EPIX MEDICAL INC
Form 10-K
March 29, 2002

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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, 2001

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from_____ to _____

Commission file number: 0-21863

EPIX MEDICAL, INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3030815**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
71 Rogers Street, Cambridge Massachusetts	**02142**
(Address of principal executive offices)	(Zip Code)

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

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

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

Common Stock, $.01 Par Value Per Share

(Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been

subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

The aggregate market value of the registrant's voting stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) on March 21, 2002 was $203,253,048, based on the last sale price as reported by The Nasdaq National Market.

As of March 21, 2002, the registrant had 16,874,602 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 12, 2002.

PART I

ITEM 1. BUSINESS

Overview

We are a specialty pharmaceutical company engaged in the development of targeted contrast agents to both improve the capability and expand the use of magnetic resonance imaging, which we refer to as MRI, as a tool for diagnosing human disease. Our lead product under development, MS-325, is an injectable intravascular contrast agent designed for multiple cardiovascular imaging applications, including peripheral vascular disease and coronary artery disease. We believe that MS-325 will significantly enhance the quality of MR images and provide physicians with a clinically superior, non-invasive (i.e., no more invasive than a peripheral intravenous injection or I.V.) and cost-effective method for diagnosing cardiovascular disease. We also believe that MS-325 will simplify the diagnostic pathway for a number of cardiovascular diseases and in many cases replace highly invasive (i.e., more invasive than a peripheral I.V., up to and including a surgical procedure) and expensive conventional X-ray angiography, which is currently considered the definitive diagnostic exam for assessing cardiovascular disease. Potential additional imaging applications for MS-325, include breast cancer, female sexual arousal dysfunction, myocardial perfusion and arthritis imaging. We are currently conducting a Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MR angiography, or MRA, for the evaluation of peripheral vascular disease.

As a major component of our corporate strategy, we have sought to enter 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 entered into strategic alliances with Schering Aktiengesellschaft, or Schering AG, Tyco/Mallinckrodt and Daiichi Radioisotope Laboratories, Ltd., or Daiichi for the development, manufacture and commercialization of MS-325 and other vascular contrast agents. We have also formed collaborations with the three major MRI scanner manufacturers, General Electric Medical Systems, Philips Medical Systems and Siemens Medical Systems, to develop advanced imaging techniques designed to facilitate the use of MS-325-enhanced MRA. We entered into these strategic alliances and collaborations, which are described in "Strategic Alliances," and we will seek to enter into future strategic alliances and collaborations with industry leaders, in order to obtain access to resources and infrastructure to leverage our strengths.

The use of MRI has grown steadily over the past 10 years due to reduced cost and improved imaging capabilities and now provides an effective diagnostic technique, or modality, for a broad range of applications. MRI manufacturers have improved the hardware and software of their systems, reducing the time per procedure dramatically while significantly enhancing image resolution. While MRI is currently used extensively to image many organs and tissues in the body, its use in imaging the arteries and veins has been limited. Prior attempts to develop contrast agents to facilitate the clinical utility of MRI, particularly for coronary arteries, have had limited success. Unlike most currently available MRI contrast agents, which are non-specific, MS-325 is an injectable intravascular contrast agent intended to enhance the quality of MR images and provide physicians with a superior method for diagnosing diseases affecting the vasculature. MS-325 is a small molecule that produces an MRI signal because of the presence of gadolinium, a highly magnetically active element favored by clinicians for enhancing MR

images. This molecule is designed with our proprietary technology to bind to albumin, the most common blood protein. In MS-325 images using standard MRI techniques, the blood gives off a strong magnetic signal and appears bright against the dark background of surrounding tissue. Because of its affinity for albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam and therefore provides the image acquisition time and signal strength needed to obtain a high contrast, high resolution image of the cardiovascular system. Like most currently available

non-specific contrast agents, MS-325 is designed to be excreted safely through the kidneys over time. We believe that MS-325 will simplify the diagnostic pathway for a number of diseases and in many cases replace highly invasive and expensive conventional X-ray angiography.

In September 2001, we settled a longstanding patent dispute with Bracco Imaging, S.p.A., or Bracco, which is described in "Management's Discussion and Analysis and Results of Operations." Also, in January 2002, we completed an equity offering raising an additional $30.2 million.

We incorporated in Delaware in 1988 and commenced operations in 1992. Our principal executive offices are located at 71 Rogers Street, Cambridge, Massachusetts 02142-1118 and our telephone number is (617) 250-6000. Our Web site is located at http://www.epixmed.com. We do not intend for the information contained in our Web site to be considered a part of this Form 10-K.

Cardiovascular Disease

Background

The human cardiovascular system consists of the heart and a vast series of arteries and veins that carry blood throughout the body. Cardiovascular disease, a broad class of diseases affecting the heart and vasculature, is the number one cause of death in the United States, with approximately 950,000 fatalities each year. One out of every 2.5 deaths in the United States is attributed to cardiovascular disease and it is estimated that over 60 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, the renal arteries, and the large vessels of the pelvis, legs and arms. Recent research in cardiovascular disease has begun to highlight the pervasive, or multi-focal nature, of this condition. Because the major risk factors tend to affect all vascular regions, many patients have multiple clinical symptoms of cardiovascular disease. Therefore, patients diagnosed with cardiovascular disease in one vascular region are at high risk of having similar disease in another vascular region. Clinicians have also begun to realize the importance of characterizing atherosclerotic plaques once they have been identified. We believe that the ability to characterize plaques may allow physicians to identify those regions of cardiovascular disease 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 extremely severe and often include one or more of the following:

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

Aortic Aneurysm. The aorta is the main blood vessel that carries blood from the heart to the rest of the body. Degenerative changes in the vessel wall often result in the enlargement or bulging of the lower part this vessel, known as abdominal aortic aneurysm. Individuals with this condition are at serious risk that the aneurysm will rupture, causing life-threatening bleeding. There are an estimated 200,000 cases of abdominal aortic aneurysm diagnosed each year in the

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

Heart Attack 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 12.4 million Americans. Coronary heart disease is responsible for over 450,000 deaths each year, making it the number one cause of death in the United States.

Hypertension. Hypertension, or high blood pressure, refers to the constriction of blood vessels, which causes the heart to work harder to supply blood to the body. This condition, which significantly elevates an individual's risk of heart attack or stroke, afflicts approximately fifty million individuals in the United States. 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 renovascular hypertension because it can be treated with various revascularization procedures; however, conventional X-ray angiography, the current definitive diagnosis for this condition, carries elevated risk for patients with renal impairment due to the toxicity of the X-ray contrast dye.

Ischemic Stroke. Blocked arteries in the head and neck can prevent areas of the brain from receiving the necessary blood supply, potentially leading to ischemic stroke. Individuals with atherosclerosis are at 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 80% of the 600,000 strokes each year in the United States are a result of atherosclerotic disease.

Diagnosing Cardiovascular Disease

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

Screening for Peripheral Vascular Disease

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

Screening for Coronary Artery Disease

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

Stress Echocardiograms. Stress Echocardiograms use ultrasound to measure motion of the walls of the heart under physical or pharmacological stress. In most cases, a lack of blood flow to a particular area of the heart will be reflected in atypical motion of the heart wall. The test is non-invasive and costs between $200 and $900. 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 2.1 million stress echocardiograms

were performed in the United States in 2000.

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, use small quantities of radiation and cost between $300 and $1,400. A patient is injected with a radioactive agent and then a radiation sensitive camera is used to detect uptake of the agent in the heart muscle. A deficiency in blood flow to particular regions of the heart is shown in the resulting images. While the test can identify the effects of coronary artery disease, it provides no information on the anatomy of the coronary arteries and it cannot determine the location of blockages. We estimate that over five million nuclear stress perfusion studies were conducted in the United States in 2000.

Definitive Diagnosis of Plaque Blockages

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, nephrotoxic X-ray contrast 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 4.3 million X-ray angiograms were performed in the United States in 2000, of which approximately 2.1 million were coronary angiograms. X-ray angiography has a number of undesirable characteristics for a diagnostic tool including:

Invasive procedure that requires extended recovery time, and results in significant risk of serious complications including limb loss, renal failure, and death;

Exposure of patients to potentially harmful ionizing radiation;

Large volumes of nephrotoxic dye may cause severe reactions;

Separate exams necessary to view both arteries and veins;

Separate exams necessary for each vascular region;

Provides only 2-dimensional images;

Relatively expensive ($700-$3,000 for peripheral angiograms, $2,000-$6,000 for coronary angiograms);

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

Inability to characterize plaques.

Another modality currently being investigated as a potential diagnostic tool for imaging blood vessels is computed tomography, or CT, which is primarily used to image solid organs. Although it does not require an arterial puncture, CT requires the use of large quantities of toxic X-ray contrast dye and exposes patients to radiation, which limits the number of vascular regions it can image in an exam. CT has shown limited

success in imaging the coronary arteries due to cardiac motion. A specialized form of CT, electron beam CT, is approved in the United States for angiographic imaging but has had limited impact on clinical practice due to the low number of electron beam CT scanners installed and its use of toxic X-ray contrast dye and radiation. CT is also being investigated for use in detecting calcium deposits in the coronary arteries, which has been advocated as predictive of atherosclerotic disease in that region. While extremely sensitive, this technique is limited by its high level of false positives.

MRI

MRI has been established as the imaging modality 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 3-dimensional images. A contrast agent is often injected into a vein in the patient's arm prior to an MRI exam to amplify the signal from the desired anatomical structure. It is estimated that contrast agents are used in 25-30% of all MRI exams. MR scanners are characterized by the strength of the magnetic field they generate. Typical MRI scanners those most commonly found in hospitals generate a relatively strong magnetic field and therefore require significant infrastructure for installation. Low-field scanners, whose magnetic fields are less than one-third the strength of traditional scanners, are often found in out-patient settings due to their relatively low cost and infrastructure requirements. The trade-off for low-field MR scanners is that a decrease in the strength of the magnetic field results in a decrease in the MR signal detected, which typically results in reduced resolution. While the use of MRI is expanding among experts, MRI has not made a significant impact on the diagnosis of cardiovascular disease to date with the exception of cerebrovascular and carotid artery studies. Non-contrast MRI exams of the vascular system, which image blood flow rather than anatomy, are often ineffective when used in patients with cardiovascular disease, because of the minimal or turbulent blood flow associated with this condition. Even for the imaging of carotid arteries, where flow-based MRI has had some clinical impact, the lack of direct anatomic data limits the ability of MRI to provide a quantitative measurement of stenosis required for accurate diagnosis. MRI exams using existing non-specific contrast agents are limited by the rapid diffusion of the agents out of the vascular system, which reduces the time during which an image can be acquired. Consequently, many experts believe MRI contrast agents which remain in the bloodstream for extended periods of time will be necessary to obtain sufficient contrast for widespread use of MRI to image the vascular system.

Plaque Characterization

Recent research suggests that plaques associated with regions of vessel wall inflammation may be at increased risk of rupture and are consequently more likely to present immediate risk to patients. The one modality currently used to characterize the content and/or shape of arterial plaques is known as intravascular ultrasound, or IVUS. An IVUS exam requires the insertion of a relatively large catheter (i.e., larger than an X-ray angiographic catheter) equipped with an ultrasound transducer through an

arterial puncture in the femoral artery. These procedures, which are more invasive than conventional X-ray angiograms, are not commonly used in the United States due to the elevated risk of complications.

Summary

In summary, the current process for diagnosing cardiovascular disease is a complicated pathway that typically involves subjecting patients to risky and invasive procedures before a definitive diagnosis can be rendered. We therefore believe that there is significant clinical need for a highly accurate, non-invasive exam which 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 MR images and provide physicians with a superior method for diagnosing cardiovascular disease. Unlike most currently available MRI contrast agents, which are non-specific and therefore leak out of the vasculature, MS-325 binds 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 contrast, high resolution image of the cardiovascular system. These images are intended to provide sufficient anatomical detail for definitive diagnosis and surgical planning.

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

MS-325-Enhanced Angiography

We believe that MS-325-enhanced MRA will be used to diagnose cardiovascular disease and has the potential to replace a significant portion of the estimated 4.3 million conventional X-ray angiograms performed each year in the United States. 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. MS-325-enhanced MRA, on the other hand, is a non-invasive exam requiring only an intravenous injection of MS-325.

No Ionizing Radiation. MRA using MS-325 involves only safe, low-energy radio waves rather than potentially harmful ionizing radiation.

Arterial and Venous Information in a Single Exam. Due to persistence in the blood, MS-325 gives MRI the potential to capture image data of both arteries and veins in a single exam. Venographic imaging plays a crucial role in identifying veins suitable to be harvested for use in bypass grafts as well as planning the route for catheter-based interventional procedures. X-ray technology requires separate exams to image arteries and veins.

Whole-Body Imaging. Whereas X-ray angiography captures data over a limited vascular region, we expect MS-325-enhanced MRA to provide clinicians with the ability to capture images of the entire vascular system. We believe that a whole-body 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.

3-Dimensional Images. MS-325-enhanced MRA captures 3-dimensional data which can be manipulated by physicians to get the best possible view of the vessels being examined. These

3-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 an MRI exam with MS-325 will cost approximately between $500 and $1,000, roughly one-third the cost of an equivalent X-ray angiogram.

Patient Monitoring. After an intervention for cardiovascular disease such as angioplasty or bypass graft, optimal patient management could include follow-up exams, or re-looks, to determine the re-forming of blockages, or restenosis, as well as proper functioning of grafts. Due to the risk, discomfort and expense associated with X-ray angiography, follow-up imaging currently is limited, which can lead to increased patient management costs and poorer outcomes due to undiagnosed restenosis and other complications. We estimate that there are currently over 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 re-look. 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 microvessels.

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

Low-Field MR Angiography

We believe that the extended blood residence time of MS-325 will prove particularly beneficial in facilitating the use of low-field MRI scanners for diagnosing cardiovascular disease. These scanners, which account for approximately 37% of the installed base of MRI scanners, pose several potential advantages over traditional scanners: they are relatively inexpensive, they use open configurations for improved patient comfort, they can be portable, they are compatible with nearby electronic equipment, and they can enable MRI for patients with pacemakers. However, low-field scanners do not currently provide the resolution required for clinically useful vascular studies. Because of its high signal at low magnetic field strengths, MS-325 may enable low-field MRI scanners to perform high-resolution imaging of the vasculature. This would potentially allow relatively inexpensive MRI exams to be performed in 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 non-invasive, integrated cardiac exam for the diagnosis of coronary artery disease. Such a procedure would be designed to provide information on coronary artery anatomy, including location of arterial blockages, as well as cardiac perfusion and cardiac function data, in one sitting early in the diagnostic work-up. Because the procedure is intended to provide physicians with more comprehensive diagnostic information at an earlier stage of the diagnostic work-up, physicians would be able to make a more informed diagnosis, and therefore arrange for appropriate patient treatment, sooner than would otherwise be possible, thereby potentially achieving better patient outcomes at a lower cost. Of the estimated 6.75 million patients in the United States who enter the diagnostic pathway for coronary artery disease each year, we believe that over half would be candidates for such an integrated cardiac exam.

