NEOPROBE CORP
Form 10KSB
March 16, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-KSB

(Mark One)

x ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended: December 31, 2006

OR

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

For the transition period from _____ to _____.

Commission file number: 0-26520

NEOPROBE CORPORATION
(Name of Small Business Issuer in Its Charter)

Delaware	31-1080091
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
425 Metro Place North, Suite 300, Dublin, Ohio	43017-1367
(Address of Principal Executive Offices)	(Zip Code)

Issuer's telephone number, including area code: (614) 793-7500
Securities registered pursuant to Section 12(b) of the Act: None
Securities registered pursuant to Section 12(g) of the Act:

Common Stock, par value $.001 per share
(Title of Class)

Check whether the issuer is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act. o

Check whether the registrant: (1) filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act during the past 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 x No o

Check if there is no disclosure of delinquent filers pursuant to Item 405 of Regulation S-B contained in this form and no disclosure will 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-KSB or any amendment to this Form 10-KSB. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act. Yes o No x

The issuer's revenues for the fiscal year ended December 31, 2006 were $6,051,071.

The aggregate market value of shares of common stock held by non-affiliates of the registrant on March 9, 2007 was $12,849,028.

The number of shares of common stock outstanding on March 9, 2007 was 59,864,910.

DOCUMENTS INCORPORATED BY REFERENCE

None.

Transitional Small Business Disclosure Format (check one): Yes o No x

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PART I

Item 1. Description of Business

Development of the Business

Neoprobe Corporation (Neoprobe, the company or we) is a biomedical company that develops and commercializes innovative products that enhance patient care and improve patient outcome by meeting the critical intraoperative diagnostic information needs of physicians and therapeutic treatment needs of patients. We were originally incorporated in Ohio in 1983 and reincorporated in Delaware in 1988. Our executive offices are located at 425 Metro Place North, Suite 300, Dublin, Ohio 43017. Our telephone number is (614) 793-7500.

From our inception through 1998, we devoted substantially all of our efforts and resources to the research and clinical development of radiopharmaceutical and medical device technologies related to the intraoperative diagnosis and treatment of cancers, including our proprietary radioimmunoguided surgery (**RIGS**®) technology. At that point, an evaluation of the status of the regulatory pathway for our **RIGS** products coupled with our limited financial resources caused us to suspend development activities related to our radiopharmaceutical business and to retrench our organization to focus on our medical device business. After achieving profitability in 2000 following this retrenchment, we set out on a strategy to expand our medical device portfolio outside the cancer field. In December 2001, we took a major step in executing this strategy with the acquisition of Biosonix Ltd., a private Israeli company limited by shares, which we subsequently renamed Cardiosonix Ltd. (Cardiosonix). Neoprobe through Cardiosonix has begun commercializing the **Quantix**® line of blood flow measurement devices for a variety of diagnostic and surgical applications in the cardiac and vascular management arena. The results of Cardiosonix's efforts to date have not met with our original expectations; however, we continue to believe that the **Quantix** products can positively impact our medical device business over the next few years.

In addition, although our strategic focus expanded in 2001 to include blood flow measurement, we continued to look for other avenues to reinvigorate our radiopharmaceutical development. During 2004, our efforts resulted in a number of positive events that caused us to take steps to re-activate development of our radiopharmaceutical and therapeutic initiatives. As a result, in 2007 we now have one of our radiopharmaceutical products, **Lymphoseek®**, involved in a variety of clinical evaluations including a Phase 2 multi-center clinical trial, and a second, **RIGScan®** CR, for which we are clarifying the regulatory pathway and identifying potential sources of funding. In early 2005, we also formed a new subsidiary, Cira Biosciences, Inc. (Cira Bio), to evaluate the current market opportunities for another technology platform, activated cellular therapy (ACT). Our unique virtual business model combines revenue generation from medical devices that contributes to covering our corporate overhead while we devote capital raised through financing efforts to incremental development such as **Lymphoseek** and look for development partners to assist us in the clinical and commercial development for **RIGScan** CR and ACT.

Our Technology

Gamma Detection Devices

Through 2006, substantially all of our revenue has been generated from the sale of a line of gamma radiation detection devices and related products used by surgeons in the diagnosis and treatment of cancer and related diseases. Our currently-marketed line of gamma detection devices has been cleared by the U.S. Food and Drug Administration (FDA) and other international regulatory agencies for marketing and commercial distribution throughout most major global markets.

Our patented gamma detection device systems consist of hand-held detector probes and a control unit. The critical detection component is a highly radiosensitive crystal contained in the tip of the probe that relays a signal through a

preamplifier to the control unit to produce both a digital readout and an audible signal. The detector element fits into a housing approximately the size of a pocket flashlight. The **neo2000®** Gamma Detection System, originally released in 1998, is the third generation of our gamma detection systems. The **neo2000** is designed as a platform for future growth of our instrument business. The **neo2000** is software upgradeable and is designed to support future surgical targeting probes without the necessity of costly remanufacture. Since 1998, we have developed and released four major software upgrades for customer units designed to improve the utility of the system and/or offer the users additional features, including our most recent release that enables our entire installed base of **neo2000** users to use our recently released Bluetooth® wireless gamma detection probes. Generally, these software upgrades have been included in new units offered for sale but have also been offered for sale separately.

Surgeons are using our gamma detection devices in a surgical application referred to as sentinel lymph node biopsy (SLNB). SLNB helps trace the lymphatic patterns in a cancer patient to evaluate potential tumor drainage and cancer spread in lymphatic tissue. The technique does not detect cancer; rather it helps surgeons identify the lymph node(s) to which a tumor is likely to drain and spread. The lymph node(s), sometimes referred to as the "sentinel" node(s), may provide critical information about the stage of a patient's disease. SLNB begins when a patient is injected at the site of the main tumor with a commercially available radioactive tracing agent. The agent is intended to follow the same lymphatic flow as the cancer would if it had metastasized. The surgeon may then track the agent's path with a hand-held gamma radiation detection probe, thus following the potential avenues of metastases and identifying lymph nodes to be biopsied for evaluation and determination of cancer spread.

Numerous clinical studies, involving a total of nearly 2,000 patients and published in peer-reviewed medical journals such as *Oncology* (January 1999) and *The Journal of The American College of Surgeons* (December 2000), have indicated SLNB is approximately 97% accurate in predicting the presence or absence of disease spread in melanoma and breast cancers. Consequently, it is estimated that more than 80% of breast cancer patients who would otherwise have undergone full axillary lymph node dissections (ALND), involving the removal of as many as 20 - 30 lymph nodes, might be spared this radical surgical procedure if the sentinel node was found to be free of cancer. Surgeons practicing SLNB have found that our gamma detection probes are well-suited to the procedure.

Hundreds of articles have been published in recent years in peer-reviewed journals on the topic of SLNB. Furthermore, a number of thought leaders and cancer treatment institutions have recognized and embraced the technology as standard of care for melanoma and for breast cancer. Our marketing partner continues to see strong sales, especially for use in breast cancer treatment. SLNB in breast cancer has been the subject of national and international clinical trials, including one major study sponsored by the U.S. Department of Defense and the National Cancer Institute (NCI) and one sponsored by the American College of Surgeons. The first of these trials completed accrual approximately two years ago and preliminary results may be available in the next year to eighteen months. Accrual on the second trial was halted early, due, we believe, to the overwhelming desire of patients to be treated with SLNB rather than be randomized in a trial whereby they might receive a full axillary dissection. We believe that once data from these trials are published there may be an additional demand for our devices from those surgeons who have not yet adopted the SLNB procedure. We also believe, based on an estimate of the total number of operating rooms in medical centers that are capable of performing the types of procedures in which our gamma detection devices are used, that while we are potentially reaching saturation at the major cancer centers and teaching institutions, a significant portion of the global market for gamma detection devices such as ours remains untapped.

