30, 2003	Fourth Quarter Ended December 31, 2003	Total Year
Revenues:					
Product development revenue	$ 2,544,165	$ 2,781,037	$ 2,834,438	$ 1,374,695	$ 9,534,335
Royalty revenue	482,800	617,396	682,116	615,081	2,397,393
License fee revenue	468,701	423,767	401,300	299,516	1,593,284
Total revenues	3,495,666	3,822,200	3,917,854	2,289,292	13,525,012
Operating expenses:					
Research Development	7,391,448	5,890,935	5,618,628	9,122,511	28,023,522
General & administrative	1,606,917	1,558,091	1,677,654	1,741,656	6,584,318
Total operating expenses	8,998,365	7,449,026	7,296,282	10,864,167	34,607,840
Other income, net	81,331	45,904	16,838	224,278	368,351
Income taxes	27,194	38,818	2,973	11,090	80,075
Net loss	$ (5,448,562)	$ (3,619,740)	$ (3,364,563)	$ (8,361,687)	$ (20,794,552)
Weighted average shares, basic and diluted	17,090,243	17,177,677	19,765,976	22,125,758	19,055,698
Net loss per share:					
Basic and diluted	$ (0.32)	$ (0.21)	$ (0.17)	$ (0.39)	$ (1.09)

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