Other Cardiovascular Applications

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

Beyond Cardiovascular

MRI Additional Applications

We believe MS-325-enhanced MRA will find significant clinical utility beyond the diagnosis of cardiovascular disease. Because of its potential for high-resolution imaging of the vasculature, for example, MS-325 is being investigated for possible use in diagnosing several conditions involving damaged or abnormal microvessels. In addition, as a marker of albumin, MS-325-enhanced MRA may play a role in diagnosing conditions which result in regions of atypical albumin concentration. We are pursuing applications for MS-325 beyond cardiovascular disease in order to fully leverage the broad diagnostic potential of this technology.

Technology Platform

Background

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. The design of these molecules is derived from the unique and highly complex intersection of chemistry, pharmacology, and biophysics. 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 three areas:

Targeting

We develop metal complexes that are engineered to bind to particular proteins and receptor molecules in the body. This binding causes increased concentration and retention of the contrast agent in the specific tissues and fluids that contain the targeted receptor molecules. The challenge in designing such agents is two-fold: one must both choose the best target the protein or cell type that most precisely characterizes the relevant disease state and identify a targeting region that binds to that target without binding to other molecules in the body. The targeting region of MS-325, for example, is designed to bind selectively to albumin, the most common blood protein, which keeps the agent localized within the bloodstream. For our thrombus MR agent, we have used combinatorial chemistry technology to select a family of highly specific peptides which bind to fibrin, the dominant protein inside clots, without binding to fibrinogen, a similar, but far less clot specific protein in blood. We have considerable expertise in peptide synthesis and in labeling the peptides with strongly enhancing clusters of gadolinium.

MRI Signal Generation

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

to increase the signal from a single targeting molecule. This involves challenges in both chemistry and biophysics to maintain the RIME effect.

Image Acquisition and 3-D Visualization

We have also developed significant expertise in the translation of raw MRI data into clinically useful 3-dimensional images. MRI is the most flexible of the major medical imaging modalities. The hardware and software of most MRI scanners allow an enormous range of 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 the agents we have already designed, but is critical for optimizing the clinical usefulness of future MRI agents.

Our Product and Development Programs

MS-325

Background

Our lead product candidate, MS-325, is a targeted intravascular contrast agent intended for use with MRI. MS-325 is a small molecule chelate which produces an MRI signal because it contains gadolinium, a highly magnetically active element favored by clinicians for enhancing MR images. This molecule is designed with our proprietary technology to bind to albumin, the most common blood protein. In MS-325 images using standard MRI techniques, the blood gives off a strong magnetic signal and appears bright against the dark background of surrounding tissue. Because of its affinity for albumin, MS-325 remains at high concentrations in the bloodstream throughout the MRI exam and therefore provides the image acquisition time and signal strength needed to obtain a high contrast, high resolution image of the cardiovascular system. Like most currently available non-specific contrast agents, MS-325 is designed to be excreted safely through the kidneys over time.

Lead Indication Peripheral Vascular Disease

We are currently conducting a Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease. In June 1999, we initiated the first trial of a two-arm Phase III study designed to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease, a common peripheral vascular disease. We completed enrollment in this trial in 2001 and reported preliminary results on March 18, 2002 at the American College of Cardiology conference. We achieved the primary clinical endpoint of this trial, which was improvement in accuracy of MS-325-enhanced MRA versus that of non-contrast MRA. The trial compared with conventional X-ray angiography demonstrated that MS-325-enhanced MRA compared favorably to conventional X-ray angiography, the current reference standard, achieving 88% accuracy 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 September 2001, we expanded our Phase III clinical trial program for MS-325 in order to broaden our lead indication to peripheral vascular disease from 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 peripheral 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 peripheral vascular disease in the renal arteries, and another to determine the efficacy of MS-325-enhanced MRA for the detection of peripheral vascular disease in the feet. We expect that a broad peripheral vascular disease indication will include the entire vasculature excluding the heart and brain, thereby providing us with the potential to significantly expand the market directly addressed by MS-325.

In addition to the expansion of our Phase III clinical trial program, we have reduced the number of patients in the second Phase III aortoiliac trial based on the statistical results of a Phase II clinical trial that was completed in June 2001. 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 peripheral vascular disease in the carotid, iliac and femoral arteries. In this Phase II study, MS-325-enhanced MRA compared favorably to conventional X-ray angiography, achieving 82% accuracy versus conventional X-ray angiography in identifying clinically significant stenoses caused by atherosclerotic disease and was safe and well-tolerated by patients. In addition, we have completed two Phase I clinical trials to date; the first in February 1997, and the second in February 1998.

Coronary Artery Disease

We are currently conducting a Phase II feasibility trial to test the safety and preliminary efficacy of MS-325-enhanced MRA for the evaluation of coronary artery disease. This trial is being conducted at multiple sites. As with the completed first arm of the Phase III aortoiliac trial and the Phase II peripheral vascular disease trial, our trial compares MS-325-enhanced MRA to X-ray angiography, the current reference standard, to determine the location and degree of plaque blockages. Clinical use of MRA for imaging the coronary arteries is particularly difficult at present due to the problem of cardiac motion which results from both the beating of the heart and respiration. We have joined with several leading MRI manufacturers, academic centers and other research organizations to develop hardware and software solutions to the problem of cardiac motion. We received promising early images from this study which indicate that MS-325 may be useful in assessing coronary artery blockages.

Potential Additional Applications

We are currently evaluating results from clinical and preclinical studies performed in the following areas to determine the potential utility of MS-325 for additional applications:

Breast Cancer

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

Female Sexual Arousal Dysfunction

In March 2001, we completed enrollment in a Phase II feasibility trial, which we conducted in collaboration with Pfizer, Inc. to explore the efficacy of MS-325-enhanced MRA in the diagnosis of female sexual arousal dysfunction. Preliminary results from this trial indicate that MS-325-enhanced MRA is able to measure changes in pelvic blood volume and organ volume during sexual arousal. We believe that this technique may prove useful in assessing how different diseases affect sexual response in women as well as examining the effects of potential treatments in restoring impaired sexual response.

Myocardial Perfusion

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

Arthritis

We are currently evaluating results from a preclinical study in a rabbit model that has shown promise in both demonstrating high-contrast images delineating synovium and joint effusion separately in inflammatory arthritis, as well as monitoring disease progression in longitudinal study of rheumatoid arthritis.

Prototype Clot Imaging Agent

Background

Thromboembolic disease refers to a class of relatively common disorders involving the formation of blood clots or, thrombi, in the veins and arteries. The most common form of this disease, deep vein thrombosis, or DVT, is characterized by the presence of thrombi in the deep veins of the leg and calf. This disease afflicts approximately two million Americans each year. The most severe consequences of DVT tend to occur when a thrombus dislodges from the vessel wall to form an embolus, which can then pass to and obstruct arteries in the lung. This condition, known as pulmonary embolism, or PE, affects an estimated 600,000 patients each year in the United States. In addition, blood clots in the carotid artery can lead to stroke, while clots in the coronary arteries can result in heart attack. We estimate that blood clots are responsible for over 400,000 deaths each year in the United States. The current method for diagnosing DVT involves a series of venous ultrasound exams typically followed by X-ray venography. The ultrasound procedure, while non-invasive, is effective primarily for diagnosing DVT in the thighs. It is ineffective for a significant portion of the patient population who may be asymptomatic and those who have clots forming below the knee, in the pelvis and in the vena cava. It is estimated that over 2.7 million ultrasound procedures are performed each year in the United States to detect DVT, which represents the current gold standard for diagnosis, requires the injection of X-ray contrast dye into the foot and carries a significant risk of complications, including the formation of new clots. The diagnosis of PE presents an even greater challenge for clinicians. In fact, research suggests that this diagnosis is missed more than 50% of the time. The primary diagnostic technique for PE, a nuclear scan, is indeterminate in a large number of patients. Nearly one million such exams were performed in the United States in 2000. In the event of an indeterminate exam, the clinician must either infer the diagnosis from the presence/absence of DVT or must perform a pulmonary angiogram. Pulmonary angiography is a highly invasive catheter-based procedure which subjects the patient to significant risk of morbidity and mortality. Clots in the carotid and coronary arteries are diagnosed in much the same way as atherosclerotic blockages, with X-ray angiography providing definitive diagnosis in most patients.

Thrombus Development Program

We are seeking to develop a targeted contrast agent that would enable MRI to illuminate blood clots. Such a product could potentially change the diagnostic work-up for many of the conditions associated with thromboembolic disease, including PE and DVT. We believe that the use of this new

approach could lead to better medical outcomes due to earlier and more definitive diagnosis. Early diagnosis is especially important for clots in the thigh, pelvis and vena cava. Because of their increased likelihood of migrating to the lungs once inside the pulmonary vasculature, these clots can be fatal. We believe that such a contrast agent could eliminate the need for the CT, ultrasound and nuclear medicine studies currently used to identify thrombotic disease, and could potentially provide a non-invasive but clinically equivalent alternative to pulmonary angiography. Further, 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. Our prototype clot-imaging agent is based on a family of highly specific peptides that bind to fibrin, the dominant protein inside clots. The selected peptide is linked to a proprietary gadolinium group, which for the first time, will provide a sufficiently strong signal to allow imaging of clots during MRI exams. In November 1999, we announced that a prototype agent, EP-862, had been shown in preclinical testing, to detect sub-millimeter blood clots in an animal model. We are continuing to advance this program, having identified several improved prototype agents. We expect to continue to devote significant resources to this program in the future and hope to file an Initial New Drug, or IND, application with the FDA which, if approved, will allow us to begin human safety trials.

Our Business Strategy

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

Establish the safety and clinical utility of MS-325 for our lead cardiovascular imaging indication of peripheral vascular disease. As previously discussed in the section "Our Product and Development Programs," "Lead Indications Peripheral Vascular Disease" we are currently conducting a Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease.

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

Establish the clinical utility of MS-325 beyond cardiovascular imaging. We are committed to leveraging the unique diagnostic properties of MS-325 across as many clinical applications as possible. We are therefore seeking to establish the clinical utility of MS-325-enhanced MRA in diagnosing conditions other than cardiovascular disease. In March 2000, we completed enrollment for a Phase II feasibility study designed to evaluate the safety and efficacy of MS-325-enhanced MRA in identifying malignant breast lesions in women with breast abnormalities. In March 2001, we completed enrollment in a Phase II feasibility trial, in conjunction with Pfizer Inc., to assess the potential utility of MS-325-enhanced MRA in diagnosing female sexual arousal dysfunction by monitoring pelvic blood volume in women. We are also currently evaluating a preclinical study to investigate the potential use of MS-325-enhanced MRA for arthritis.

Develop an MRI imaging agent for thromboembolic disease imaging. We are currently developing thrombosis-specific MRI contrast agents based on our proprietary technology platform, and we hope to file an IND application with the FDA which, if approved, will allow us to begin human safety trials.

Maximize the value of strategic alliances. We have established collaborations with Schering AG, Tyco/Mallinckrodt, General Electric Medical Systems, Philips Medical Systems, Siemens Medical

Systems, and Pfizer. We entered into these alliances, and will seek to enter into future strategic alliances with pharmaceutical, imaging agent and MRI equipment industry leaders, in order to obtain access to resources and infrastructure to leverage our strengths. See "Strategic Alliances and Collaborations."

Strategic Alliances and Collaborations

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

Co-Development, Sales & Marketing

Schering AG

In June 2000, we entered into a strategic collaboration agreement 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 United States. Schering AG will lead clinical activities for the product outside the United States. In addition, we granted Schering AG an exclusive option to develop and market 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 withTyco/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 $20.0 million in milestone payments under the strategic collaboration agreement, of which $2.5 million will be earned upon NDA filing and up to $2.5 million will be earned upon product approval. Under the terms of the December 2000 amendment, Schering AG paid us an up-front fee of $3.0 million and may be required to pay us an additional $7.0 million upon our achievement of certain milestones.

Also, under the strategic collaboration agreement, we have options to acquire certain participation rights with respect to two of Schering AG's products currently in clinical trials, SHU 555C and Gadomer-17. We are entitled to exercise these options on a region-by-region basis upon the payment of certain fees. We are entitled to exercise the SHU 555C option for a period of twelve months after the date the option becomes exercisable. Once we exercise the SHU 555C option, we 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. We are entitled to exercise the Gadomer-17 option for a period of 120 days following Schering AG's performance of certain milestones.

Once we exercise the Gadomer-17 option, we will enter into a definitive agreement with Schering AG with respect to Gadomer-17, pursuant to which we will share development costs incurred from the date of the option exercise, as well as profits, equally with Schering AG. Under the terms of the strategic collaboration agreement, either party may terminate the agreement upon thirty days notice if there is a material breach of the contract or if either party fails to meet certain milestones. In addition, Schering AG may terminate the agreement at any time on a region-by-region basis or in its entirety, upon six months written notice to us; and we may terminate the agreement with respect to development of MS-325 in the European Union, or EU, at any time after June 9, 2001 upon ninety days written notice to Schering AG, if Schering AG has failed to meet its obligations in connection with the regulatory approval of MS-325 in the EU.

On May 8, 2000, we granted to Schering AG a worldwide, royalty-bearing license to patents covering Schering AG's development project, Eovist injection, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 8, 2000, Schering AG granted us a non-exclusive, royalty-bearing license to certain of its Japanese patents. We agreed to withdraw our invalidation claim of Schering AG's Japanese patent 1,932,626 in the Japanese Patent Office pursuant to this license agreement. See "Patents and Proprietary Rights." Schering AG had been an opposing party in our European patent case prior to the licensing agreement. On May 9, 2000, the Opposition Division of the European Patent Office maintained our European patent in a slightly amended form. The patent is owned by the Massachusetts General Hospital 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 such 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 may pay up to an additional $5.0 million in milestone payments, of which $2.5 million will be paid upon NDA filing and $2.5 million will be paid upon product approval. We will also pay Tyco/Mallinckrodt a share of our MS-325 operating profit margins in the US and a royalty on MS-325 gross profits outside the US, except in Japan where no payments are due Tyco/Mallinckrodt.

In October 1999, we entered into a Non-Negotiable Promissory Note and Security Agreement, or the Loan, 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. 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 balance due under the Loan as of December 31, 2000 and 2001 was $3,004,607 and represents our share of the third and fourth quarter MS-325 development costs in 1999. No additional funding is available to us under the Loan. The Loan bears interest, adjustable on a quarterly basis, at the Prime Rate published in the Wall Street Journal and is repayable in full on October 1, 2002. The loan is secured by a first priority security interest in all of our intellectual property.

Daiichi

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

our reacquisition from Daiichi of the MS-325 development and marketing rights in Japan, we assigned these rights to Schering AG as described above.

MRI Equipment Manufacturers

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

General Electric Medical Systems

In January 1998, we announced the formation of a collaboration with General Electric Medical Systems to accelerate the development of cardiovascular MRI. In particular, the collaboration focuses on reducing the effects of cardiac motion on MR images, providing user-friendly computer tools as a means of visualizing arteries and veins in 3-dimensional space and optimizing MRI sequences for intravascular MRI contrast agents, including MS-325. Under the terms of this non-exclusive agreement, research is performed at several centers in addition to our facilities, including General Electric's corporate research facility in Schenectady, NY; General Electric Medical Research in Milwaukee, WI, 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 and Philips Medical Systems will combine our resources to optimize imaging technology and improve 3-dimensional visualization of arteries and veins in patients undergoing MR angiography. Research and development is being carried out at several international Philips research centers, as well as at our facilities.