In addition to lymphatic mapping, surgeons are investigating the use of our devices for other gamma-guided surgery applications, such as evaluating the thyroid function, in determining the state of disease in patients with vulvar and penile cancers, and for SLNB in prostate, gastric, colon, head and neck, and non-small cell lung cancers. Expanding the application of SLNB beyond the current primary uses in the treatment of breast cancer and melanoma is the primary focus of our strategy regarding our gamma-guided surgery products. To support that expansion, we continue to work with our marketing and distribution partners to develop additional software-based enhancements to the **neo2000** platform as well as our new Bluetooth wireless probes introduced in October 2006. To that end, our goals for our gamma detection device business for 2007 center around introducing additional improvements to our **neo2000** system and working with our marketing partners to further penetrate the breast care market and identify ways to expand the application of SLNB to other indications beyond breast cancer and melanoma. We also believe that our development of **Lymphoseek** could be an integral step in helping expand the application of SLNB.

Blood Flow Measurement Devices

Accurate blood flow measurement is essential for a variety of clinical needs, including:

· real-time monitoring;

· intra-operative quantification;

· non-invasive diagnostics; and

· evaluation of cardiac function.

Blood flow velocity measurements are often confused with volume blood flow. These two variables, however, are normally different parameters that respond differently to pathological conditions and provide different data. Blood flow velocity is used primarily for determining the existence of a stenosis (narrowing or obstruction) in the vascular surgery setting, while the applications of blood flow volume have potential impact across a much broader range of medical disciplines.

Cardiosonix has developed and is commercializing the **Quantix** line of products that employ a unique and proprietary technology that allows for measurement of blood flow volume, velocity and several other hemodynamic parameters that permit the real-time assessment of conduit hemodynamic status.

The **Quantix** technology utilizes a special application of the Doppler method through simultaneous projection of a combination of narrow beams with a known angle between them. Thus, based on trigonometric and Doppler considerations, the angle of insonation can be obtained, resulting in accurate, angle-independent blood flow velocity measurements that do not require the use of complicated, expensive imaging systems. In order to obtain high-resolution velocity profiles, the **Quantix** devices use a multi-gated pulse wave Doppler beam. With this method, specific sample volumes along the ultrasound beam can be separately evaluated, and the application of a flow/no flow criterion can be made. The Cardiosonix technology applies a special use of digital Doppler technology, which with the digital signal processing power of the system allows hundreds of sample volumes to be sampled and processed simultaneously, thus providing high resolution velocity profiles for both angle and vascular diameter calculations, and subsequently volume blood flow measurements. At present, Cardiosonix has two products in the early stages of commercialization designed to provide blood flow measurement and cardiac output information to physicians in cardiac/vascular surgery and neurosurgery. The technology also has the potential to be applied in other healthcare settings where measurement of blood flow may be beneficial.

Quantix/OR™ is designed to permit cardiovascular surgeons to obtain intraoperative volume blood flow readings in various targeted blood vessels within seconds. The system consists of an insonation angle-independent ultrasound probe and digital numerical displays of blood flow rate. Thus, the surgeon obtains immediate, real-time and quantitative readings while focused on the target vessel. Quantifying blood flow can be very beneficial during anastomostic or other bypass graft procedures to determine adequate blood flow. While measurement is advisable whenever a blood vessel is exposed and manipulated intra-operatively, generally this is not the current practice.

Ultimately, in practice, the surgeon generally resorts to using his or her eyes and fingers in a process called finger palpation to qualitatively assess vessel flow. The **Quantix/OR** offers the surgeon immediate and simple quantitative assessment of blood flow in multiple blood vessels and grafts. The primary advantage of finger palpation is that it is fast, simple and low cost; the disadvantages are that it requires a good deal of experience, it is difficult to perform in vessels embedded in tissue, it can become difficult to interpret in large vessels, and it permits only a very qualitative and subjective assessment. A significant partial occlusion (or even a total occlusion) will result in significant vessel “distention” and strong pulse that may mislead the surgeon. Rather than rely on such a subjective clinical practice,

which is highly experience-dependent, the **Quantix/OR** is designed to allow the surgeon to rely on more quantifiable and objective information. We believe that **Quantix/OR** represents a measurable improvement over existing technologies to directly measure blood flow intraoperatively. Other technologies that attempt to measure intraoperative blood flow directly are generally more invasive and are impractical when non-skeletonized vessel measurements are required. As a result, a majority of surgeons generally resort to finger palpation to qualitatively, rather than quantitatively, measure vessel perfusion.

The initial physician and distributor evaluation of the flagship product, the **Quantix/OR**, during 2004 indicated a number of design deficiencies that needed to be corrected before further commercial distribution of the product was advisable. The development activities for the **Quantix/OR** over the last year have therefore involved modification of the user interface software functions and a redesign of the **Quantix/OR** probe ergonomics to enhance system performance, improve ease of measurement and expand physician acceptance of the system. The **Quantix/OR** device has received CE mark regulatory clearance for marketing in the European Union (EU) as well as FDA 510(k) clearance for marketing in the United States.

Quantix/ND™ is intended to allow neurosurgeons and neurologists, as well as intensive care unit or emergency room physicians, to non-invasively measure the internal carotid artery blood flow in a simple, real-time manner. **Quantix/ND** consists of a control unit and an ultrasound probe that obtains signals directly from the carotid artery in a non-invasive manner. **Quantix/ND** is designed primarily for use in monitoring head trauma patients in neuro-intensive care units and emergency rooms. Periodic blood flow measurements may minimize the risk of brain impairment. To date, we have placed the **Quantix/ND** device with only a limited number of thought leaders. While we are unaware of any competitive measurement system on the market today that provides real-time, bedside, non-invasive, continuous, direct and accurate measurements of a complete suite of hemodynamic parameters including blood flow, we also believe that the current market for the **Quantix/ND** may be primarily as a research tool until additional feedback is received from those who are evaluating the device. The **Quantix/ND** device has received CE mark regulatory clearance for marketing in the EU as well as FDA 510(k) clearance for marketing in the United States.

Our strategy related to Cardiosonix products for 2007 is to close on a significant portion of the sales leads we began to generate during the latter part of 2006 and to continue to increase the number of competitive product evaluations to which we are invited. We cannot assure you, however, that any of Cardiosonix's products will achieve market acceptance. See Risk Factors.

Lymphoseek

Our gamma detection devices are primarily capital in nature; as such, they generate revenue only on the initial sale. To complement the one-time revenue stream related to capital products, we are working on developing recurring revenue or "procedural" products that would generate revenue based on each procedure in which they were used. The product we are working on with the greatest near-term potential in this area involves a proprietary drug compound under exclusive worldwide license from the University of California, San Diego (UCSD) that we refer to as **Lymphoseek**. The UCSD license grants Neoprobe the commercialization rights to **Lymphoseek** for diagnostic imaging and intraoperative detection applications. If proven effective and cleared for commercial sale, **Lymphoseek** would be the first radiopharmaceutical specifically designed and labeled for the targeting of lymphatic tissue.

Neoprobe and UCSD completed the initial pre-clinical evaluations of **Lymphoseek** in 2001. Since that time, UCSD has initiated five Phase I clinical trials involving **Lymphoseek**. The status of these trials is listed below:

Indication	Number of Patients	Status
Breast (peritumoral injection)	24	Completed
Melanoma	24	Completed
Breast (intradermal injection, next day surgery)	60	Completed
Prostate	20	Ongoing
Colon	20	Ongoing

These Phase I studies have been supported, including being substantially funded through research grants, by a number of organizations such as the Susan G. Komen Breast Cancer Research Foundation, the American Cancer Society (ACS) and the NCI. Research data from these clinical evaluations of **Lymphoseek** have been presented at recent meetings of the Society of Nuclear Medicine, the Society of Surgical Oncology and the World Sentinel Node Congress. The prostate and colon studies are being conducted under Neoprobe's investigational new drug (IND) application that has been cleared with FDA using drug product supplied by Neoprobe.

In November 2003, we met with the Interagency Council on Biomedical Imaging in Oncology (Interagency Council), an organization representing FDA, the NCI and the Centers for Medicare and Medicaid Services, to discuss the regulatory approval process and to determine the objectives for the next clinical trial involving **Lymphoseek**. During 2004, we prepared and submitted an IND application to FDA to support the marketing clearance of **Lymphoseek**.