Siemens Medical Systems

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

Potential New Applications

Pfizer

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

Competition

The healthcare industry is characterized by extensive research efforts and rapid technological change and there are many companies that are working to develop products similar to ours. There are currently no FDA-approved targeted vascular contrast agents for use with MRI. However, there are a number of non-specific MRI agents approved for marketing in the United States and in certain foreign markets that are likely to compete with MS-325 if approved for MR angiography. Such products include Magnevist® by Schering-AG, Dotarem® by Guerbet, S.A., Omniscan® by Nycomed Imaging ASA or Nycomed, ProHance and MultiHance® by Bracco and OptiMARK by Tyco/Mallinckrodt. We are aware of six agents under clinical development, Nycomed's NC100150, Schering AG's Gadomer-17, SHU555C, Guerbet's P792, or 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 can not assure you that our competitors will not succeed in the future in developing products that are more effective than any that we are developing. We believe that our ability to compete within the MRI contrast agent market is dependent on a number of factors including the success and timeliness with which we complete FDA trials, the breadth of applications, if any, for which our products receive approval, and the effectiveness, cost, safety and ease of use of our products in comparison to the products of our competitors. Our success will also be dependent 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. Several other nuclear medicine agents, including Draxis Health's FibrImage® and Schering AG's P748, are in clinical testing for DVT and PE, respectively. We believe another radiopharmaceutical under clinical development by Schering AG, P-773, is being investigated for use in imaging atherosclerotic plaque. In addition, while no ultrasound contrast agent has yet been approved for myocardial perfusion imaging, several of these agents are undergoing clinical testing for this indication, including, DuPont's Definity, Alliance Pharmaceutical's Imagent, and Nycomed's Sonazoid and Optison. Finally, we are aware of one ultrasound agent, ImaRx's MRX-408, under preclinical development for imaging DVT. We cannot guarantee that we will be able to compete successfully in the future or that developments by others will not render MS-325, or our future product candidates obsolete or non-competitive or that our collaborators or customers will not choose to use competing technologies or products.

Patents and Proprietary Rights

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

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

Two U.S. patents exclusively licensed from MGH as well as their cognate patents and applications in foreign countries. Five additional patents that had been exclusively licensed to Epix from MGH have been transferred back to MGH.

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

Eight utility applications in prosecution and four provisional utility applications on twelve different subject matters as well as their cognate patents and applications in foreign countries.

Our two licensed U.S. patents which broadly cover RIME technology, albumin binding with metal chelates, and liver targeting metal chelates, have been issued a patent in Europe similar to those United States patents, and have received notice of allowance for a similar patent application in Japan. These two United States patents were involved in an interference proceeding with an application owned by Tyco/Mallinckrodt, but the interference was terminated in our favor. Our Japanese patent application had been opposed. The sole issue in these proceedings is whether the Japanese Patent Office should have granted and/or allowed patents to us.

The legal proceedings between Bracco, Schering AG and others against us and MGH involving national patents derived from European Patent 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 222,886 and its worldwide counterparts was executed on September 25, 2001. We received various payments, including royalties on a quarterly basis pursuant to the license with Bracco, which is described in "Management's Discussion and Analysis and Results of Operations." Previously, on May 7, 2000, we granted to Schering AG a worldwide royalty-bearing license to our patents covering Schering AG's development project, Eovist®, an MRI contrast agent for imaging the liver, currently in Phase III clinical trials. Also on May 7, 2000, Schering AG granted us a non-exclusive royalty-bearing license to its Japanese patents, 1,932,626, 1,968,413 and its Japanese Application, WO99/16474. We have agreed to withdraw our invalidation claim of Schering AG's Japanese patent, 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, there are currently no legal actions involving this patent family.

We have received an additional United States patent covering novel metal chelates. We have also received a patent in the United States covering the process by which MS-325 is manufactured (U.S. Patent Number 5,919,967; granted July 6, 1999; expires April 11, 2017). Finally, we have patent applications pending in the United States, Japan and Europe covering various aspects of our RIME technology. Our patent protection for MS-325 currently extends to 2006 in the United States and Europe. If the currently pending patent applications issue, this protection will be extended until 2015. Protection for the manufacturing process in the United States is already extended until 2017, and will be extended until 2017 in Europe and Japan if the currently pending patent applications issue. In addition, during 1999 and early 2000 we filed four new patent applications for additional products and processes involving compounds, compositions, and methods for imaging. In 2001, we filed

one patent application and four provisional patent applications.

An issued patent grants to the owner the right to exclude others from practicing inventions claimed therein. In the United States, a patent filed before June 8, 1995 is enforceable for 17 years from the date of issuance or 20 years from the deemed date of filing the underlying patent applications, whichever is longer. Patents based on applications filed from June 8, 1995 expire 20 years from the deemed date. The General Agreement on Tariffs and Trade provides that patents whose

applications were filed on or after June 8, 1995 are effective for 20 years from filing. This new rule is generally regarded as unfavorable to pharmaceutical companies, where the time period between patent filing and commercialization of the patented product may be extended many years because of the lengthy development cycle and regulatory process.

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

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

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

Many of our competitors are continuing to actively pursue patent protection for activities and discoveries similar to ours. There can be no assurance that these competitors, many of which have substantially greater resources than us and have made substantial investments in competing technologies, will not in the future seek to assert that our products or chemical processes infringe their existing patents and/or will not seek new patents that claim to cover aspects of our technology. Furthermore, patent applications in the United States, 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 and MGH have entered into a license agreement pursuant to which MGH has granted us an exclusive worldwide license to the patents and patent applications, which relate to our only product candidate, MS-325. The MGH license imposed certain due diligence obligations with respect to the development of products covered by the license, all of which have been fulfilled to date. The MGH license requires us to pay royalties on our net sales of MS-325. We must also pay MGH a percentage of all royalties received from our sublicensees. Accordingly, we will be required to make payments to MGH on profits generated under the Schering collaboration, if any. Our failure to comply with these requirements could result in the conversion of the license from being exclusive to non-exclusive in nature or termination of the license agreement itself. Any such event would have a material adverse effect on our business, financial condition and results of operations.

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

operations.

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

Manufacturing

We do not have, nor do we currently have plans to develop, full-scale manufacturing capability for MS-325. We intend to rely on Tyco/Mallinckrodt as the primary manufacturer of MS-325 for Phase III clinical trials, as well as for any future human clinical trials and commercial use. In the event that Tyco/Mallinckrodt fails to fulfill its manufacturing responsibilities satisfactorily, Schering AG has the right to purchase MS-325 from a third party or to manufacture the compound itself. However, either course of action could materially delay the manufacture and development of MS-325, 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 our product candidates are subject to extensive governmental regulation in the United States and other countries. Pharmaceuticals, including contrast-imaging agents for use with MRI, are regulated in the United States by the FDA under the Food, Drug and Cosmetic Act, 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 United States, a company seeking approval to market a new pharmaceutical must obtain FDA approval of a new drug application, or

NDA. Before an NDA may be filed, however, a certain procedure is typically followed. This includes: (i) performance of preclinical laboratory and animal studies; (ii) submission to the FDA of an application for an IND, which must become effective before human clinical trials may commence; (iii) completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the pharmaceutical for its intended use; (iv) submission to the FDA of an NDA; and (v) approval of the NDA by the FDA prior to any commercial sale or shipment of the agent. In November 1997, the Food and Drug Administration Modernization Act of 1997, or the Act, was passed and signed into law. The Act, most of which became effective in February 1998, promises, among other things, to streamline the approval process for drugs and enable patients with serious diseases to more easily access experimental products. The effect, if any, of the Act on us, MS-325 and our other product candidates is not known at this time.

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

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

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

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

NDA will be required to gain approval for the use of an approved product in indications other than those for which the NDA was approved initially.

After an NDA is approved, we would continue to be subject to pervasive and continuing regulation by the FDA, including record keeping requirements, reporting of adverse experience from the use of the agent and other requirements imposed by the FDA. FDA regulations also require FDA approval of an NDA supplement for certain changes if they affect the safety and efficacy of the pharmaceutical, including, but not limited to, new indications for use, labeling changes, the use of a different facility to manufacture, process or package the product, changes in manufacturing methods or quality control systems and changes in specifications for the product. Our failure to receive approval of an NDA supplement could have a material adverse effect on our business, financial condition and results of operations. The advertising of most FDA-regulated products is subject to FDA and Federal Trade Commission jurisdiction, but the FDA has sole jurisdiction over advertisements for prescription drugs. We are and may be subject to regulation under state and Federal law regarding occupational safety, laboratory practices, handling of chemicals, environmental protection and hazardous substance control. We also will be subject to 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 United States are subject to regulatory requirements that vary widely from country to country. In the EU, the general trend has been towards coordination of common standards for clinical testing of new agents, leading to changes in various requirements imposed by each EU country. The level of regulation in the EU and other foreign jurisdictions varies widely. The time required to obtain regulatory approval from comparable regulatory agencies in each foreign country may be longer or shorter than that required for FDA approval. In addition, in certain foreign markets we may be subject to governmentally mandated prices for our products.

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. For example, Medicare pays hospitals a prospectively determined amount for an in-patient stay based on a Medicare

beneficiary's discharge diagnosis related group, or DRG. This payment 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. In 2001, the Centers for Medicare and Medicaid Services (formerly HCFA) created additional payment categories for contrast- enhanced diagnostic procedures performed in outpatient settings, thus improving the reimbursement situation for such agents. Certain new contrast agents may be eligible for additional pass-through payments. 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 United States over the next decade. We believe that the managed care approach to healthcare and the growth in capitated arrangements and other arrangements under which the providers are at financial risk for the services that are provided to their patients will facilitate the market acceptance of our products, as we believe that the use of our products will significantly lower the overall costs and improve the effectiveness of managing patient populations. We cannot assure you, however, that our products will be available, will lower costs of care for any patients or that providers will choose to utilize them even if they do, or if reimbursement will be available.

In foreign markets, reimbursement is obtained from a variety of sources, including governmental authorities, private health insurance plans and labor unions. In most foreign countries, there are also private insurance systems that may offer payments for alternative therapies. Although not as prevalent as in the United States, 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 United States and in foreign markets. We believe that the overall escalating cost of medical products and services has led to, and will continue to lead to, increased pressures on the health care industry, both foreign and domestic, to reduce the cost of products and services, including products offered by the Company. There can be no assurance, in either the United States or foreign markets, that third party reimbursement will be available or adequate, that current reimbursement amounts will not be decreased in the future or that future legislation, regulation, or reimbursement policies of third-party payors will not otherwise adversely affect the demand for our product candidates or our ability to sell our product candidates on a profitable basis, particularly if MRI exams enhanced with our contrast agents are more expensive than competing vascular imaging techniques that are equally effective. The unavailability or inadequacy of third-party payor coverage or reimbursement could have a material adverse effect on our business, financial condition and results of operations.

Employees

As of December 31, 2001 we employed 88 persons on a full-time basis, of which 65 were involved in research and development and 23 in administration and general management. Twenty seven of our employees hold Ph.D. or M.D. degrees. We believe that our relations are good with all of our employees. None of our employees are a party to a collective bargaining agreement.

Research and Development

During the years ended December 31, 2001, 2000, and 1999, we incurred research and development expenses of $22,903,780, $25,833,243 and $14,667,370 respectively.

Risk Factors

The risks and uncertainties described below are those that we currently believe may materially affect our company. Additional risks and uncertainties that we are unaware of or that we currently deem immaterial also may be important factors that affect our Company.

All of our product candidates are in research or development and we have not generated revenues from commercial sales of our products.

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

We anticipate future losses and may never become profitable.

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of December 31, 2001 were approximately $92.0 million. These losses have resulted primarily 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 increase significantly in the future, and we expect to incur substantial losses over at least the next several years. We may never generate revenues from the sale of our products. Moreover, even if we generate product revenues, we may not be able to achieve or sustain profitability.

Our financial results fluctuate quarterly, which could negatively affect our stock price.

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

the timing of fees and milestone payments that we receive from strategic partners;

whether we form new strategic alliances;

the timing of expenditures in connection with research and development activities, including clinical trials;

the timing of product introductions and associated launch, marketing and sales activities; and

the timing and extent of product acceptance for different indications and geographical areas of the world.

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

For the forseeable future, we will depend on our only product candidate, MS-325, for revenues.

MS-325 is currently our only product candidate in human clinical trials and we can not guarantee that any of our other development projects will yield a product candidate suitable for entry into clinical trials. As a result, our initial revenues and profits, if any, will be derived

from sales of MS-325. If MS-325 fails to achieve regulatory approval and market acceptance, our business, financial condition and results of operations will be materially adversely effected.

Because development of our targeted contrast agents will involve a lengthy and complex process, we are not certain that we will be able to commercialize any of our product candidates currently in development.

Our product candidates are currently in research and development and will require additional research and development, extensive clinical testing and regulatory approval prior to any commercial sales. We cannot predict if or when we will be able to commercialize any of our product candidates under development. We must complete clinical trials in the United States and demonstrate the safety and efficacy of MS-325, currently in Phase III clinical trials, prior to obtaining Food and Drug Administration approval. Our clinical trials may not be successful and we may not complete them in a timely manner. We could report serious side effects as the clinical trial proceeds. Our results from early clinical trials may not predict results that we will obtain in large scale clinical trials, as a number of companies have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. We may not conduct additional Phase II or Phase III clinical trials for MS-325 and such trials, if begun, may not demonstrate any efficacy or will be completed successfully in a timely manner, if at all. The rate of completion of our clinical trials depends upon, among other things, the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the clinical protocol under which MS-325 will be studied, the proximity of the patient to a clinical site and the eligibility criteria for the study. Delays in planned patient enrollment may result in increased costs, regulatory filing delays, or both. Furthermore, we, the FDA or other regulatory authorities may alter, suspend or terminate clinical trials at any time. If we do not successfully complete clinical trials, we will not have a product to market.

If MRI manufacturers are not able to enhance their hardware and software, we will not be able to market our contrast agents for cardiac indications.

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

If MRI technology becomes obsolete, we will not have a market for our product candidates.

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

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

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

safety;

price;

ease of administration;

effectiveness; and

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

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

Our competitors 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. Many of these competitors have substantially greater capital and other resources than we have and may represent significant competition for us. These companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. In addition, these companies may be more successful than we are in developing, manufacturing and marketing products. Our strategic partners or customers may choose to use competing technologies or products. As a result, we may not be able to compete successfully in the future.

We depend on exclusively licensed technology from the Massachusetts General Hospital and if we lose this license, it is unlikely we could obtain this technology elsewhere.

Under the terms of a license agreement that we have with MGH, we are the exclusive licensee to certain technology, including patents and patent applications, which relate to our product candidates, including MS-325. The license agreement imposes various commercialization, sub-licensing, royalty and other obligations on us. If we fail to comply with these and other requirements our license could convert from exclusive to non-exclusive or terminate entirely. It is unlikely that we would be able to obtain this technology elsewhere. Any such event would have a material adverse effect on our business, financial condition and results of operations.