In the first quarter of 2005, we announced that FDA had accepted our application to establish a corporate IND for **Lymphoseek**. With the transfer of the UCSD physician IND to Neoprobe, we assumed full clinical and commercial responsibility for the development of **Lymphoseek**. Following the establishment of the corporate IND, Neoprobe's clinical and regulatory personnel began discussions with FDA regarding the clinical development program for **Lymphoseek**.

As a "first in class" drug, Neoprobe was advised that additional non-clinical studies needed to be completed before additional clinical testing of the drug could occur in humans. The non-clinical testing was successfully completed in the fourth quarter of 2005 and the reports were filed with FDA in December. The seven studies included repeat administrations of **Lymphoseek** at dosages significantly in excess of the anticipated clinical dosage. None of the non-clinical studies revealed any toxicity issues associated with the drug.

In preparation for the commencement of the multi-center clinical study, Neoprobe engaged the services of a global clinical research organization (CRO) to oversee and monitor the conduct of the Phase 2 and Phase 3 clinical studies. Neoprobe and the CRO began working with some of the leading cancer treatment hospitals in the United States that Neoprobe had identified to participate in the clinical studies. We developed and reviewed with the clinical sites and regulatory agencies the Phase 2 protocol, investigator's brochure and case report forms to obtain regulatory clearance and institutional clearance from the clinical sites to commence patient enrollment in the Phase 2 study. An investigator's meeting was held with the Phase 2 clinical investigators at the Society of Surgical Oncology (SSO) meeting in March 2006 in preparation for the initiation of patient enrollment in the Phase 2 study. In addition, we used the SSO meeting as a venue to meet with and recruit potential investigators for the planned Phase 3 study of **Lymphoseek** to be initiated later in 2007.

Upon the submission of the IND and draft Phase 2 protocol, FDA advised Neoprobe that commercially produced **Lymphoseek** would need to be used in the Phase 2 clinical study, as opposed to using drug previously manufactured in laboratories at UCSD. Also, the regulatory agencies raised a number of Chemistry, Manufacturing and Control (CMC) questions regarding the drug compound and its complete characterization. Neoprobe began the transfer of bulk

drug manufacturing to Reliable Biopharmaceutical early in 2005 and engaged Cardinal Health to develop and validate procedures and assays to establish commercial standards for the formulation, filling and lyophilization of the drug compound. We submitted an initial CMC response to FDA in April 2006.

We were notified by FDA in May 2006 that they completed their review of our submissions and that we were released from clinical hold to commence patient enrollment for a Phase 2 clinical study of **Lymphoseek**. The first of our Phase 2 clinical sites received clearance from its internal clinical review committee or Institutional Review Board (IRB) in July 2006. The IRB clearance permitted us to finalize arrangements to begin patient screening and enrollment activities for the Phase 2 trial, and we began patient enrollment in September. We had originally hoped to provide top-line results for the first 40 patients in our Phase 2 trial of **Lymphoseek** during the fourth quarter of 2006. Unfortunately, the time required to obtain the necessary IRB approvals and to then execute the research contracts at some of the participating clinical institutions has taken significantly longer than expected. We announced positive efficacy results from the Phase 2 trial (**Lymphoseek** identified lymphatic tissue in 39 of 40 (97.5%) treated patients) earlier in March 2007. Based upon the positive efficacy results of the drug from the first stage of the trial, Neoprobe has commenced enrollment in the second stage of the Phase 2 study and has submitted its proposed Phase 3 protocols to FDA. The second stage of the Phase 2 study will involve an additional 40 patients with either melanoma or breast cancer. Patients are now being enrolled at all five of the leading cancer centers in the United States who we have identified as participating in the Phase 2 study. The participating institutions are the John Wayne Cancer Center, University of California San Francisco, MD Anderson Cancer Center, University Hospital Cleveland and the University of Louisville. We currently expect enrollment in the Phase 2 trial to be completed during the second quarter of 2007.

The submission to FDA includes separate Phase 3 studies to be conducted in patients with either melanoma and breast cancer. We expect each Phase 3 study to involve approximately 200 evaluable patients. We currently expect the Phase 3 trials will likely now begin sometime during the second half of 2007. To facilitate enrollment, we currently plan to increase the number of participating institutions in the Phase 3 trials to approximately 25 centers in each trial. This should enable us to enroll patients at a more rapid rate than was experienced in the Phase 2. Our ability to commence the Phase 3 study in the third quarter will be dependent upon FDA approving the design and scope of the Phase 3 protocols prior to the completion of the Phase 2 study. The approval of the Phase 3 protocols and investigator's brochure will permit us to commence the review of the Phase 3 by the IRBs at the study sites. The IRB review process was one of the limiting factors in the commencement of the Phase 2 study and we are endeavoring to expedite the process for the Phase 3 study. To further facilitate these reviews, a preliminary investigators meeting is being held at the March 2007 meeting of the SSO.

Our goal is to file the NDA for **Lymphoseek** in 2008, which will be dependent upon the ability to commence the Phase 3 clinical studies in a timely fashion. Depending on the timing and outcome of the FDA regulatory review cycle, we believe that **Lymphoseek** can be commercialized in 2009. As a result of the delays we have experienced and modifications made to the number of patients we expect to enroll, as well as revisions in our regulatory pathway, our current estimate of total out-of-pocket development costs has increased to approximately $9 million. In addition, Neoprobe has discussed the drug approval and registration process through the centralized European drug evaluation procedures with the European Medicinal Evaluation Agency (EMEA) in London. We intend to use the results from the Phase 3 clinical evaluation of **Lymphoseek**, which we currently intend to include sites in the EU, to support the drug registration application process with the EMEA. We cannot assure you, however, that this product will achieve regulatory approval, or if approved, that it will achieve market acceptance. See Risk Factors.

RIGS

From inception until 1998, Neoprobe devoted significant efforts and resources to the development of its proprietary **RIGS** technology. The **RIGS** system combines a patented hand-held gamma radiation detection probe, proprietary radiolabeled cancer-specific targeting agents, and patented surgical methods to provide surgeons with real-time information to locate tumor deposits not detectable by conventional methods. The **RIGS** system is designed to assist the surgeon in the more thorough removal of the cancer, thereby leading to improved surgical treatment of the patient. The targeting agents used in the **RIGS** process are monoclonal antibodies, labeled with a radioactive isotope that emits low energy gamma rays. The device used is a very sensitive radiation detection instrument that is capable of

detecting small amounts of radiation bound to the targeting agent. Before surgery, a cancer patient is injected with one of the targeting agents which circulates throughout the patient’s body and binds specifically to cancer cell antigens or receptors. Concentrations of the targeting agent are then located during surgery by Neoprobe's gamma detection device, which emits an audible tone to direct the surgeon to targeted tissue.

RIGScan CR is an intraoperative agent consisting of a radiolabeled murine monoclonal antibody (MAb CC49). The radiolabel used is ^{125}I, a 27 - 35 KeV emitting isotope. The MAb used in **RIGScan** CR is the CC49 MAb developed by the NCI and licensed to Neoprobe by the National Institutes of Health (NIH). The CC49 MAb is produced from a murine cell line generated by the fusion of splenic lymphocytes from mice immunized with tumor-associated glycoprotein-72 (TAG-72) with non-immunoglobulin secreting P3-NS-1-Ag4 myeloma cells. The CC49 MAb localizes or binds to TAG-72 and shows a strong reactivity with both LS-174T colon cancer extract and to a breast cancer extract.

RIGScan CR is the biologic component for the **RIGS** system to be used in patients with colon or rectal cancer. The **RIGS** system was conceived to be a diagnostic aid in the intraoperative detection of clinically occult disease. **RIGScan** CR is intended to be used in conjunction with other diagnostic methods, for the detection of the extent and location of tumor in patients with colorectal cancer. The detection of clinically occult tumor provides the surgeon with a more accurate assessment of the extent of disease, and therefore may impact the surgical and therapeutic management of the patient. Clinical trials suggest that **RIGScan** CR provides additional information outside that provided by standard diagnostic modalities (including surgical exploration) that may aid in patient management. Specifically, **RIGScan** CR used as a component of the **RIGS** system confirms the location of surgically suspicious metastases, evaluates the margins of surgical resection, and detects occult tumor in perihepatic (portal and celiac axis) lymph nodes.