We depend on our strategic collaborators for support in product development and the regulatory approval process, and these efforts may suffer if we experience problems with our collaborators.

We depend on strategic collaborators for support in product development and the regulatory approval process as well as a variety of other activities including manufacturing, marketing and distribution of our products in the United States and abroad, when and if the FDA and corresponding foreign agencies approve our product candidates for marketing. To date, we have entered into several strategic alliances, including a collaboration agreement with Schering AG, to develop and commercialize MS-325 and other MRI vascular agents worldwide and an agreement with Tyco/Mallinckrodt, granting Tyco/Mallinckrodt rights to enter into an agreement with Schering AG to manufacture MS-325 for clinical development and commercial use. We may not receive milestone payments from these alliances should MS-325 fail to meet certain performance targets in clinical trials. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development, and commence marketing, of MS-325 in their respective territories, or they may not successfully market MS-325. Schering AG and Mallinckrodt currently manufacture imaging agents for other modalities that will compete against MS-325. Schering AG will be responsible for setting the price of the product worldwide. However, Schering AG may not set prices in a manner that maximizes revenues for us. Our failure to receive milestone payments, a reduction or discontinuance of efforts by our partners, or the termination of these alliances would have a material adverse effect on our business, financial condition and results of operations.

We may not successfully enter into additional strategic alliances for the development and commercialization of future product candidates. In addition, any future alliances may not be on terms favorable to us or may not be successful. If we are unable to enter into future strategic alliances with capable partners on commercially reasonable terms, we may delay the development and commercialization of future product candidates and could possibly postpone them indefinitely.

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

The protection of our proprietary technologies is material to our business prospects. We pursue a comprehensive patent program for our product candidates in the United States and in other countries where we believe that significant market opportunities exist. We own or have an exclusive license to patents and patent applications on the critical aspects of our core technology as well as many specific applications of this

technology. However, the patent positions of pharmaceutical and biopharmaceutical firms, including us, generally include complex legal and factual questions. The issued patents that we own or license, or any patents that we obtain in the future, may not effectively protect our technology or provide a competitive advantage. In addition, any of our patents, patent applications or licensed patents may be challenged, invalidated or circumvented in the future.

Many of our competitors actively pursue patent protection for activities and discoveries similar to our activities and discoveries. These competitors, many of which have made substantial investments in competing technologies, could seek to assert that our products or chemical processes infringe on their existing patents and/or will seek new patents that claim to cover aspects of our technology. Furthermore, patent applications in the United States are maintained in secrecy until patents are issued, and patent applications in foreign countries are maintained in secrecy for a specified period after filing. Publication of discoveries in the scientific or patent literature tends to lag behind actual discoveries and the filing of related patent applications. In addition, patents issued and patent applications filed relating to pharmaceuticals are numerous. Therefore, we may not be aware of all competitive patents, either pending or issued, that relate to our product candidates or processes used or those products or processes that we propose to use. If our patents fail to protect our business, we may not be able to compete effectively.

We may incur substantial costs as a result of litigation or other proceedings relating to our patent and other intellectual property rights.

The pharmaceutical and biotechnology industries are characterized by extensive litigation regarding patents and other intellectual property rights. We intend to protect and defend our intellectual property vigorously. We may need to bring costly and time-consuming litigation to enforce our issued patents, to protect our trade secrets and know-how, or to determine the enforceability, scope and validity of the proprietary rights of others. We may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office or by foreign agencies to determine the priority of inventions. Any litigation surrounding these issues could result in extensive costs to us as well as be a significant distraction for management. Such costs could have a material adverse effect on our business, financial condition and results of operations.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We typically require our employees, consultants and advisors to execute confidentiality and assignment of invention agreements in connection with their employment, consulting or advisory relationships with us. These agreements could be breached or we may not have adequate remedies for any breach. Furthermore, our competitors could independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our proprietary technology, and we might not be able to meaningfully protect our rights in unpatented proprietary technology. Several of our management and scientific personnel were formerly associated with other pharmaceutical and biotechnology companies and academic institutions. In some cases, these individuals are conducting research in similar areas with which they were involved prior to joining us. As a result, we, as well as these individuals, could be subject to claims of violation of trade secrets and similar claims.

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

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

We are subject to extensive U.S. and foreign governmental regulatory requirements and lengthy approval processes for our product candidates. The development and commercial use of our product candidates will be regulated by numerous federal, state, local and foreign governmental authorities in the U.S., including the FDA and foreign regulatory agencies abroad. The nature of our research and development and manufacturing processes requires the use of hazardous substances and testing on certain laboratory animals. Accordingly, we are subject to extensive federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials and wastes, as well as the use of and care for laboratory animals. Although we believe we are in compliance with all such laws and maintain policies and procedures to ensure that we remain in compliance, it is possible that accidents will happen that would expose us to legal risk and/or financial loss. Furthermore, current laws could change and new laws could be passed that may force us to change our policies and procedures, an event which could impose significant costs on us.

The regulatory approval process for new MRI contrast agents, including required pre-clinical studies and clinical trials, is lengthy and expensive. Although some of our employees have experience in

obtaining regulatory approvals, we have only limited experience in filing or pursuing applications necessary to gain regulatory approvals. 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 can not be sure as to the length of the clinical trial period or the number of patients that will be required to be tested in the clinical trials in order to establish the safety and efficacy of MS-325 or any of our future product candidates. We may encounter unanticipated delays or significant costs in our efforts to secure necessary approvals. We may not obtain regulatory approval, even after the performance of clinical trials and the passage of time and the expenditure of such resources, for MS-325 or any other product candidates that we develop. Our analysis of data obtained from pre-clinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent FDA regulatory approval. Future United States legislative or administrative actions also could prevent or delay regulatory approval of our product candidates. Even if we obtain regulatory approvals, they may include significant limitations on the indicated uses for which we may market a product. A marketed product also is subject to continual FDA and other regulatory agency review and regulation. Later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market, as well as possible civil or criminal sanctions. Further, many academic institutions and companies conducting research and clinical trials in the MRI contrast agent field are using a variety of approaches and technologies. If researchers obtain any adverse results in pre-clinical studies or clinical trials, it could adversely affect the regulatory environment for MRI contrast agents generally. In addition, if we obtain marketing approval, the FDA may require post-marketing testing and surveillance programs to monitor the product's efficacy and side effects. Results of these post-marketing programs may prevent or limit the further marketing of the monitored product.

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

If we do not raise additional funds necessary to fund our operations, we may not be able to implement our business plan.

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

the progress and scope of clinical trials;

the timing and costs of filing future regulatory submissions;

the timing and costs required to receive both United States and foreign governmental approvals;

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

the extent to which our products gain market acceptance;

the timing and costs of product introductions; the extent of our ongoing research and development programs;

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

the costs of developing marketing and distribution capabilities.

Additional financing may not be available on terms acceptable to us, or at all. If we cannot fund our capital requirements, it would have a material adverse effect on our business, financial condition and results of operations. If adequate funds are not available, we may have to curtail operations significantly or obtain funds by entering into arrangements with strategic partners or others that may require us to relinquish rights to certain of our technologies, product candidates, products or potential markets. To the extent that we raise additional capital through the sale of equity or securities convertible into equity, the issuance of such securities could result in dilution to our existing stockholders.

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

We do not have, nor do we currently have plans to develop, full-scale manufacturing capability for MS-325. While we do manufacture small amounts of MS-325 for research and development efforts, we intend to rely on Tyco/Mallinckrodt as the primary manufacturer of MS-325 for Phase III clinical trials, as well as for any future human clinical trials and commercial use. In the event that Tyco/Mallinckrodt fails to fulfill its manufacturing responsibilities satisfactorily, Schering AG has the right to purchase MS-325 from a third party or to manufacture the compound itself. However, either course of action could materially delay the manufacture and development of MS-325. Schering AG may not be able to find an alternative manufacturer. In addition, Schering AG may not be able to manufacture MS-325 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.

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

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

If we fail to get adequate levels of reimbursement from third party payors for our product candidates after they are approved in the U.S. and abroad, we will not be able to commercialize our product candidates.

We could be adversely affected by changes in reimbursement policies of governmental or private healthcare payors, particularly to the extent any such changes affect reimbursement for procedures in which our product candidates would be used. Failure by physicians, hospitals and other users of our products to obtain sufficient reimbursement from third-party payors for the procedures in which our products would be used or adverse changes in governmental and private third-party payors' policies toward reimbursement for such procedures would have a material adverse effect on our business,

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

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

Our future business and operating results depend in significant part upon the continued contributions of our key technical and senior management personnel, many of whom would be difficult to replace and some of whom perform important functions for us beyond those functions suggested by their respective job title or description. Our future business and operating results also depend in significant part upon our ability to attract and retain qualified management, operational and technical personnel. Competition for this personnel is intense, and we may not be successful in attracting or retaining such personnel. Although we maintain key life insurance on the lives of some key officers, the loss of any key employee, the failure of any key employee to perform in his or her current position, or our inability to attract and retain skilled employees, as needed, could have a material adverse effect on our business, financial condition and results of operations.

Future issuances and sales of shares of our common stock upon the exercise of options may result in dilution of our common stock.

Dilution is likely to occur upon exercise of outstanding stock options.

We do not intend to pay cash dividends on our common stock.

We have not paid cash dividends since our inception and do not intend to pay cash dividends in the foreseeable future. Therefore, you will have to rely on appreciation in our stock price in order to achieve a gain on your investment.

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. For example, we are subject to Section 203 of the General Corporation Law of the State of Delaware which, subject to certain exceptions, restricts certain transactions and business combinations between a corporation and a stockholder owning 15% or more of the corporation's outstanding voting stock for a period of three years from the date the stockholder becomes an interested stockholder. These provisions may have the effect of delaying or preventing a change of control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

ITEM 2. PROPERTIES

We lease a total of 22,950 square feet of space at 71 Rogers Street and adjacent locations, and 13,310 square feet at 161 First Street, all in Cambridge, Massachusetts. The current leases at 71 Rogers Street and adjacent locations, and our lease at 161 First Street run until December 31, 2002. We have an option to extend the lease at 71 Rogers Street and adjacent locations for an additional three or five years. Our current facilities are adequate to meet our needs until the expiration of the leases in December 31, 2002. We are currently involved in negotiating extensions for our current facilities.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings that would materially adversely affect our business, results of operations or financial condition.

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, 2001.

PART II

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

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

	High	Low
2000		
First Quarter	$ 26.75	$ 8.88
Second Quarter	22.63	12.75
Third Quarter	18.94	13.19
Fourth Quarter	14.06	4.88
2001		
First Quarter	$ 13.63	$ 8.03
Second Quarter	12.35	7.10
Third Quarter	12.26	7.02
Fourth Quarter	14.60	6.24

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

On March 21, 2002, the last reported bid for the Common Stock was $14.15 per share. As of March 21, 2002, there were approximately 91 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,				
	2001	2000	1999	1998	1997
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenues	$ 9,569	$ 6,924	$ 1,144	$ 1,781	$ 4,228
Operating loss	(18,841)	(23,745)	(17,935)	(15,825)	(7,462)
Loss before provision for income taxes	(18,156)	(22,957)	(16,983)	(13,998)	(6,112)
Provision for income taxes	1,092				
Loss before cumulative effect of change in accounting principle	(19,248)	(22,957)	(16,983)	(13,998)	(6,112)
Cumulative effect of change in accounting principle (1)		(4,363)			
Net loss	$ (19,248)	$ (27,320)	$ (16,983)	$ (13,998)	$ (6,112)
Weighted average common shares outstanding:					
Basic	14,007	12,445	11,556	11,354	8,333
Diluted	14,007	12,445	11,556	11,354	8,333
Loss per share:					
Loss before cumulative effect of change in accounting principle	$ (1.38)	$ (1.85)	$ (1.47)	$ (1.23)	$ (0.73)
Cumulative effect of change in accounting principle		$ (0.35)			
Net loss, basic and diluted	$ (1.38)	$ (2.20)	$ (1.47)	$ (1.23)	$ (0.73)
Pro forma amounts assuming the accounting change is applied retroactively (1):					
Net loss		$ (22,957)	$ (15,892)	$ (12,907)	$ (7,021)
Net loss per share basic and diluted		$ (1.85)	$ (1.38)	$ (1.14)	$ (0.84)

	December 31,				
	2001	2000	1999	1998	1997
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 24,966	$ 24,713	$ 14,140	$ 29,101	$ 42,813
Working capital	8,277	15,020	10,514	25,593	39,673
Total assets	26,911	29,681	17,886	32,903	44,775
Long-term liabilities	12,844	10,050	2,281	1,374	279
Total stockholders' equity (deficit)	(3,210)	6,566	10,764	27,503	41,046

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

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

Overview

Since commencing operations in 1992, we have been principally engaged in the research and development of our product candidates, as well as seeking various regulatory clearances and patent protection. We have had no revenues from product sales and have incurred cumulative losses since inception through December 31, 2001 aggregating approximately $92.1 million.

We have received revenues, as more fully described under "Strategic Alliances and Collaborations," in connection with licensing and strategic alliances with Bracco, Schering AG, Tyco/Mallinckrodt and Daiichi. In September 2001, pursuant to a Settlement and Release Agreement and Worldwide License Agreement known as the License Agreement, we granted Bracco a worldwide, non-exclusive royalty bearing sub-license to our patents. The patents sub-licensed to Bracco are owned by MGH and are licensed exclusively to us. We received $10.0 million ($9.0 million net of Italian income taxes) in up-front payments pursuant to the License Agreement, which consisted of a $2.0 million license fee, $1.0 million of royalties on past sales of MultiHance®, $4.0 million of prepaid royalties and a $3.0 million contingent license fee based upon marketing approval in the US. In addition, Bracco is obligated to pay us a quarterly royalty on its sales of MultiHance® beginning in January 2001 and ending on the patent expiration date in each country that MultiHance® is sold. During 2001, we recorded a total of $2.1 million of revenue related to this agreement, consisting of $2.0 million of royalties and $100,000 of license fee revenue. Of the $2.0 million in revenues, $1.0 million related to sales of MultiHance® prior to January 1, 2001 and the remaining $1.0 million related to sales on MultiHance® for the year ended December 31, 2001. Upon termination of the License Agreement, any remaining balance of the prepaid future royalties, $3.6 million at December 31, 2001, must be repaid to Bracco.

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

Our initial product candidate, MS-325, is currently our only product candidate undergoing human clinical trials. We filed an IND application for MS-325 in July 1996. We initiated a Phase I clinical trial in 1996 and a Phase I dose escalation study in 1997, both of which have been completed. We completed a Phase II clinical trial in June 1998 to test the safety and preliminary efficacy of MS-325-enhanced MRA for the evaluation of PVD, and also completed a Phase II trial in June 2001 that was designed to compare the diagnostic accuracy of five different doses of MS-325-enhanced MRA with that of X-ray angiography in the aortoiliac vascular bed. In 2001, we completed enrollment in the first study of a two-arm Phase III clinical trial, which was initiated in June 1999, and was designed to determine the efficacy of MS-325-enhanced MRA for the detection of aortoiliac occlusive disease. In September 2001, we expanded our initial target indication for MS-325 to a broad peripheral vascular disease indication from only aortoiliac occlusive disease, after discussions with the FDA. As a result of this expansion, we added two new Phase III trials to our Phase III clinical trial program, one in the renal arteries and one in the feet. We expect to complete enrollment in the Phase III trials by approximately the end of the third quarter of 2002. We are also currently conducting a Phase II feasibility trial to test the safety and feasibility of MS-325-enhanced MRA for the evaluation of coronary artery disease. In addition, in March 2000, we completed enrollment in a Phase II clinical trial to test the safety and feasibility of MS-325 for detecting breast cancer, and in March 2001, we completed enrollment in a Phase II feasibility trial which we conducted in collaboration with Pfizer, Inc. to explore the efficacy of MS-325-enhanced MRA in the diagnosis of female sexual arousal disfunction.