Neoprobe conducted two Phase 3 studies, NEO2-13 and NEO2-14, of **RIGScan** CR in the mid-1990s in patients with primary and metastatic colorectal cancer, respectively. Both studies were multi-institutional involving cancer treatment institutions in the United States, Israel, and Europe. The primary endpoint of both studies was to demonstrate that **RIGScan** CR detected pathology-confirmed disease that had not been detected by traditional preoperative (*i.e.,* CT Scans) or intraoperative (*i.e.*, surgeon's visual observations and palpation) means. That is, the trials were intended to show that the use of **RIGScan** CR assisted the surgeon in the detection of occult tumor. In 1996, Neoprobe submitted applications to the EMEA and FDA for marketing approval of **RIGScan** CR for the detection of metastatic colorectal cancer.

Clinical study NEO2-14, which was submitted to FDA in the **RIGScan** CR Biologic License Application (BLA), enrolled 151 colorectal cancer patients with either suspected metastatic primary colorectal disease or recurrent colorectal disease. During FDA's review of the BLA, 109 of the enrolled patients were determined to be evaluable patients. Clinical study NEO2-13 was conducted in 287 enrolled patients with primary colorectal disease. The primary end-point for clinical study NEO2-13 was the identification of occult tumor.

NEO2-14 was the pivotal study submitted with Neoprobe's referenced BLA. Two additional studies evaluating patients with either primary or metastatic colorectal disease, NEO2-11 (a multi-center study) and NEO2-18 (a single institution study), were included in the BLA and provided supportive proof of concept (*i.e.*, localization and occult tumor detection) and safety data. A study summary report for NEO2-13 was submitted under the BLA; however, FDA undertook no formal review of the study.

Following review of our applications, we received requests for further information from FDA and from the European Committee for Proprietary Medicinal Products on behalf of the EMEA. Both FDA and the EMEA acknowledged that our studies met the diagnostic endpoint of the Phase 3 clinical study, which was to provide incremental information to the surgeon regarding the location of hidden tumor. However, both agencies wanted to know how the finding of additional tumor provided clinical benefit that altered patient management or outcome for patients with metastatic colorectal cancer. In a series of conversations with FDA, the product claims were narrowed to the intraoperative detection of hepatic and perihepatic disease in patients with advanced colorectal cancer and patients with recurrent colorectal cancer.

FDA determined during its review of the BLA that the clinical studies of **RIGScan** CR needed to demonstrate clinical utility in addition to identifying additional pathology-confirmed disease. In discussions between Neoprobe and the agency, an FDA-driven post hoc analysis plan was developed to limit the evaluation of **RIGScan** CR to patients with hepatic and perihepatic disease with known metastasis to the liver. Findings of occult disease and subsequent changes in patient management (*i.e*., abandoning otherwise risky hepatic resections) in this limited population would serve as a measure of patient benefit. FDA's analysis of the patients enrolled in NEO2-14 matching the limited criteria was evaluated with a determination to confirm the surgical resection abandonment outcome. The number of evaluable patients in this redefined patient population was deemed too small by the agency and the lack of pre-stated protocol guidance precluded consistent sets of management changes given similar occult findings. The number of evaluable patients for any measure of clinical utility, therefore, was too small to meet relevant licensing requirements and FDA ultimately issued a not approvable letter for the BLA on December 22, 1997, describing certain clinical and manufacturing deficiencies. Neoprobe withdrew its application to the EMEA in November 1997.

We developed a clinical response plan for both agencies during the first half of 1998. However, following our analysis of the regulatory pathways for approval that existed at that time, we determined that we did not have sufficient financial resources to conduct the additional studies requested and sought to identify others with an interest in continuing the development process.

In recent years, we have obtained access to survival analyses of patients treated with **RIGScan** CR which have been prepared by third parties, indicating that **RIGScan** CR may be predictive of, or actually contribute to, a positive outcome when measuring survival of the patients that participated in our original BLA studies. The data or its possible significance was unknown at the time of the BLA review given the limited maturity of the follow-up experience. The data includes publication by some of the primary investigators involved in the Phase 3 **RIGS** trials who have independently conducted survival follow-up analyses to their own institution’s **RIGS** trial patients with apparently favorable results relating to the long-term survival prognosis of patients who were treated with **RIGS**. In addition, we learned that FDA has held the BLA originally filed with FDA in 1996 open. Based primarily on these pieces of information, we requested a meeting with FDA to discuss the possible next steps for evaluating the survival related to our previous Phase 3 clinical trials as well as the possible submission of this data, if acceptable, as a prospective analysis in response to questions originally asked by FDA in response to our original BLA.

The April 2004 meeting with FDA was an important event in the re-activation of the **RIGS** program. The meeting was very helpful from a number of aspects: we confirmed that the **RIGS** BLA remains active and open. We believe this will improve both the cost effectiveness and timeliness of future regulatory submissions for **RIGScan** CR. Additionally, FDA preliminarily confirmed that the BLA may be applicable to the general colorectal population; and not just the recurrent colorectal market as applied for in 1996. Applicability to a general colorectal population could result in a greater market potential for the product than if applicable to just the recurrent population. During the meeting, FDA indicated that it would consider possible prognostic indications for **RIGScan** CR and that survival data from one of our earlier Phase 3 studies could be supportive of a prognostic indication. We provided FDA with a draft protocol for a Phase 3 prognostic/therapeutic trial.

Neoprobe received a response from FDA that the prognostic/therapeutic trial design appeared to meet their guidelines. FDA’s response to our clinical submission included an invitation for Neoprobe to seek a special protocol assessment (SPA) of its proposed Phase 3 study. Neoprobe intends to seek a SPA review of the complete Phase 3 package including the clinical protocol, training materials and data collection forms later this year. In concert with our meetings with FDA, we met with representatives of the European regulatory body, the EMEA, to seek guidance for the **RIGScan** CR program in Europe. The guidance from the EMEA was consistent with the input from FDA with the additional recommendation that any future clinical studies be conducted with the humanized version of the **RIGScan** CR antibody. It is possible that the regulatory pathway may continue to evolve as we seek to reach a consensus with the regulatory agencies on the reactivation of the BLA for **RIGScan** CR.

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In addition, the **RIGScan** CR biologic drug has not been produced for several years and we believe it is likely we would have to perform some additional work related to ensuring the drug cell line is still viable and submit this data to FDA for their evaluation before approval could be considered. We have initiated discussions with established biologic manufacturing organizations to determine the costs and timelines associated with the production of commercial quantities of the CC49 antibody. In addition, we will need to establish radiolabeling capabilities for the CC49 antibody in order to meet the regulatory needs for the **RIGScan** CR product.

In parallel with our discussions with the regulatory authorities, we have discussed the clinical and regulatory strategy for **RIGScan** CR with reimbursement consultants who provided us with valuable input regarding the potential target pricing for a **RIGScan** product.

In November 2005, Neoprobe submitted a corporate IND application for the modified humanized version of **RIGScan** CR. With the establishment of the corporate IND, responsibility for the clinical and commercial development of the humanized version of **RIGScan** CR was officially transferred from a physician sponsored IND to Neoprobe. Prior to the evaluation of the modified antibody in a Phase I clinical trial, all clinical development of **RIGScan** CR had been conducted with a murine (i.e., mouse DNA-based) version of a monoclonal antibody. The Phase I trial was the first test in human patients using a modified version of the antibody from which the prominent parts of the mouse DNA chain had been removed. In early 2006, we filed an IND amendment that included a final report to FDA of the Phase I study.