We anticipate fluctuation in our quarterly results of operations due to several factors, including: the timing of fees and milestone payments received from strategic partners; the formation of new

strategic alliances by us; the timing of expenditures in connection with research and development activities; the timing of product introductions and associated launch, marketing and sales activities; and the timing and extent of product acceptance for different indications and geographical areas of the world.

Critical Accounting Policies

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

Revenue Recognition

In the fourth quarter of 2000, we adopted SEC Staff Accounting Bulletin No. 101, or SAB 101, "Revenue Recognition in Financial Statements" retroactively to January 1, 2000, changing our method of recognizing revenue. Under SAB 101, we recognize revenues from non-refundable license fees and milestone payments not specifically tied to a separate earning process ratably over the period during which we have a substantial continuing obligations to perform services under the contract. When the period of deferral cannot be specifically identified from the contract, we estimate the period of deferral based upon our obligations under the contract. We continually review these estimates, which could result in a change in the deferral period. Payments received from Schering AG for development cost sharing obligations are recorded as revenue when the underlying costs are incurred. Non-refundable payments received for which revenue has not been earned are recorded as deferred revenue. Contract advances represent refundable amounts received in advance of services rendered.

Accrued Product Development Expense

In order to conduct the clinical trials required for our initial product, MS-325, we enter into contracts with vendors who render services over an extended period of time. Upon signing a contract, we determine the expected timing of when services are to be provided and record expense ratably over time based upon the initial forecasted timetable. Periodically, we review both the timetable of services to be rendered and the timing of services actually received. Based upon this review, revisions may be made to the forecasted timetable or to the extent of services performed, or both, in order to reflect our most current estimate of the contract.

The above listing is not intended to be a comprehensive list of all of our accounting policies. In many cases, the accounting treatment of a particular transaction is specifically dictated by generally accepted accounting principles, with no need for our judgment in their application. There are also areas in which our judgment in selecting any available alternative would not produce a materially different result. See our audited financial statements and notes thereto, which begin on page F-1 of this Annual Report on Form 10-K and which contain our accounting policies and other disclosures required by generally accepted accounting principles.

Results of Operations

Comparison of Years ended December 31, 2001 and December 31, 2000

Revenues

Revenues for the years ended December 31, 2001 and 2000 were $9.6 million and $6.9 million, respectively. Revenues for 2001 consisted of $5.8 million of product development revenue from Schering AG, $2.1 million of royalty and license fee revenue related to the Bracco agreement signed in September 2001 and $1.7 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 is a result of $2.1 million related to the Bracco agreement and $600,000 in license fee revenue associated with the granting of Schering AG's rights to market MS-325 in Japan.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2001 were $22.9 million as compared to $25.8 million for 2000. In the year 2000, a one-time charge of $4.9 million was included in research and development expenses, which related to the reacquisition of the Japanese rights to develop and commercialize MS-325 from Daiichi, causing an overall decrease in research and development expenses from

2000 to 2001. Excluding this one-time charge in 2000, research and development expenses increased $2.0 million from 2000 to 2001 primarily due to increased costs for personnel and other resources to support research and development of the Company's thrombus imaging program and higher costs associated with advancing MS-325 through clinical trials.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2001 were $5.5 million as compared to $4.8 million for 2000. General and administrative expenses increased $670,000 during 2001 as compared to 2000 primarily as a result of ongoing corporate activities, royalty expense associated with the Bracco agreement and increased personnel and related expenses.

Interest Income and Interest Expense

Interest income for the year ended December 31, 2001 was $1.0 million as compared to $1.3 million for 2000. The $300,000 decrease was primarily due to lower interest rates during 2001 compared to 2000 offset by a higher average cash, cash equivalent and marketable securities balance in 2001 as compared to 2000. Interest expense for the year ended December 31, 2001 was $339,000 as compared to $468,000 in 2000. The $129,000 decrease was attributable to lower interest rates in the year ended December 31, 2001 along with lower interest expense associated with our decreasing capital lease obligation and the repayment of our note payable. This decrease was offset by increased interest expense associated with the Bracco agreement.

Provision for Income Taxes

The provision for income taxes of $1.1 million represents Italian income taxes related to the Bracco agreement signed in September 2001 for which we are unable to offset against net operating losses. Any future payments received from Bracco are subject to Italian income tax withholding.

Comparison of Years ended December 31, 2000 and December 31, 1999

In the fourth quarter of 2000, we adopted SAB 101, "Revenue Recognition in Financial Statements" retroactively to January 1, 2000, changing our method of recognizing revenue. We recorded a cumulative effect of change in accounting principle in accordance with the adoption of SAB 101 in the amount of $4.4 million, which related to up-front and guaranteed milestone fees paid in

1996 and 1997 by Tyco/Mallinckrodt, our previous marketing partner for MS-325. Prior to the adoption of SAB 101, we recognized revenues from non-refundable license fees upon execution of the underlying license agreement. Revenues from milestone payments under collaborative agreements were recorded as revenue based upon the provisions of each agreement. Under the new accounting method, after the adoption of SAB 101, we now 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 a substantial continuing obligation to perform services under the contract. Included in 2000 revenues is $1.1 million of revenue that was recognized in prior years relating to the adoption of SAB 101. The remaining $3.3 million of revenue to be recognized in future years that is included in the cumulative effect of change in accounting principle will be recognized ratably over the future period during which we have a substantial continuing obligation to perform services under the contract.

The following discussions relating to revenue for the year ended December 31, 2000 and revenue for the year ended December 31, 1999 reflect pro forma results as if we had followed SAB 101 from our inception.

Revenues

Revenues for the year ended December 31, 2000 and 1999 totaled $6.9 million and $2.2 million, respectively. Excluding $1.1 million of SAB 101 revenues in both periods, revenues were derived from work performed in connection with product development contracts with Schering AG in the year ended December 31, 2000 and Tyco/Mallinckrodt in the year ended December 31, 1999. The increase in revenues was due to the impact of the development funding terms under the strategic collaboration agreement entered into with Schering AG in June 2000.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2000 were $25.8 million as compared to $14.7 million for 1999. The $11.1 million increase resulted primarily from higher costs associated with advancing MS-325 through clinical trials and the related effect of new development funding terms under the strategic collaboration agreement with Schering AG, increased costs for personnel and other

resources associated with advancing our thrombus imaging program and $4.9 million of expenses incurred in December 2000 associated with the reacquisition of the Japanese rights to develop and commercialize MS-325 from Daiichi. These increased costs were partially offset by lower manufacturing costs of material produced in connection with our strategic alliance with Daiichi.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2000 were $4.8 million as compared to $4.4 million for 1999. The $400,000 increase was due to increased costs related to corporate communications and marketing activities. These increased costs were partially offset by lower legal costs related to ongoing patent activities.

Interest Income and Interest Expense

Interest income for the year ended December 31, 2000 was $1.3 million as compared to $1.2 million for 1999. The $100,000 increase was primarily due to slightly higher average levels of cash, cash equivalents and marketable securities during 2000. Interest expense for the year ended December 31, 2000 was $468,000 as compared to $222,000 in 1999. The increase in interest expense was attributable to a higher average balance in our loan payable to Tyco/Mallinckrodt in the year ended December 31, 2000.

Research and Development General

We are currently performing research and development activities for two products, MS-325, which is in Phase III clinical trials and Thrombus, which is in the research stage.

MS-325

MS-325 is an injectable intravascular contrast agent intended to enhance the quality of MR images and provide physicians with a superior method for diagnosing diseases affecting the vasculature.

We are currently conducting a Phase III clinical trial program to test the safety and efficacy of MS-325-enhanced MRA for the evaluation of peripheral vascular disease. We expect to complete enrollment in the three remaining studies in our Phase III clinical trial program by approximately the end of the third quarter of 2002 and we expect to file our NDA with the FDA in 2003. The FDA review process of an NDA filing can vary widely. If granted expedited review, we could receive product approval within six months from the date of the NDA filing date. However, historically the FDA has required approximately twelve months to review a product NDA prior to approval. Once approved by the FDA, our partner, Schering AG will be responsible for the launch and marketing of MS-325.

Both the time-frame and costs involved in completing the development of MS-325, gaining FDA approval and commercializing the product may vary greatly for several reasons:

We rely on third party clinical trial centers to find suitable patients for our Phase III clinical trial program. If these third parties do not find suitable patients in the time-frame for which we have planned, we will not be able to complete our Phase III clinical trial program according to our expected schedule. Such a delay would result in an increase in costs to the development of our MS-325 program, a delay in filing an NDA with the FDA, and a delay in commercialization of the product.

We conduct our Phase III clinical trial program in accordance with specific protocols, which we have filed with the FDA. If the FDA modifies the protocols we have filed with them or requires us to perform additional studies, we could incur significant additional costs and additional time to complete our Phase III clinical trial program according to the revised plan. This would also result in a delay in our ability to file an NDA with the FDA and a delay in the commercialization of our product.

The length of time that the FDA takes to review our NDA can also vary widely, causing a delay in the commercialization of MS-325. Such a delay would result in an increase in costs and a delay in the commercialization of our product.

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

Our current timetable for completing the development of MS-325 and achieving commercialization reflects our best estimate of the time involved in completing the remaining steps 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 the existing timetable to changes caused by them. Any such delays could result in a significant increase in costs to complete development of MS-325 as well as a delay in product launch, which could enable competition to intensify.

Thrombus

We are seeking to develop a targeted contrast agent that would enable MRI to illuminate blood clots. Such a product could potentially change the diagnostic work-up for many of the conditions associated with thromboembolic disease, including PE and DVT. We believe that the use of this new approach could lead to better medical outcomes due to earlier and more definitive diagnosis. We further believe that our proprietary technology platform could enable MRI to differentiate old and new clot formation, potentially identifying those clots that pose the most risk to patients and those that are the most treatable.

We have not yet entered into a strategic collaboration with a third party for the development and marketing of our Thrombus program. Therefore, we have generated no revenues from this program and have fully funded its costs to date.

The amounts of the expenditures that will be necessary to execute our thrombus business plan are subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Completion of product candidates may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate.

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

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

Significant unexpected change in the current market conditions;

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.

Liquidity and Capital Resources

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities, of $25.0 million at December 31, 2001. On January 18, 2002 we raised $30.2 million pursuant to our previously filed shelf registration, bringing our cash, cash equivalents and marketable securities to $53.8 million as of that date. In September 2000, we entered into an agreement with Acqua Wellington North American Equities Fund Ltd., or Acqua Wellington, for an equity financing facility. During 2001, we received $8,666,346 and in 2000, we received $885,397 in net proceeds using this facility. This equity financing facility was terminated in January 2002, in accordance with the terms of the equity financing facility agreement, as a result of our sale of all of the remaining shares available on our effective S-3 shelf offering. Our January 2002 offering raised $30.2 million in net proceeds, and we issued an additional 2.575 million shares. Acqua Wellington did not purchase any shares in the January offering.

We currently receive quarterly cash payments from Schering AG for their share of development costs of MS-325, quarterly royalty payments from Bracco on their sales of MultiHance® and interest income earned on our cash, cash equivalents and available-for-sale marketable securities. In the future, we may also receive proceeds from a shelf registration statement filed with the SEC on March 20, 2002 whereby we requested to register 5 million shares of common stock. Such filing has not yet been declared effective by the SEC. Certain additional future cash flows depend on the successful filing of an NDA, FDA approval and product launch of MS-325, and include up to $27.0 million in

milestone

payments from Schering AG and our share of the profits earned on sales of MS-325 worldwide. We may also receive royalties on sales of Schering AG's Eovist product once it is approved for sale.

Known outflows, in addition to our ongoing research and development and general and administrative expenses, include the $3.0 million Loan due Tyco/Mallinckrodt in October 2002, semi-annual royalties we owe MGH on sales by Bracco of MultiHance®, and $2.4 million we owe Daiichi in December 2003 under the terms of the Reacquisition Agreement. Other potential future outflows depend on the successful filing of an NDA, FDA approval and product launch of MS-325, which include $5.0 million of milestone payments due Tyco/Mallinekrodt, a share of profits due Mallinekrodt on sales of MS-325 worldwide except Japan, 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 estimate that cash, cash equivalents and marketable securities on hand as of December 31, 2001, as well as the $30.2 million raised in January 2002, will be sufficient to fund our operations through November 2003. We believe that we will need to raise additional funds for research, development and other expenses through equity or debt financing, strategic alliances or otherwise, in order to achieve commercial introduction of any of our product candidates. 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 United States and foreign governmental approvals; the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; the extent to which our products gain market acceptance; the timing and costs of product introductions; the extent of our ongoing research and development programs; the costs of training physicians to become proficient with the use of our products; and, if necessary, once regulatory approvals are received, the costs of developing marketing and distribution capabilities.

Because of anticipated spending to support development of MS-325, thrombus and new research programs, we do not expect positive cash flow from operating activities for any future quarterly or annual period prior to commercialization of MS-325, which is currently forecast to be in 2004. We anticipate continued investments in fixed assets, including equipment and facilities expansion to support new and continuing research and development programs. We have in place a lease agreement that will enable us to utilize our current principal scientific facilities through December 31, 2002, and we have an option to extend the lease for an additional three or five years at a rental rate equal to approximately 95% of fair market value. We also have a lease for nearby office space, which expires in December 2002. We are currently involved in negotiating extensions for our current facilities.

Our major outstanding contractual obligations relate to our capital leases from equipment financings, our facilities leases and our obligations to strategic partners.

Below is a table that represents our contractual obligations and commercial commitments as of December 31, 2001:

		Payments due by period		
	Total	2002	2003	2004
Capital leases	$ 81,037	$ 81,037	$	$
Operating leases	$ 1,794,589	1,355,044	400,781	38,764
Loan payable to strategic partner	$ 3,004,607	$ 3,004,607		
Accrued reacquisition costs	$ 2,400,000		$ 2,400,000	
	$ 7,280,233	$ 4,440,688	$ 2,800,781	$ 38,764

We have incurred tax losses to date and therefore have not paid significant federal or state income taxes since inception. As of December 31, 2001, we had loss carryforwards of approximately $71.0 million available to offset future taxable income. These amounts expire at various times through

2020. As a result of ownership changes resulting from sales of equity securities, our ability to use the loss carryforwards is subject to limitations as defined in Sections 382 and 383 of the Internal Revenue Code of 1986, or the Code, as amended. We currently estimate that the annual limitation on our use of net operating losses through May 31, 1996 will be approximately $900,000. Pursuant to Sections 382 and 383 of the Code, the change in ownership resulting from public equity offerings in 1997 and any other future ownership changes may further limit utilization of losses and credits in any one year. We also are eligible for research and development tax credits that can be carried forward to offset federal taxable income. The annual limitation and the timing of attaining profitability may result in the expiration of net operating loss and tax credit carryforwards before utilization.