Over the past few years, we devoted significant effort toward the identification of potential development partners for **RIGScan** CR. Our efforts to date have resulted in discussions with a number of parties, some of which have led to due diligence and potential partnership discussions. We continue to believe it will be necessary for Neoprobe to identify a development partner or an alternative funding source in order to prepare for and to fund the pivotal clinical testing that will be necessary to gain marketing clearance for **RIGScan** CR. However, while we have parties who have indicated an interest in the technology, none of the discussions to date have resulted in definitive agreements with any party or parties. In addition, we do not believe these efforts will result in a partnership until further clarity can be added to the **RIGScan** regulatory approval pathway, such as perhaps obtaining a positive SPA determination from FDA. However, even if we are able to make such arrangements on satisfactory terms, we believe that the time required for continued development, regulatory approval and commercialization of a **RIGS** product would likely be a minimum of five years before we receive any significant product-related royalties or revenues. We cannot assure you that we will be able to complete definitive agreements with a development partner for the **RIGS** technology and do not know if a partner will be obtained on a timely basis on terms acceptable to us, or at all. We also cannot assure you that FDA or the EMEA will clear our **RIGS** products for marketing or that any such products will be successfully introduced or achieve market acceptance. See Risk Factors.

Activated Cellular Therapy

Through various research collaborations, we performed early-stage research on another technology platform, ACT, based on work originally done in conjunction with the **RIGS** technology. ACT is intended to boost the patient's own immune system by removing lymph nodes identified during surgery and then, in a cell processing technique, activating and expanding "helper" T-cells found in the nodes. Within 10 to 14 days, the patient's own immune cells, activated and numbering more than 20 billion, are infused into the patient in an attempt to trigger a more effective immune response to the cancer.

In the course of our research into ACT performed with **RIGS**, we learned that these lymph node lymphocytes containing helper T-cells could be activated and expanded to treat patients afflicted with viral and autoimmune disease as well as oncology patients. We have seen promising efficacy of this technology demonstrated from six Phase I clinical trials covering the oncology, viral and autoimmune applications.

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In 2005, we formed a new subsidiary, Cira Bio, to explore the development of ACT. Neoprobe owns approximately 90% of the outstanding shares of Cira Bio with the remaining shares being held by the principals of a private holding company, Cira LLC. In conjunction with the formation of Cira Bio, an amended technology license agreement also was executed with The Ohio State University, from whom both Neoprobe and Cira LLC had originally licensed or optioned the various cellular therapy technologies. As a result of the cross-license agreements, Cira Bio has the exclusive development and commercialization rights to three issued U.S. patents that cover the oncology and autoimmune applications of its technology. In addition, Cira Bio has exclusive licenses to several pending patent applications.

Cira Bio engaged the Battelle Memorial Institute to complete a technology and manufacturing process assessment of the cellular therapy approach. In addition, a scientific advisory group is being formed to develop a clinical and regulatory approach for the Cira Bio technology. Following the completion of these assessments and the formation of a commercialization strategy, Cira Bio intends to raise the necessary capital to move this technology platform forward. The means by which this funding is obtained will likely dilute Neoprobe's ownership interest in Cira Bio; however, we believe that moving forward such a promising technology will only yield positive results for the Neoprobe stockholders and the patients who could benefit from these treatments. However, we do not know if we will be successful in obtaining additional funding, on terms acceptable to us, or at all.

In addition, although the prospects for ACT may be improved depending on the outcome of a decision to renew development efforts for **RIGS**, we currently do not intend to fund any significant ACT-related research and development beyond the evaluation work already performed until a source of further funding is identified. We cannot assure you that we will be successful in obtaining additional funding, or if obtained, that any ACT products will be successfully developed, tested or licensed, or that any such products will gain market acceptance. See Risk Factors.

Market Overviews

The medical device marketplace is a fast growing market. *Medical Device & Diagnostic Industry* magazine reports an annual medical device and diagnostic market of $75 billion in the U.S. and $169 billion internationally.

Cancer Market Overview

Cancer is the second leading cause of death in the U.S. and Western Europe and is responsible for over 500,000 deaths annually in the U.S. alone. The NIH estimates the overall annual costs for cancer (the primary focus of our gamma detection and pharmaceutical products) for the U.S. in the year 2006 at $206.3 billion: $78.2 billion for direct medical costs, $17.9 billion for indirect morbidity, and $110.2 billion for indirect mortality. Our line of gamma detection systems is currently used primarily in the application of SLNB in breast cancer and melanoma which, according the ACS, are expected to account for 12% and 4%, respectively, of new cancer cases in the U.S. in 2006.

The NIH has estimated that breast cancer will annually affect approximately 500,000 women in North America, Western Europe, and other major economic markets. Breast cancer is the second leading cause of death from cancer among all women in the U.S. According to the ACS, nearly 181,000 new cases of invasive breast cancer were expected to be diagnosed and approximately 41,000 women were expected to die from the disease during 2007 in the U.S. alone. The incidence of breast cancer increases with age, rising from about 100 cases per 100,000 women at age 40 to about 400 cases per 100,000 women at age 65. Thus, we believe that the significant aging of the population, combined with improved education and awareness of breast cancer and diagnostic methods, will lead to an increased number of breast cancer surgical diagnostic procedures.

Approximately 80% of the patients diagnosed with breast cancer undergo a lymph node dissection (either ALND or SLNB) to determine if the disease has spread. While many breast cancer patients are treated in large cancer centers or university hospitals, regional and/or community hospitals currently treat the majority of breast cancer patients. Over

10,000 hospitals are located in the markets targeted for our gamma detection SLNB products. While we are aware of no published statistics on the number of institutions that are currently using gamma detection devices in SLNB, we believe that approximately 50% of the total potential global market for gamma detecting devices remains to be penetrated at this time. However, if the potential of **Lymphoseek** as a radioactive tracing agent is ultimately realized, it has the potential to address not only the current breast and melanoma markets on a procedural basis, but also to assist in the clinical evaluation and staging of solid tumor cancers and expanding SLNB to additional indications, such as gastric, non-small cell lung and other solid tumor cancers.

We estimate the total market potential for **Lymphoseek**, if ultimately approved for all of these indications, could exceed $200 million. However, we cannot assure you that **Lymphoseek** will be cleared to market, or if cleared to market, that it will achieve the prices or sales we have estimated.

The ACS estimates that over 147,000 new incidences of colon and rectal cancers will occur in the U.S. in 2006. Based on an assumed recurrence rate of 40%, this would translate into total potential surgical procedures of over 200,000 annually in the U.S. alone. We believe the number of procedures in other markets of the world to be approximately two times the estimated U.S. market. As a result, we believe the total potential global market for **RIGScan** CR could be in excess of $3 billion annually, depending on the level of reimbursement allowed. However, we cannot assure you that **RIGScan** CR will be cleared to market, or if cleared to market, that it will receive the reimbursement or achieve the level of sales we have currently estimated.

Blood Flow Measurement Market Overview

Cardiovascular disease is the number one killer of men and women in the U.S. and in a majority of countries in the rest of the world that track such statistics. The National Center for Healthcare Services (NCHS) registered over 6.3 million inpatient cardiovascular procedures in the U.S. during 2004 with a primary dignosis of cardiovascular disease. In the U.S. in 2004, the NCHS estimates that there were 427,000 coronary artery bypass surgeries performed on 249,000 patients. We, as well as our competitors and other industry analysts, generally estimate the rest of the world's incidence of such modalities at approximately equal to as much as two time U.S. estimates.

The American Heart Association (AHA) estimates the total cost of cardiovascular diseases and stroke in the United States will exceed $431 billion in 2007. A substantial portion of these expenditures is expected to be for non-invasive image and intravascular examination. We are focused on two distinct markets within the hospital setting for Cardiosonix' products:

- intraoperative blood flow assessment (**Quantix/OR**); and

- non-invasive diagnostic blood flow assessment (**Quantix/ND**).

Based on data obtained from the AHA, the Society of Thoracic Surgeons and the American Hospital Association, it is estimated that there are approximately 500,000 vascular and cardiovascular procedures performed in the U.S. that could benefit from qualitative blood flow measurement. Based on these estimates, information obtained from industry sources and data published by our competitors and other medical device companies, we estimate the worldwide total of target procedures to be approximately equal to as much as two times the U.S. totals.

Based on the above number of procedures, assuming we are able to achieve market prices that are comparable to what our competitors are achieving (estimated at averaging $20,000 per system or $130 per procedural use), we believe the worldwide market potential for blood flow measurement products in the niches which our products address to be more than $200 million. However, at the present state of market development and acceptance of blood flow measurement within the medical community, the penetrable market is likely significantly less. At present, we would estimate that only 15% of by-pass procedures involve blood flow measurement. We believe that gaining a modest share of the penetrable market could result in meaningful supplemental annual revenues for our company. We cannot assure you, however, that Cardiosonix products will achieve market acceptance and generate the level of sales or prices anticipated.

Marketing and Distribution

Gamma Detection Devices

We began marketing the current generation of our gamma detection systems, the **neo2000**, in October 1998. Since October of 1999, our gamma detection systems have been marketed and distributed throughout most of the world through Ethicon Endo-Surgery, Inc. (EES), a Johnson & Johnson company. In Japan, however, we market our products through a pre-existing relationship with Century Medical, Inc.

The heart of the **neo2000** system is a control unit that is software-upgradeable, permitting product enhancements without costly remanufacturing. Since the original launch of the **neo2000** system, we have introduced an enhanced version of our 14mm reusable probe optimized for lymphatic mapping procedures, a laparoscopic probe intended for certain minimally invasive procedures, and three Bluetooth probes for a variety of applications. We have also developed four major software version upgrades for the system that have been made available for sale to customers. We intend to continue developing additional SLNB-related probes and instrument products in cooperation with EES to maintain our leadership position in the SLNB field.

Physician training is critical to the use and adoption of SLNB products by surgeons and other medical professionals. Our company and our marketing partners have established relationships with leaders in the SLNB surgical community and have established and supported training courses internationally for lymphatic mapping. We intend to continue to work with our partners to expand the number of SLNB training courses available to surgeons.

We entered into our current distribution agreement with EES effective October 1, 1999 for an initial five-year term with options to extend for two successive two-year terms. In March 2004, EES exercised its first two-year extension option, and in March 2006 EES exercised its option for the second and final two-year term extension, thus extending the term of our current agreement through December 31, 2008. Under this agreement, we manufacture and sell our SLNB products almost exclusively to EES, who distributes the products globally (except for Japan). EES has no ongoing purchase or reimbursement commitments to us other than the rolling four-month binding purchase commitment for gamma detection devices as outlined in the distribution agreement. Our agreement with EES also contains certain termination provisions and licenses to our intellectual property that take effect only in the event we fail to supply product, or for other reasons such as a change of control. See Risk Factors.

Gamma Detection Radiopharmaceuticals

We have not established a marketing or distribution channel for either **RIGScan** CR or **Lymphoseek**. We have had initial discussions with parties who may be interested in marketing and distribution of these products; however, such discussions to date have been preliminary in nature and have not resulted in any definitive arrangements. We believe the most preferable and likely distribution partners for **Lymphoseek** would be entities with global radiopharmaceutical distribution channels although it is possible that other, more traditional oncology pharmaceutical portfolios may also have interest. With respect to **RIGScan** CR, we believe there are development milestones that can be achieved prior to the need for significant capital investment in **RIGScan** CR such as preparing the request for a SPA and completing a final protocol review. However, we continue to believe it will be necessary for us to identify a development partner or an alternative funding source in order to prepare for and to fund the pivotal clinical testing that will be necessary to gain marketing clearance for **RIGScan** CR. At the present time, while we have parties who have indicated an interest in entering into a development relationship, we do not believe these efforts will result in a definitive partnership at least until a positive SPA is obtained. We anticipate continuing discussions for both **Lymphoseek** and **RIGScan** CR as we move forward with the clinical development for each product; however, we cannot assure you that we will be able to secure marketing and distribution partners for either product, or if secured, that such arrangements will result in significant sales of either product.

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Blood Flow Measurement Devices

Both of our blood flow measurement devices, the **Quantix/ND** and **Quantix/OR** have received marketing clearance in the U.S. and the EU and certain other foreign markets. Our goal is to ensure sales and distribution coverage through third parties of substantially all of the U.S., the EU, the Pacific Rim of Asia and selective markets in the rest of the world. Currently, we have in place or have executed or reached agreement in principle with distributors and/or master distributors for the **Quantix/OR** covering the United States, all major market countries in the EU, and substantially all countries that comprise the Pacific Rim of Asia. In addition, we have distribution arrangements in place covering major portions of Central and South America.

We anticipate spending a significant amount of time and effort in 2007 to close on leads generated regarding the **Quantix/OR** and to develop new sales leads. The sales cycle for medical devices such as our blood flow products is typically a four- to six-month cycle. This sales cycle, coupled with the timetable necessary to train the new distributors we engaged during 2006 has resulted in disappointing sales levels of our blood flow measurement equipment to date. We are also investigating alternative pricing strategies such as per-use fees or leasing that may affect the adoption rates for our blood flow measurement devices. As a result, we anticipate that the product development and market support costs we will incur in 2007 will be greater than the revenue we generate from the sales of blood flow devices. We are still evaluating our outlook for 2007 but believe the coming quarters are important to demonstrating the ultimate viability of this product line.

Manufacturing

Gamma Detection Devices

We rely on independent contract manufacturers, some of which are single-source suppliers, for the manufacture of the principal components of our current line of gamma detection system products. See Risk Factors. We have devoted significant resources to develop production capability for our gamma detection systems at qualified contract manufacturers. Production of the **neo2000** control unit, the 14mm probe, the 11mm laparoscopic probe, and the Bluetooth probes involve the manufacture of components by a combination of subcontractors, including but not limited to eV Products, a division of II-VI Corporation (eV), and TriVirix International, Inc. (TriVirix). We also purchase certain accessories for our line of gamma detection systems from other qualified manufacturers.

In December 1997, we entered into a supply agreement with eV for the supply of certain crystals and associated electronics to be used in the manufacture of our proprietary line of hand-held gamma detection probes. The original term of the agreement with eV expired on December 31, 2002 and was automatically extended through December 31, 2005. Since the expiration of the agreement with eV, they have continued to supply crystals under purchase orders. eV supplies 100% of the crystals used in our products. While eV is not the only potential supplier of such crystals, any prolonged interruption of this source could restrict the availability of our probe products, which would adversely affect our operating results.

In February 2004, we executed a Product Supply Agreement with TriVirix for the manufacture of the **neo2000**, 14mm probe and 11mm laparoscopic probe. The initial term of this agreement expired in February 2007 but was automatically extended through February 2008. The Agreement is automatically extended for successive one-year periods unless six months notice is provided by either party.

We cannot assure you that we will be able to maintain agreements with our subcontractors on terms acceptable to us, or that our subcontractors will be able to meet our production requirements on a timely basis, at the required levels of performance and quality. In the event that any of our subcontractors is unable or unwilling to meet our production requirements, we cannot assure you that an alternate source of supply could be established without significant interruption in product supply or without significant adverse impact to product availability or cost. Any significant

supply interruption or yield problems that we or our subcontractors experience would have a material adverse effect on our ability to manufacture our products and, therefore, a material adverse effect on our business, financial condition, and results of operations until a new source of supply is qualified. See Risk Factors.

Gamma Detection Radiopharmaceuticals

In preparation for the commencement of multi-center clinical evaluation of **Lymphoseek**, Neoprobe engaged drug manufacturing organizations to produce the drug for use in the Phase 2 and pivotal (i.e., Phase 3) clinical trials. Neoprobe selected Reliable Biopharmaceutical Corporation (Reliable) to produce the basic chemical compound and Cardinal Health, Inc. (Cardinal) to perform final product manufacturing including final drug formulation, lyophilization (i.e., freeze-drying) and packaging processes. Once packaged, the vialed drug can then be shipped to a hospital or regional commercial radiopharmacy where it can be made radioactive (i.e., radiolabeled) with Tc99m to become **Lymphoseek**. The commercial manufacturing processes at Reliable and Cardinal have been validated and both organizations have assisted Neoprobe in the preparation of the chemistry, manufacturing and control sections of our submissions to FDA. Both Reliable and Cardinal are registered manufacturers with FDA. At this point, our agreements with Reliable and Cardinal cover only product to be used in the clinical trials and regulatory registration process for **Lymphoseek**. Further commercial supply and distribution agreements have yet to be negotiated with both Reliable and Cardinal. We cannot assure you that we will be successful in reaching such agreements with Reliable or Cardinal on terms satisfactory to us or at all.