We do not believe that inflation has had a material impact on our operations.

Strategic Agreements

In September 2001, pursuant to a Settlement and Release Agreement and Worldwide License Agreement, known as the License Agreement, we granted Bracco a worldwide, non-exclusive royalty bearing sub-license to our patents. We received $10.0 million ($9.0 million after payment of Italian withholding taxes) in up-front payments pursuant to the License Agreement. In addition, Bracco is obligated to pay us a quarterly royalty on its sales of MultiHance® beginning in January 2001 and ending on the patent expiration date in each country that MultiHance® is sold. During 2001, we recorded a total of $2.1 million of revenue related to this agreement, consisting of $2.0 million of royalties and $100,000 of license fee revenue of the $2.0 million in revenues, $1.0 million related to sales of MultiHance® prior to January 1, 2001 and the remaining $1.0 million related to sales on MultiHance® for the year ended December 31, 2001. If upon termination of the License Agreement, any balance remains of the prepaid future royalties, originally $4.0 million, this balance, $3.6 million at December 31, 2001 must be repaid to Bracco.

In connection with the 2000 Schering strategic collaboration agreement, as amended, Schering AG paid us an up-front fee of $10.0 million, which we then paid to Tyco/Mallinckrodt. Schering AG also made a $20.0 million dollar equity investment in us at $17.98 per share of common stock, through its affiliate, Schering Berlin Venture Corporation ("Schering BV"). In return for their investment, we issued 1,112,075 shares of our common stock to Schering BV. We may receive up to an additional $20.0 million in milestone payments under the strategic collaboration agreement, of which $2.5 million will be earned upon NDA filing and up to $2.5 million will be earned upon product approval. Under the terms of the December 2000 amendment, Schering AG paid us an up-front fee of $3.0 million and may be required to pay us an additional $7.0 million upon our achievement of certain milestones.

In connection with the amendment to the Tyco/Mallinckrodt agreement, we paid in June 2000 Tyco/Mallinckrodt an up-front fee of $10.0 million and may be required to pay up to an additional $5.0 million in milestones, $2.5 million will be paid upon NDA filing and $2.5 million will be paid upon product approval. The first milestone is the submission of an NDA to the FDA, which is planned for 2003. We will also pay Tyco/Mallinckrodt a share of operating margins in the US and a royalty on gross profits outside the US on sales of MS-325.

In October 1999, we entered into a Loan with Tyco/Mallinckrodt. The Loan balance at December 31, 2001 and 2000 of $3,004,607 represents our share of third and fourth quarter 1999 MS-325 development costs. No additional funding is available to us under the Loan. The Loan bears interest, adjustable on a quarterly basis, payable twice a year, at the Prime Rate published in the Wall Street Journal and is repayable in full on October 1, 2002. The Loan is secured by a first priority security interest in all of the Company's intellectual property.

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. In December 2000 we reacquired the rights to develop and commercialize MS-325 in from Daiichi. Under the terms of this Reacquisition Agreement, we agreed to pay Daiichi a total of $5.2 million. In January 2001, we paid Daiichi $2.8 million in fees and we will pay an additional $2.4 million upon the earlier of regulatory approval of MS-325 in either U.S. or Japan or December 31, 2003. Daiichi will also receive a royalty from us on net sales of MS-325 in Japan.

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; the early stage of our initial product development and 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

relationshiops 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.

Accounting Pronouncements

Recently Issued Accounting Standards

In July 2001, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standard, or SFAS, No. 141, Business Combinations, and SFAS No. 142, Goodwill and Other Intangible Assets. SFAS No. 141 applies to all business combinations completed after June 30, 2001 which, among other things, requires the use of the purchase method of accounting. SFAS No. 141 also establishes new criteria for determining whether intangible assets should be recognized separately from goodwill. SFAS No. 142 provides that goodwill and intangible assets with indefinite lives will not be amortized, but rather will be reviewed for impairment at least annually. SFAS No. 142 is effective for fiscal years beginning after December 31, 2001 and accordingly, the Company will apply SFAS No. 142 beginning in the first quarter of 2002. Management does not expect that the application of SFAS No. 141 or No. 142 will have a significant impact on the results of operations or financial position of the Company.

In August 2001, the FASB issued SFAS No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets, which superseded SFAS No. 121, Accounting for Long-Lived Assets and for Long-Lived Assets to Be Disposed Of. The Company is required to adopt SFAS No. 144 in the first quarter of fiscal 2003. The adoption of SFAS No. 144 is not expected to have a material effect on the Company's financial position or results of operations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

Investments in both fixed rate and floating rate interest earning instruments carry a degree of interest rate risk. Fixed rate securities may have their fair market value adversely impacted due to a rise in interest rates, while floating rate securities may produce less income than expected if interest rates fall. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates or we may suffer losses in principal if forced to sell securities that have seen a decline in market value due to changes in interest rates. A hypothetical 10% increase or decrease in interest rates would result in a decrease in the fair market value of our total portfolio of approximately $40,000, and an increase of approximately $39,000, respectively, at December 31, 2001.

The interest rate on our loan payable to Tyco/Mallinckrodt is adjustable on a quarterly basis and therefore subjects the Company to interest rate risk. However, based on the outstanding loan balance of $3,004,607 and prime rate of 4.75% at December 31, 2001, a 10% increase in the prime rate would increase the Company's annual interest expense by approximately $15,000.

The interest rate of our agreement with Bracco S.p.A. is adjustable on a quarterly basis and therefore subjects the Company to interest rate risk. However, based on the outstanding balance of $4,000,000, a portion of total deferred revenue, and an interest rate of 4.75% (prime plus 1%) at December 31, 2001, a 10% increase in the prime rate would increase the Company's annual interest expense by approximately $23,000.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Financial Statements and supplementary data appear at pages F-1 through F-19 of this Annual Report on Form 10-K.

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

None

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

(a) The information required under this item is incorporated herein by reference to the section entitled "Management" in our definitive Proxy Statement for our 2002 Annual Meeting of Stockholders (2002 Proxy Statement) to be filed with the Commission not later than April 30, 2002.

ITEM 11. EXECUTIVE COMPENSATION

The information required under this item is incorporated herein by reference to the section entitled "Executive Compensation" in the 2002 Proxy Statement.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required under this item is incorporated herein by reference to the section entitled "Security Ownership of Certain Beneficial Owners And Management" in the 2002 Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required under this item is incorporated herein by reference to the section entitled "Certain Transactions" in the 2002 Proxy Statement.

PART IV

ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

a. Documents filed as part of this Report:

1. Financial Statements:

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

b. No reports on Form 8-K were filed in the fourth quarter of 2001.

c. Exhibits

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 herewith.
3.3	Form of Amended and Restated By-Laws of the Company. Filed as Exhibit 4.2 to the Company's Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.
4.1	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.1	Short Form Lease from Trustees of the Cambridge East Trust to the Company dated July 1, 1992. Filed as Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.2	First Amendment Lease From Trustees of the Cambridge Trust to the Company dated October 20, 1993. Filed as Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.3	Second Amendment Lease From Trustees of the Cambridge East Trust to the Company dated September 17, 1994. Filed as Exhibit 10.12 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.

10.4+	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.
10.5	Third Amendment Lease From Trustees of the Cambridge East Trust to the Comp any dated May 1, 1996. Filed as Exhibit 10.20 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.6	Third Amended and Restated Stockholders' Rights Agreement by and among the Company and certain of its stockholders named therein dated May 29, 1996. Filed as Exhibit 10.22 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.7	Amendment No. 1 to Third Amended and Restated Stockholders' Rights Agreement dated May 31, 1996. Filed as Exhibit 10.24 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.8	Amendment No. 2 to Third Amended and Restated Stockholders' Rights Agreement dated December 6, 1996. Filed as Exhibit 10.27 to the Company's Registration Statement on Form S-1 (File No. 333-17581) and incorporated herein by reference.
10.9#	Amended and Restated 1992 Equity Incentive Plan. Filed as Exhibit 99.1 to the Company's Registration Statement on Form S-8 (File No. 333-30531) and incorporated herein by reference.
10.10#	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.
10.11	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.
10.12#	Amended and Restated 1996 Employee Stock Purchase Plan. Filed as Appendix B to the Company's 2002 Definitive Proxy Statement on Schedule 14A (File No. 000-21863) and incorporated herein by reference.
10.13#	Amended and Restated 1996 Director Stock Option Plan. Filed as Appendix C to the Company's 2002 Definitive Proxy Statement on Schedule 14A (File No. 000-21863) and incorporated herein by reference.
10.14	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.
10.15	Sublease dated as of October 31, 1997 between the Company and SatCon Technology Corporation. Filed as Exhibit 10.40 to the Company's Annual Report on Form 10-K for the period ended December 31, 1998 (File No. 000-21863) and incorporated herein by reference.
10.16	First Amendment to Sublease dated as of July 15, 1998 between the Company and SatCon Technology Corporation. Filed as Exhibit 10.41 to the Company's Annual Report on Form 10-K for the period ended December 31, 1998 (File No. 000-21863) and incorporated herein by reference.
10.17	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.

10.18	Sublease extension election for an additional three years, beginning January 1, 2000 and ending December 31, 2002 pursuant to Article 5 of the First Amendment to Sublease dated as of July 15, 1998 between the Company and SatCon Technology Corporation. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 1999 (File No. 000-21863) and incorporated herein by reference.

10.19	Non-Negotiable Promissory Note dated October 8, 1999 between the Company and Tyco/Mallinckrodt Inc. Filed as Exhibit 10.47 to the Company's Annual Report on Form 10-K for the period ended December 31, 1999 (File No. 000-21863) and incorporated herein by reference.
10.20	Security Agreement dated October 8, 1999 between the Company and Tyco/Mallinckrodt Inc. Filed as Exhibit 10.48 to the Company's Annual Report on Form 10-K for the period ended December 31, 1999 (File No. 000-21863) and incorporated herein by reference.
10.21	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.
10.22++	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.
10.23++	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.
10.24	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.
10.25	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.
10.26	Common Stock Purchase Agreement dated as of September 18, 2000 by and between the Company and Acqua Wellington North American Equities Fund, Ltd. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated September 18, 2000 (File No. 000-21863) and incorporated herein by reference.
10.27++	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, 2001 (File No. 000-21863) and incorporated herein by reference.
10.28	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, 2001 (File No. 000-21863) and incorporated herein by reference.
10.29++	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.
10.30	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.
23.1	Consent of Ernst & Young LLP. Filed herewith.

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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.

#

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

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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, we have duly caused this report to be signed on our behalf by the undersigned, thereto duly authorized.

EPIX MEDICAL, INC.

March 28, 2002 By: /s/ MICHAEL D. WEBB

Michael D. Webb

Chief Executive Officer

We the undersigned officers and directors of EPIX Medical, Inc., hereby severally constitute Michael D. Webb, Pamela E. Carey, and William T. Whelan, and each of them singly, our true and lawful attorneys, with full power to them and each of them to sign for use, in our names and in the capacity indicated below, any and all amendments to this annual report on this Form 10-K for the fiscal year ended December 31, 2001, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each said attorneys-in-fact may cause to be done by virtue hereof.

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 28, 2002
/s/ PAMELA E. CAREY Pamela E. Carey	Chief Financial Officer	March 28, 2002
/s/ CHRISTOPHER F. O. GABRIELI Christopher F. O. Gabrieli	Chairman of the Board and Director	March 28, 2002
/s/ STANLEY T. CROOKE, M.D., PH.D Stanley T. Crooke, M.D., Ph.D	Director	March 28, 2002
/s/ PETER WIRTH Peter Wirth	Director	March 28, 2002
/s/ RANDALL B. LAUFFER, PH.D. Randall B. Lauffer, Ph.D.	Director	March 28, 2002

EPIX MEDICAL, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT AUDITORS

Board of Directors and Stockholders EPIX Medical, Inc.

We have audited the accompanying balance sheets of EPIX Medical, Inc. as of December 31, 2001 and 2000, and the related statements of operations, stockholders' (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of EPIX Medical, Inc. at December 31, 2001 and 2000, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 12, 2002

EPIX MEDICAL, INC.

BALANCE SHEETS

	December 31,	
	2001	**2000**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 13,609,883	$ 402,621
Marketable securities	11,355,785	24,310,253
Due from strategic partner		3,000,000
Royalties receivable	96,948	
Prepaid expenses and other assets	491,702	371,318

	December 31,	
Total current assets	25,554,318	28,084,192
Property and equipment, net	1,243,842	1,461,443
Other assets	112,533	134,952
Total assets	$ 26,910,693	$ 29,680,587
LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY		
Current liabilities:		
Accounts payable	$ 1,431,013	$ 1,800,046
Accrued expenses	4,981,255	3,677,833
Contract advances	5,169,953	2,462,340
Accrued reacquisition costs		2,800,000
Current portion of capital lease obligations	78,760	259,308
Current portion of note payable		373,783
Loan payable to strategic partner	3,004,607	
Deferred revenue	2,611,961	1,690,909
Total current liabilities	17,277,549	13,064,219
Capital lease obligations, less current portion		64,440
Accrued reacquisition costs, less current portion	2,400,000	2,400,000
Loan payable to strategic partner		3,004,607
Deferred revenue	10,443,636	4,581,818
Commitments and contingencies		
Stockholders' (deficit) equity:		
Preferred Stock, $0.01 par value, 1,000,000 shares authorized at December 31, 2001 and 2000, no shares issued and outstanding at December 31, 2001 and 2000 respectively		
Common stock, $.01 par value, 40,000,000 shares authorized at December 31, 2001 and 2000, 14,238,087 and 13,203,991 shares issued and outstanding at December 31, 2001 and 2000, respectively	142,381	132,040
Additional paid-in capital	88,620,094	79,144,912
Accumulated deficit	(91,966,743)	(72,718,720)
Accumulated other comprehensive income (loss)	(6,224)	7,271
Total stockholders' (deficit) equity	(3,210,492)	6,565,503
Total liabilities and stockholders' (deficit) equity	$ 26,910,693	$ 29,680,587

See accompanying notes.

EPIX MEDICAL, INC.