In preparation for the initiation of the next phase of clinical evaluation of **RIGScan** CR, we have also initiated discussions with potential biologic manufacturers and radiolabeling organizations. We have held discussions with parties who may assist in the manufacturing validation and radiolabeling of the **RIGScan** product; however, we have not yet finalized agreements with these entities. We anticipate finalizing these discussions following securing a development partner in order to accommodate the commencement of future **RIGScan** CR clinical trials. We cannot assure you that we will be successful in securing and/or maintaining the necessary biologic, product and/or radiolabeling capabilities. See Risk Factors.

Blood Flow Measurement Devices

The **Quantix** blood flow measurement devices distributed through early 2006 were manufactured by our subsidiary, Cardiosonix Ltd. In early 2006, we received approval from the Office of the Chief Scientist in Israel to transfer manufacturing rights for the **Quantix** devices to Neoprobe. See Risk Factors. Future assembly of **Quantix** blood flow control units will therefore be done under the terms of the Product Supply Agreement we have in place with TriVirix for the assembly of our gamma devices. Assembly of the **Quantix/OR** control units started at TriVirix in March 2006. We currently purchase ultrasound transducer modules and probe subassemblies from Vermon S.A. (Vermon) of France under purchase orders. The ultrasound probe assemblies are then completed by Technical Services for Electronics, Inc. (TSE), also under purchase orders.

We cannot assure you that we will be able to finalize supply and service agreements with Vermon, TSE or other subcontractors for the **Quantix** products, that we will be able to maintain our agreement with TriVirix, or that our subcontractors will be able to meet our production requirements on a timely basis, at the required levels of performance and quality. In the event that any of our subcontractors is unable or unwilling to meet our production requirements, we cannot assure you that an alternate source of supply could be established without significant interruption in product supply or without significant adverse impact to product availability or cost. Any significant supply interruption or yield problems that we or our subcontractors experience would have a material adverse effect on our ability to manufacture our products and, therefore, a material adverse effect on our business, financial condition, and results of operations until a new source of supply is qualified. See Risk Factors.

Competition

We face competition from medical product and biotechnology companies, as well as from universities and other non-profit research organizations in the field of cancer diagnostics and treatment. Many emerging medical product companies have corporate partnership arrangements with large, established companies to support the research, development, and commercialization of products that may be competitive with our products. In addition, a number of large established companies are developing proprietary technologies or have enhanced their capabilities by entering into arrangements with or acquiring companies with technologies applicable to the detection or treatment of cancer and the measurement of blood flow. Many of our existing or potential competitors have substantially greater financial, research and development, regulatory, marketing, and production resources than we have. Other companies may develop and introduce products and processes competitive with or superior to those of ours. See Risk Factors.

For our products, an important factor in competition is the timing of market introduction of our products or those of our competitors' products. Accordingly, the relative speed with which we can develop products, complete the regulatory clearance processes and supply commercial quantities of the products to the market is an important competitive factor. We expect that competition among products cleared for marketing will be based on, among other things, product efficacy, safety, reliability, availability, price, and patent position.

Gamma Detection Devices

With the emergence of ILM, a number of companies have begun to market gamma radiation detection instruments. Most of the competitive products have been designed from an industrial or nuclear medicine perspective rather than being developed initially for surgical use. We compete with products produced and/or marketed by Care Wise Medical Products Corporation, Intra-Medical Imaging LLC (distributed by GE Healthcare), SenoRx, Pol.Hi.Tech. Srl, and other companies.

It is often difficult to glean accurate competitive information within the lymphatic mapping field, primarily because most of our competitors are either subsidiaries or divisions of a large corporation or privately held corporations, whose sales revenue or volume data is, therefore, not readily available or determinable. In addition, lymphatic mapping does not currently have a separate reimbursement code in most healthcare systems. As such, determining trends in the actual number of procedures being performed using lymphatic mapping is difficult. We believe, based on our understanding of EES' success rate in competitive bid situations, that our market share has remained relatively constant or increased slightly in light of changes in the competitive landscape over the past few years. As we have discussed, we believe that current sales levels indicate that some prospective customers may be waiting on the results of important international clinical trials prior to adoption the SLNB procedure and purchasing a gamma detection device. We expect the results from these trials, when announced, will likely have a positive impact on sales volumes. We believe our intellectual property portfolio will be a barrier to competitive products; however, we cannot assure you that competitive products will not be developed, be successful in eroding our market share or affect the prices we receive for our gamma detection devices. See Risk Factors.

Gamma Detection Radiopharmaceuticals

We do not believe there are any directly competitive intraoperative diagnostic radiopharmaceuticals with **RIGScan** CR that would be used intraoperatively in the colorectal cancer application that **RIGScan** CR is initially targeted for. There are other radiopharmaceuticals that are used as preoperative imaging agents; however, we are unaware of any that could be used as a real-time diagnostic aid during surgery such as **RIGScan** CR.

Surgeons who practice the lymphatic mapping procedure that **Lymphoseek** is intended for currently use other radiopharmaceuticals such as a sulphur-colloid compound in the U.S. and other colloidal compounds in other markets. However, these drugs are being used "off-label" (i.e., they are not specifically indicated for use as a lymphatic targeting

agent). As such, we believe that **Lymphoseek**, if ultimately approved, would be the first drug specifically labeled for use as a lymphatic tissue targeting agent.

Blood Flow Measurement Devices

There are several technologies on the market that measure or claim to measure indices of blood flow. These products can be categorized as devices that measure blood flow directly and devices that only obtain an estimation of flow conditions. We believe our device is most directly competitive with Transit Time Ultrasound (TT) Flowmetry. TT is the leading modality for blood flow measurement in the operating room today. TT systems monitor blood flow invasively and are restricted to isolated vessels. They require probe adaptation to the vessel size, and do not provide additional vascular parameters. The technology requires the operator to encircle the blood vessel with a probe that includes two ultrasound transmitters/receivers on one side, and a mirror reflector on the opposite side of the vessel. By measuring the transit time of the ultrasound beam in the upstream and downstream directions, volume blood flow estimates can be evaluated. In addition, there are other competitive technologies which utilize Doppler ultrasound. Doppler technology has been around for several decades, and is being widely used in non-invasive vascular diagnostics. Duplex ultrasound systems have the potential to measure blood flow non-invasively. Duplex systems are designed for imaging the anatomical severity of pathology. This method is technician-dependent, often cumbersome and does not offer monitoring capabilities. Plain Doppler systems provide only blood flow velocity rather than volume flow.

Cardiosonix products are designed to address blood flow measurement across a variety of clinical and surgical settings, and there are a number of companies already in the marketplace that offer products related to blood flow measurement. However, most of these products do not directly compete with Cardiosonix products. The companies that do offer potentially competitive products are, for the most part, smaller, privately held companies, with which we believe we can effectively compete. Indeed, due to our belief in the technical superiority of our products, we believe the existence of competitors will help to educate the marketplace regarding the importance of blood flow measurement. As we have discussed, adoption of blood flow monitoring devices for the measurement of hemodynamic status will likely take an involved education process as it often involves a change in clinical or surgical management. While there is not a clear leader in these markets, the following companies compete most directly with Cardiosonix: Transonic Systems, Inc., Medi-Stim AS, and Carolina Medical, Inc.

Patents and Proprietary Rights

We regard the establishment of a strong intellectual property position in our technology as an integral part of the development process. We attempt to protect our proprietary technologies through patents and intellectual property positions, in the United States as well as major foreign markets. Approximately 20 instrument patents issued in the United Sates as well as major foreign markets protect our SLNB technology.

Cardiosonix has also applied for patent coverage for the key elements of its Doppler blood flow technology in the U.S. The first of the two patents covering Cardiosonix technology was issued in the U.S. in January 2003 and claims for the second patent have been allowed.