STATEMENTS OF OPERATIONS

Year ended December 31,

	2001	2000	1999
Revenues:			
Product development revenue	$ 5,720,148	$ 5,832,841	$ 1,144,056
Royalty revenue	2,052,397		
License fee revenue	1,796,170	1,090,909	
Total revenues	9,568,715	6,923,750	1,144,056
Operating expenses:			
Research and development	22,903,780	25,833,243	14,667,370
General and administrative	5,505,807	4,835,160	4,411,194
Total operating expenses	28,409,587	30,668,403	19,078,564
Operating loss	(18,840,872)	(23,744,653)	(17,934,508)
Interest income	1,023,659	1,256,323	1,173,136
Interest expense	(339,204)	(468,277)	(221,781)
Loss before provision for income taxes	(18,156,417)	(22,956,607)	(16,983,153)
Provision for income taxes	1,091,606		
Loss before cumulative effect of change in accounting principle	$ (19,248,023)	$ (22,956,607)	$ (16,983,153)
Cumulative effect of change in accounting principle		(4,363,636)	
Net loss	$ (19,248,023)	$ (27,320,243)	$ (16,983,153)
Weighted average shares:			
Basic and diluted	14,007,165	12,444,622	11,555,964
Net loss per share, basic and diluted:			
Loss before cumulative effect of change in accounting principle	$ (1.38)	$ (1.85)	$ (1.47)
Cumulative effect of change in accounting principle		(.35)	
Net loss	$ (1.38)	$ (2.20)	$ (1.47)
Pro forma amounts assuming the accounting change is applied retroactively:			
Net loss	$	$ (22,956,607)	$ (15,892,244)
Net loss per share, basic and diluted	$	$ (1.85)	$ (1.38)

See accompanying notes.

EPIX MEDICAL, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-In Capital	Stock Holder Loans	Accumulated Deficit	Accumulated Other Comprehensive Income/(loss)	Total Stockholders' (Deficit) Equity
	Shares	Amount					
Balance at December 31, 1998	$ 11,458,401	$ 114,584	$ 55,839,411	$ (123,119)	$ (28,415,324)	$ 87,453	$ 27,503,005
Issuance of common stock upon exercise of options	142,037	1,420	119,388				120,808
Issuance of common stock under employee stock purchase plan	24,323	243	116,659				116,902
Issuance of compensatory stock option plan	55,554	556	249,438				249,994
Issuance of compensatory stock option loan				(249,994)			(249,994)
Compensatory stock option expense			98,956				98,956
Disqualifying disposition of compensatory stock option			96,828				96,828
Interest income on compensatory stock options loans				(14,317)			(14,317)
Net loss					(16,983,153)		(16,983,153)
Available-for-sale marketable securities unrealized loss						(175,100)	(175,100)
Comprehensive loss							(17,158,253)
Balance at December 31, 1999	11,680,315	116,803	56,520,680	(387,430)	(45,398,477)	(87,647)	10,763,929
Issuance of common stock upon exercise of options	332,803	3,328	1,615,179				1,618,507
Issuance of common stock under employee stock purchase plan	14,708	147	120,018				120,165
Issuance of common stock	1,176,165	11,762	20,873,635				20,885,397
Compensatory stock option loan expense			15,400				15,400
Repayment of stock option loans				387,430			387,430
Net loss					(27,320,243)		(27,320,243)
Available-for-sale marketable securities unrealized gain						94,918	94,918
Comprehensive loss							(27,225,325)
Balance at December 31, 2000	13,203,991	132,040	79,144,912		(72,718,720)	7,271	6,565,503
Issuance of common stock upon exercise of options	98,266	983	363,366				364,349
Issuance of common stock under employee stock purchase plan	18,822	188	152,870				153,058
Issuance of common stock	917,008	9,170	8,657,176				8,666,346
Compensatory stock option expense			301,770				301,770
Net loss					(19,248,023)		(19,248,023)
Available-for-sale marketable securities unrealized loss						(13,495)	(13,495)
Comprehensive loss							(19,261,518)
Balance at December 31, 2001	14,238,087	$ 142,381	$ 88,620,094	$	$ (91,966,743)	$ (6,224)	$ (3,210,492)

See accompanying notes.

EPIX MEDICAL, INC.

STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2001	**2000**	**1999**
Operating activities:			
Net loss	$ (19,248,023)	$ (27,320,243)	$ (16,983,153)
Adjustments to reconcile net loss to net cash used in operating activities:			
Cumulative effect of change in accounting principle		4,363,636	
Depreciation and amortization	915,177	938,839	996,461
Stock compensation expense	301,770	15,400	195,784
Loss on sale of fixed assets			18,071
Changes in operating assets and liabilities:			
Due from strategic partner	3,000,000	519,757	(519,757)
Royalties receivable	(96,948)		
Prepaid expenses and other current assets	(120,384)	323,854	(177,471)
Notes receivable from officer		356,159	(20,271)
Other long term assets	22,419	(18,843)	(28,957)
Accounts payable	(369,033)	26,834	993,534
Accrued expenses	1,303,422	1,697,209	79,165
Accrued reacquisition costs	(2,800,000)	5,200,000	
Contract advances	2,707,613	2,153,385	(302,083)
Deferred revenue	6,782,870	(1,090,909)	
Receipt of cash from Schering AG for marketing rights		10,000,000	
Disbursement of cash to Tyco/Mallinckrodt for marketing rights		(10,000,000)	
Net cash used in operating activities	(7,601,117)	(12,834,922)	(15,748,677)
Investing activities:			
Purchases of fixed assets	(697,576)	(342,000)	(101,778)
Proceeds from sale of fixed assets			45,000
Purchases of marketable securities	(188,438,532)	(522,346,251)	(164,384,194)
Sale or redemption of marketable securities	201,379,505	511,840,896	179,230,860
Net cash provided by (used in) investing activities	12,243,397	(10,847,355)	14,789,888
Financing activities:			
Repayment of capital lease obligations	(244,988)	(379,911)	(438,483)
Proceeds from loan payable from strategic partner		1,421,050	1,583,557
Repayment of note payable	(373,783)	(397,864)	(349,009)
Proceeds from repayment of stock option loan and related interest		387,430	
Proceeds from Employee Stock Purchase Plan	153,058	120,165	116,902
Proceeds from stock options and warrants	364,349	1,618,507	106,492
Proceeds from sale of Common Stock	8,666,346	20,885,397	
Net cash provided by financing activities	8,564,982	23,654,774	1,019,459

	Year Ended December 31,		
Net increase (decrease) in cash and cash equivalents	13,207,262	(27,503)	60,670
Cash and cash equivalents at beginning of period	402,621	430,124	369,454
Cash and cash equivalents at end of period	$ 13,609,883	$ 402,621	$ 430,124
Supplemental disclosure of noncash investing and financing activities:			
Capital lease obligations incurred in connection with acquisition of fixed assets	$	$	$ 154,759
Issuance of stock option loan for exercise of stock options and related interest	$	$	$ 264,311
Supplemental cash flow information:			
Cash paid for interest	$ 344,452	$ 468,279	$ 221,781

See accompanying notes.

EPIX MEDICAL, INC.

NOTES TO FINANCIAL STATEMENTS

December 31, 2001

1. Business

EPIX Medical, Inc. ("EPIX" or the "Company") was formed on November 29, 1988 as a Delaware corporation and commenced operations in 1992. The Company is developing targeted contrast agents both to improve the capability and expand the use of magnetic resonance imaging ("MRI") as a tool for diagnosing human disease. The Company's principal product under development, MS-325, is an injectable vascular contrast agent designed for multiple vascular imaging indications, including peripheral vascular disease ("PVD") and coronary artery disease ("CAD").

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.

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. All marketable securities must be classified as one of the following: held-to-maturity, available-for-sale, or trading. 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/(loss).

Fair Value of Financial Instruments

At December 31, 2001 and 2000, the Company's financial instruments consisted of cash and cash equivalents, available-for-sale marketable securities, a portion of deferred revenue, a loan payable to Tyco/Mallinckrodt and accrued reacquisition costs.

The carrying value of cash equivalents approximate fair value due to their short-term maturities. The carrying value of the available-for-sale marketable securities, the loan payable to Tyco/Mallinckrodt, a portion of deferred revenue and accrued reacquisition costs are discussed in Notes 3, 6, 8 and 12, respectively.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and available-for-sale marketable securities. In accordance with the Company's investment policy, marketable securities are principally restricted to United States government issues, high-grade bank obligations, high-grade corporate bonds and certain money market funds. The Company had $24,965,668 of cash, cash equivalents and available-for-sale marketable securities invested with two financial institutions as of December 31, 2001.

Property and Equipment

Property and equipment are recorded at historical cost. Depreciation on laboratory equipment, furniture and fixtures and other equipment is determined using the straight-line method over the estimated useful lives of the related assets, ranging from 3 to 5 years. Leasehold improvements are amortized using the straight-line method over the shorter of the asset life or the remaining life of the lease. Expenditures for maintenance and repairs are charged to expense; betterments are capitalized.

Capital Lease Obligations

Assets and liabilities relating to capital leases are recorded at the present value of the future minimum rental payments using interest rates appropriate at the inception of the lease.

Income Taxes

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

Revenue

In the fourth quarter of 2000, the Company adopted SEC Staff Accounting Bulletin No. 101 ("SAB 101") "*Revenue Recognition in Financial Statements*" retroactively to January 1, 2000, changing its method of recognizing revenue. The Company recorded a cumulative effect of change in accounting principle, in accordance with the adoption of SAB 101, in the amount of $4.4 million, which related to up-front and milestone fees paid in 1996 and 1997 by Tyco/Mallinckrodt, the Company's previous marketing partner for MS-325. Under the new accounting method, after the adoption of SAB 101, the Company recognizes revenues from non-refundable license fees and milestone payments not specifically tied to a separate earning process ratably over the period during which the Company has a substantial continuing obligation to perform services under the contract. Included in 2001 and 2000 revenues is $1.1 million of revenue that was recognized in prior years relating to the adoption of SAB 101. As of December 31, 2001 the remaining $2.2 million of revenue to be recognized in future years that is included in the cumulative effect of change in accounting principle will be recognized ratably over the future period during which the Company has a substantial continuing obligation to perform services under the contract. In September 2001, pursuant to a Settlement and Release Agreement, the Company entered into a License Agreement with Bracco Imaging S.p.A. ("Bracco"). Under the License Agreement, the Company sub-licensed certain patents relating to Bracco products, including Bracco's proprietary product MultiHance®. The patents sub-licensed to Bracco are owned by the MGH and are licensed exclusively to the Company for which we pay a royalty.

The Company received from Bracco $10,000,000 ($9,000,000 net of Italian income taxes) in up-front payments consisting of a license fee, royalties on past sales of MultiHance®, prepayment of

future royalties and a contingent licensing fee based upon marketing approval of MultiHance® in the United States. The license fee of $2,000,000, will be recognized ratably over the term of the License Agreement because of ongoing obligations of the Company over such term. $1,000,000 of royalties on past sales of MultiHance® made by Bracco prior to January 1, 2001 was recognized as revenue in the third quarter of 2001. Prepaid future royalties total $4,000,000; $3,000,000 of which is required, pursuant to the License Agreement, to be applied against a portion of royalties earned commencing January 1, 2001; the remaining $1,000,000 will be applied against royalties earned commencing on January 1, 2005. The remaining $3,000,000 represents a contingent licensing fee for MultiHance® FDA approval, which will be recognized as revenue ratably in the period beginning with FDA approval through the remaining term of the License Agreement, because of ongoing obligations of the Company over such term. The $3,000,000 contingent license fee for MultiHance® FDA approval and the $1,000,000 of prepaid royalties commencing on January 1, 2005 bear interest at prime plus 1%. Interest that accrues on these balances is charged to interest expense. The carrying value of this amount approximates fair value due to the variable interest rate.

Upon termination of the License Agreement, any remaining balance of the prepaid future royalties, $3.6 million at December 31, 2001, must be repaid to Bracco.

Of the $10,000,000 received from Bracco, any amount not recognized as revenue in the year ended December 31, 2001 has been recorded on the balance sheet as deferred revenue, classified as short term and long term according to when the amount is expected to be recognized as revenue.

For the years ended December 31, 2001, 2000 and 1999, one source represented 66%, 84% and 100% of revenues, another source represented 11%, 16% and 0% and a third source represented 23%, 0% and 0%, respectively. The 1999 revenue percentages do not reflect the effect of SAB 101.

Use of Estimates

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

Research and Development

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

Stock-Based 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, rather than the alternative fair value accounting method provided for under SFAS No. 123, "*Accounting for Stock-Based Compensation*" ("SFAS 123"). The Company has provided the required disclosures pursuant to SFAS 123.

Earnings (Loss) Per Share

The Company computes net 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. Diluted net loss per share includes the effect of dilutive common equivalent shares from stock options and warrants using the treasury stock method. Basic and diluted loss per share are the same for all periods presented, due to the Company's operating losses.

Comprehensive Income (Loss)

The Company reports and presents comprehensive income and its components in accordance with the provisions of SFAS No. 130, "*Reporting Comprehensive Income*." Comprehensive income/(loss) is reflected in the statements of stockholders' equity and relates to unrealized gains and losses in marketable securities.

Recent Accounting Pronouncements

The Company adopted Financial Accounting Standards Board Statement (FASB) SFAS No. 133, "*Accounting for Derivative Instruments and Hedging Activities*." This statement provides a comprehensive and consistent standard for the recognition and measurement of derivatives and hedging activities. Adoption of this standard had no material effect on the Company's financial position or results of operations.

In July 2001, the FASB issued SFAS No. 141, "*Business Combinations*," and SFAS No. 142, "*Goodwill and Other Intangible Assets*." SFAS No. 141 applies to all business combinations completed after June 30, 2001, which, among other things, requires the use of the purchase method of accounting. SFAS No. 141 also establishes new criteria for determining whether intangible assets should be recognized separately from goodwill. SFAS No. 142 provides that goodwill and intangible assets with indefinite lives will not be amortized, but rather will be reviewed for impairment at least annually. SFAS No. 142 is effective for fiscal years beginning after December 31, 2001. The Company will apply SFAS No. 142 beginning in the first quarter of fiscal 2002. Management does not expect that the application of SFAS No. 141 or No. 142 will have a significant impact on the results of operations or financial position of the Company.

In August 2001, the FASB issued SFAS No. 144, "*Accounting for the Impairment or Disposal of Long-Lived Assets,*" which superseded SFAS No. 121, "*Accounting for Long-Lived Assets and for Long-Lived Assets to Be Disposed Of*." The Company is required to adopt SFAS No. 144 in the first quarter of fiscal 2003. The adoption of SFAS No. 144 is not expected to have a material effect on the Company's financial position or results of operations.

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 carrying value of available-for-sale marketable securities approximates their fair value. The estimated fair value and cost of marketable securities are as follows:

	Fair Value		Cost	
	December 31,			
	2001	2000	2001	2000
Federal agency obligations	$ 11,355,785	$ 2,034,306	$ 11,228,140	$ 2,036,594
U.S. Treasury obligations		2,732,721		2,735,881
Bank obligations		18,525,188		18,518,689
Corporate obligations		1,018,038		1,011,818
	$ 11,355,785	$ 24,310,253	$ 11,228,140	$ 24,302,982

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

	December 31,	
	2001	2000
Due within one year		$ 24,310,253
Due after one year through two years	$ 11,355,785	
	$ 11,355,785	$ 24,310,253

Gross unrealized gains on marketable securities, amounted to $137,165 and $113,594 in 2001 and 2000 respectively. Gross unrealized losses on marketable securities, amounted to $9,520 and $106,323 in 2001 and 2000, respectively.

4. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2001	2000
Leasehold improvements	$ 2,221,947	$ 2,120,601
Laboratory equipment	1,030,371	734,254
Furniture, fixtures and other equipment	880,339	580,225
Assets under capital lease	1,375,691	1,375,692
	5,508,348	4,810,772
Less accumulated depreciation and amortization	(4,264,506)	(3,349,329)
	$ 1,243,842	$ 1,461,443

Depreciation and amortization expense, which includes amortization of assets recorded under capital leases, was $915,177, $938,839 and $996,461 in 2001, 2000 and 1999, respectively.

5. Accrued Expenses

Accrued expenses consist of the following:

	December 31,	
	2001	2000
Accrued product development expenses	$ 3,261,548	$ 2,152,101
Accrued legal expense	74,598	110,000
Accrued compensation	885,757	815,514
Other accrued expenses	759,352	600,218
	$ 4,981,255	$ 3,677,833

6. Loan Payable to Strategic Partner

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

7. Leases

Assets under capital leases, the majority of which are for laboratory equipment, totaled $1,375,691 as of December 31, 2001 and 2000. During the years ended December 31, 2001, 2000 and 1999, the Company incurred amortization expense relating to assets under capital leases of $237,933, $371,300 and $427,740, respectively. Accumulated amortization relating to assets under capital leases was $1,319,253 and

$1,081,320 at December 31, 2001 and 2000, respectively.

In addition, the Company leases office space and certain office equipment under operating lease arrangements. The leases for the two principal facilities expire in December 2002. The Company has an option to extend the lease at one of its principal facilities and adjacent locations for an additional three or five-year period.

7. Leases (Continued)

Future minimum commitments under leases with non-cancelable terms of one or more years are as follows at December 31, 2001:

	Capital Leases	Operating Leases
2002	$ 81,037	$ 1,355,044
2003		400,781
2004		38,764
Total minimum lease payments	81,037	$ 1,794,589
Less amounts representing interest	2,277	
Present value minimum lease payments	78,760	
Less amounts due within one year	(78,760)	
	$	

Rent expense amounted to $694,395, $614,268 and $598,694 for 2001, 2000 and 1999, respectively.

8. Stockholders' (Deficit) Equity

In September 2000, we entered into an agreement with Acqua Wellington North American Equities Fund Ltd. ("Acqua Wellington") for an equity financing facility covering the sale of up to $45 million of our common stock over a 28 month period. During 2001, we received $8,666,346 and in 2000, we received $885,397 in net proceeds under this facility. These shares were sold at our discretion at a small discount to the market price of our shares at the time of the sale. The total amount of the investment was dependent, in part, on our stock price, with us controlling the amount and timing of the stock sold. This equity financing facility was terminated in January 2002, in accordance with the terms of the equity financing facility agreement, as a result of our sale of all of the remaining shares available on our effective S-3 shelf offering. The January 2002 offering raised $30.2 million in net proceeds, and we issued 2.575 million shares. Acqua Wellington did not purchase any shares in the January offering.

Warrants

In connection with the issuance of certain notes payable and the sale of Series D preferred stock in 1996, the Company issued warrants to purchase 40,000 shares of Series D preferred stock. Effective with the Company's initial public offering and the conversion of Series D preferred stock into the Company's common stock, the holders of the warrants became entitled to exercise the warrants for an aggregate of 26,665 shares of common stock at a cost equal to $4.50 per common share. These warrants, which expire in February 2002, remain outstanding as of December 31, 2001, but were exercised in February 2002.

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 2001, the Company amended the Equity Plan to, among other things, 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 5,099,901 shares of Common Stock, 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. As of December 31, 2001, 3,977,480 shares of Common Stock are reserved for issuance under the Equity Plan.

Stock option information relating to the Equity Incentive 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, 1998	1,737,592	$ 0.42 $13.88	$ 5.64	118,548	559,631	$ 3.04
Granted	881,322	$ 4.50 $11.13	$ 5.84			
Exercised	(197,591)	$ 0.42 $9.94	$ 1.88			
Canceled	(41,361)	$ 4.50 $13.88	$ 8.81			
December 31, 1999	2,379,962	$ 0.42 $13.88	$ 5.97	78,587	703,485	$ 4.28
Granted	615,915	$ 6.75 $22.50	$ 12.75			
Exercised	(332,803)	$ 0.42 $13.88	$ 4.86			
Canceled	(278,411)	$ 0.83 $22.25	$ 7.55			
December 31, 2000	2,384,663	$ 0.42 $22.50	$ 7.69	1,191,083	786,682	$ 5.25
Granted	1,061,532	$ 6.91 $12.13	$ 8.44			
Exercised	(98,266)	$ 0.42 $11.50	$ 3.67			
Canceled	(99,453)	$ 5.13 $22.50	$ 10.65			
December 31, 2001	3,248,476	$ 0.42 $21.63	$ 8.00	729,004	1,076,447	$ 6.56

1996 Directors 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. As of December 31, 2001, there are 200,000 shares of Common Stock reserved for issuance under the Director Plan. Effective January 1, 2001, the numbers of shares underlying the option granted to each eligible director upon election or re-election was increased from 15,000 to 25,000 shares. Each option becomes exercisable with respect to 8,333 shares on each anniversary date of grant for a period of three years, provided that the option holder is still a director of the Company at the opening of business on such date. The options have a term of ten years and a vesting schedule of three years. The exercise price for the options is equal to fair value at the date of grant. The exercise price may be paid in cash or shares of Common Stock or combination of both.

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

	Options Exercisable
	Number

	Options Outstanding	Option Price Range Per Share	Weighted Average Exercise Price	Available for Grant	Options Exercisable	Weighted Average Exercise Price
December 31, 1998	45,000	$ 8.50 $13.25	$ 11.80	55,000	15,000	$ 12.83
Granted	15,000	$ 7.00	$ 7.00			
December 31, 1999	60,000	$ 7.00 $13.25	$ 10.60	40,000	28,666	$ 12.42
Granted	15,000	$ 17.75	$ 17.75			
December 31, 2000	75,000	$ 7.00 $17.75	$ 12.03	25,000	42,333	$ 11.53
Granted	50,000	$ 7.98 $10.00	$ 8.99			
Cancelled	(11,334)	$ 8.50 $17.75	$ 16.66			
December 31, 2001	113,666	$ 7.00 $17.75	$ 10.23	86,334	58,666	$ 11.56

Combined Option Information

The following table summarizes information about options outstanding at December 31, 2001:

	Outstanding			Exercisable	
Range of Exercise Prices	Options Outstanding at December 31, 2001	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Options Exercisable at December 31, 2001	Weighted Average Exercise Price
$ 0.42 $5.38	927,167	5.84	$ 4.09	584,249	$ 3.43
$ 5.50 $8.69	988,313	8.68	$ 7.49	142,732	$ 6.28
$ 8.75 $11.00	821,305	7.56	$ 9.18	192,089	$ 9.34
$ 11.13 $21.63	625,357	7.78	$ 13.10	216,043	$ 13.16
	3,362,142	7.45	$ 8.00	1,135,113	$ 6.56

1996 Employee Stock Purchase Plan

The Company sponsors the Amended and Restated 1996 Employee Stock Purchase Plan (the "Purchase Plan") under which employees may purchase shares of Common Stock at a discount from fair market value at specified dates. In May 2001, the Company amended the Purchase Plan to increase the number of shares of common stock that may be purchased under the Purchase Plan by 50,000 shares to an aggregate of 116,666. Employees purchased 18,822 shares in 2001 at an average price of $8.13 per share and 14,708 shares in 2000 at an average price of $8.17 per share. At December 31, 2001, 40,470 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 are paid through payroll deductions. The Purchase Plan terminates in December 2006.

FAS 123 Pro Forma Information

The pro forma information required by FAS 123 is presented below and has been determined as if the Company accounted for its stock-based awards under the fair value method per FAS 123. The fair value of the Company's stock-based awards to employees was estimated using the Black-Scholes option-pricing model and assuming no expected dividends and the following weighted-average assumptions:

	Options			ESPP		
	Year Ended December 31,					
	2001	2000	1999	2001	2000	1999
Weighted-average life (years)	5.0	4.90	4.96	.50	.50	0.50
Weighted-average contractual life (years)	7.45	7.62	7.92			
Expected stock price volatility	0.86	1.14	0.81	1.2	1.14	0.81
Risk-free interest rate	4.72%	6.20%	5.50%	4.72%	6.20%	5.50%

The following is a summary of weighted-average grant date fair values generated by the application of the Black-Scholes model:

	Date Fair Value Year Ended December 31,		
	2001	2000	1999
Stock option plans	$ 5.61	$ 10.18	$ 3.70
ESPP	$ 3.71	$ 5.64	$ 2.80

As required under FAS 123, the following pro forma net loss and loss per share presentation reflects the amortization of the option grant fair value. For purposes of this disclosure, the estimated fair value of the options is amortized to expense over the options' vesting periods. The Company's pro forma information follows:

	Year Ended December 31,		
	2001	2000	1999
Pro forma net loss	$ (22,532,215)	$ (29,696,369)	$ (18,386,545)
Pro forma basic and diluted loss per share	$ (1.61)	$ (2.39)	$ (1.59)

The effects on 2001, 2000 and 1999 pro forma net loss and net loss per share of expensing the estimated fair value of stock options and common stock issued pursuant to the stock option plans are not necessarily representative of the effects on reported results of operations for future years as the periods presented include only two, three and four years, respectively, of option grants and share purchases under the Company's plans.

9. Income Taxes

The Company has reported losses since inception and, due to the degree of uncertainty related to the ultimate use of the loss carry forwards, fully reserved this tax benefit. The Company has the following deferred tax assets as of December 31, 2001 and 2000:

	December 31,	
	2001	2000
Deferred tax assets:		
Net operating loss carry forwards	$ 29,010,000	$ 23,760,000
Research and development tax credits	3,359,000	2,953,000
Book over tax depreciation and amortization	1,225,000	1,299,000
Deferred revenue	4,350,000	2,073,000

	December 31,	
Other	1,090,000	1,045,000
Total deferred tax assets	39,034,000	31,130,000
Valuation allowances	(39,034,000)	(31,130,000)
Deferred income taxes, net	$	$

As of December 31, 2001, the Company has net operating loss carry forwards for income tax purposes of approximately $71.0 and $64.4 million, which expire through the year 2020 and 2005, for Federal and State purposes, respectively. The valuation allowance increased by $7,904,000 during the twelve months ended December 31, 2001. The tax net operating loss carry forwards differ from the accumulated deficit principally due to temporary differences in the recognition of certain revenue and expense items for financial and tax reporting purposes.

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

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

	Years ended December 31,		Years ended December 31,	
	2001	2000	2001	2000
Tax at U.S. statutory rate	$ (6,173,000)	$ (7,805,000)	(34.00)%	(34.00)%
State taxes, net of federal benefit	(1,089,000)	(1,377,000)	(6.00)%	(6.00)%
Non-deductible items	200,606	53,000	1.10%	0.23%
Foreign taxes, net of benefit	655,000		3.61%	
Tax credits	(406,000)	(1,601,000)	(2.24)%	(6.98)%
Change in valuation allowance	7,904,000	10,730,000	45.50%	46.75%
Income tax expense	$ 1,091,606	$	7.97%	0.00%

10. Defined Contribution Plan

The Company offers a defined contribution 401(k) plan, which covers substantially all employees. The plan permits participants to make contributions from 1% to 15% of their compensation. Beginning in 1999, the Company began matching up to 3% of employees' contributions. During 2001, 2000, and 1999 the Company's match amounted to $173,412, $154,061, and $134,355, respectively.

11. Subsequent Events

Sale of Common Stock

On January 18, 2002, the Company raised approximately $30.2 million in net proceeds from the sale of 2,575,000 shares of common stock. The shares of common stock were sold pursuant to the Company's effective shelf registration statement, representing all of the available shares thereunder.

Exercise of Warrants

In February 2002, the holders of the warrants described in Note 8 exercised their warrants, and the Company issued 17,848 shares of common stock. The Company received no cash proceeds pursuant to these exercises as the warrant holders elected to exercise their warrants on a net stock issue basis. As a result of these warrant exercises, there are no remaining warrants outstanding.

12. Quarterly Financial Information (unaudited)

	First Quarter Ended March 31, 2001	Second Quarter Ended June 30, 2001	Third Quarter Ended September 30, 2001	Fourth Quarter Ended December 31, 2001
Revenues	$ 1,731,673	$ 2,197,422	$ 3,615,864	$ 2,023,756
Operating expenses:				
Research Development	5,322,031	6,352,953	5,358,701	5,870,095
General & administrative	1,586,835	1,264,498	1,337,407	1,317,067
Total operating expenses	6,908,866	7,617,451	6,696,108	7,187,162
Other income, net	206,807	293,148	137,761	46,739
Income taxes			1,082,000	9,606
Net loss	$ (4,970,386)	$ (5,126,881)	$ (4,024,483)	$ (5,126,273)
Weighted average shares, basic and diluted	13,638,913	14,022,893	14,160,239	14,198,579
Net loss per share:				
Basic and diluted	$ (0.36)	$ (0.37)	$ (0.28)	$ (0.36)

	First Quarter Ended March 31, 2000		Second Quarter Ended June 30, 2000		Third Quarter Ended September 30, 2000		Fourth Quarter Ended December 31, 2000	
	As Previously Reported	As Restated	As Previously Reported	As Restated	As Previously Reported	As Restated	As Previously Reported	As Restated
Revenues	$ 859,400	$ 1,132,127	$ 2,286,729	$ 2,559,456	$ 1,635,827	$ 1,908,554	$ 4,050,886	$ 1,323,613
Operating expense:								
Research & development	5,050,906	5,050,906	5,456,370	5,456,370	5,535,849	5,535,849	9,790,117	9,790,117
General & administrative	1,042,083	1,042,083	1,439,641	1,439,641	1,041,168	1,041,168	1,312,271	1,312,271
Total operating expenses	6,092,989	6,092,989	6,896,011	6,896,011	6,577,017	6,577,017	11,102,388	11,102,398
Other Income, net	73,004	73,004	38,864	38,864	361,430	361,430	314,750	314,750
Loss before cumulative effect of change in accounting principle	(5,160,585)	(4,887,858)	(4,570,418)	(4,297,691)	(4,579,760)	(4,307,033)	(6,737,752)	(9,464,025)
Cumulative effect of change in accounting principle		(4,363,636)						
Net loss	$ (5,160,585)	$ (9,251,494)	$ (4,570,418)	$ (4,297,691)	$ (4,579,760)	$ (4,307,033)	$ (6,737,752)	$ (9,464,025)

	First Quarter Ended March 31, 2000		Second Quarter Ended June 30, 2000		Third Quarter Ended September 30, 2000		Fourth Quarter Ended December 31, 2000	
Weighted average shares, basic and diluted	11,720,515	11,720,515	11,869,515	11,869,515	13,022,045	13,022,045	13,152,290	13,152,290
Net loss per share, basic and diluted:								
Loss before cumulative effect of change in accounting principle	$ (0.44)	$ (0.42)	$ (0.39)	$ (0.36)	$ (0.35)	$ (0.33)	$ (0.51)	$ (0.72)
Cumulative effect of change in accounting principle		(0.37)						
Net loss	$ (0.44)	$ (0.79)	$ (0.39)	$ (0.36)	$ (0.35)	$ (0.33)	$ (0.51)	$ (0.72)

QuickLinks