Lymphoseek is also the subject of patents and patent applications in the United States and certain major foreign markets. The patents and patent applications are held by The Regents of the University of California and have been licensed exclusively to Neoprobe for lymphatic tissue imaging and intraoperative detection. The first composition of matter patent covering **Lymphoseek** was issued in the United States in June 2002. The claims of the composition of matter patent covering **Lymphoseek** have been allowed in the EU and issued in the majority of EU countries in 2005. The composition of matter patent is being prosecuted in Japan.

We continue to maintain proprietary protection for the products related to **RIGS** and ACT in major global markets such as the U.S. and the EU, which although not currently integral to our near-term business plans, may be important to a potential **RIGS** or ACT development partner. The original methodology aspects of our **RIGS** technology are claimed in the United States in U.S. Patent No. 4,782,840, which expired in August 2005. However, Neoprobe has

recently gained access to additional methodology applications related to our **RIGS** technology that are covered by patents that provide additional patent coverage through 2018, unless extended. In addition to the **RIGS** methodology patents, composition of matter patents have been issued in the U.S. and EU that cover the antibodies used in clinical studies. The most recent of these patents was issued in 2004 and additional patent applications are pending.

The activated cellular therapy technology of Cira Bio is the subject of issued patents in the United States to which Neoprobe has exclusive license rights. European patent statutes do not permit patent coverage for treatment technologies such as Cira Bio's. The oncology applications of Cira Bio's treatment approach are covered by issued patents with expiration dates of 2018 and 2020, unless extended. The autoimmune applications are covered by an issued patent with an expiration date of 2018, unless extended. The viral applications are the subject of patent applications and other aspects of the Cira Bio technology that are in the process of being reviewed by the United States Patent and Trademark Office. Cira Bio has received favorable office action correspondence on both applications.

The patent position of biotechnology and medical device firms, including our company, generally is highly uncertain and may involve complex legal and factual questions. Potential competitors may have filed applications, or may have been issued patents, or may obtain additional patents and proprietary rights relating to products or processes in the same area of technology as that used by our company. The scope and validity of these patents and applications, the extent to which we may be required to obtain licenses thereunder or under other proprietary rights, and the cost and availability of licenses are uncertain. We cannot assure you that our patent applications will result in additional patents being issued or that any of our patents will afford protection against competitors with similar technology; nor can we assure you that any of our patents will not be designed around by others or that others will not obtain patents that we would need to license or design around. See Risk Factors.

We also rely upon unpatented trade secrets. We cannot assure you that others will not independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets, or disclose such technology, or that we can meaningfully protect our rights to our unpatented trade secrets.

We require our employees, consultants, advisers, and suppliers to execute a confidentiality agreement upon the commencement of an employment, consulting or manufacturing relationship with us. The agreement provides that all confidential information developed by or made known to the individual during the course of the relationship will be kept confidential and not disclosed to third parties except in specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual will be the exclusive property of our company. We cannot assure you, however, that these agreements will provide meaningful protection for our trade secrets in the event of an unauthorized use or disclosure of such information.

Government Regulation

Most aspects of our business are subject to some degree of government regulation in the countries in which we conduct our operations. As a developer, manufacturer and marketer of medical products, we are subject to extensive regulation by, among other governmental entities, FDA and the corresponding state, local and foreign regulatory bodies in jurisdictions in which our products are sold. These regulations govern the introduction of new products, the observance of certain standards with respect to the manufacture, safety, efficacy and labeling of such products, the maintenance of certain records, the tracking of such products and other matters.

Failure to comply with applicable federal, state, local or foreign laws or regulations could subject us to enforcement action, including product seizures, recalls, withdrawal of marketing clearances, and civil and criminal penalties, any one or more of which could have a material adverse effect on our business. We believe that we are in substantial compliance with such governmental regulations. However, federal, state, local and foreign laws and regulations regarding the manufacture and sale of medical devices are subject to future changes. We cannot assure you that such changes will not have a material adverse effect on our company.

For some products, and in some countries, government regulation is significant and, in general, there is a trend toward more stringent regulation. In recent years, FDA and certain foreign regulatory bodies have pursued a more rigorous enforcement program to ensure that regulated businesses like ours comply with applicable laws and regulations. We devote significant time, effort and expense addressing the extensive governmental regulatory requirements applicable to our business. To date, we have not received any notifications or warning letters from FDA or any other regulatory bodies of alleged deficiencies in our compliance with the relevant requirements, nor have we recalled or issued safety alerts on any of our products. However, we cannot assure you that a warning letter, recall or safety alert, if it occurred, would not have a material adverse effect on our company.

In the early- to mid-1990s, the review time by FDA to clear medical products for commercial release lengthened and the number of marketing clearances decreased. In response to public and congressional concern, FDA Modernization Act of 1997 (the 1997 Act) was adopted with the intent of bringing better definition to the clearance process for new medical products. While FDA review times have improved since passage of the 1997 Act, we cannot assure you that FDA review process will not continue to delay our company's introduction of new products in the U.S. in the future. In addition, many foreign countries have adopted more stringent regulatory requirements that also have added to the delays and uncertainties associated with the release of new products, as well as the clinical and regulatory costs of supporting such releases. It is possible that delays in receipt of, or failure to receive, any necessary clearance for our new product offerings could have a material adverse effect on our business, financial condition or results of operations.

While we are unable to predict the extent to which our business may be affected by future regulatory developments, we believe that our substantial experience dealing with governmental regulatory requirements and restrictions on our operations throughout the world, and our development of new and improved products, should enable us to compete effectively within this environment.

Gamma Detection and Blood Flow Measurement Devices

As a manufacturer of medical devices sold in various global markets, we are required to manufacture the devices under quality system regulations (QSR) and maintain appropriate technical files and quality records. Our medical devices are regulated in the United States by FDA and in the EU according to the Medical Device Directive (93/42/EEC). Under this regulation, we must obtain CE Mark status for all products exported to the EU.

Our initial generation gamma detection instruments received 510(k) marketing clearance from FDA in December 1986 with modified versions receiving similar clearances in 1992 through 1997. In 1998, FDA reclassified "nuclear uptake detectors" as being exempt from the 510(k) process. We believe the **neo2000** device is exempt from the 510(k) process because it is substantially equivalent to previously cleared predecessor devices. We obtained the CE Mark for the **neo2000** device in January 1999, and therefore, must continue to manufacture the devices under a quality system compliant to the requirements of ISO 9001/EN 46001 and maintain appropriate technical files. We maintain a license to import our gamma detection devices into Canada, and therefore must continue to manufacture the devices under a quality system compliant to the requirements of ISO 13485 and relevant Canadian regulations.

Cardiosonix has received 510(k) and CE mark clearance to market the **Quantix/ND** device in the U.S. and EU for non-invasive applications. The **Quantix/OR** has also received CE Mark clearance to market in the EU and 510(k) clearance to market in the U.S. Our distribution partners in certain foreign markets other than the EU are seeking marketing clearances, as required, for both the **Quantix/ND** and **Quantix/OR**.

Gamma Detection Radiopharmaceuticals (Lymphoseek and RIGScan)

Our radiolabeled targeting agents and biologic products, if developed, would require a regulatory license to market by FDA and by comparable agencies in foreign countries. The process of obtaining regulatory licenses and approvals is costly and time consuming, and we have encountered significant impediments and delays related to our previously proposed biologic products.

The process of completing pre-clinical and clinical testing, manufacturing validation and submission of a marketing application to the appropriate regulatory bodies usually takes a number of years and requires the expenditure of substantial resources, and we cannot assure you that any approval will be granted on a timely basis, if at all. Additionally, the length of time it takes for the various regulatory bodies to evaluate an application for marketing approval varies considerably, as does the amount of preclinical and clinical data required to demonstrate the safety and efficacy of a specific product. The regulatory bodies may require additional clinical studies that may take several years to perform. The length of the review period may vary widely depending upon the nature and indications of the proposed product and whether the regulatory body has any further questions or requests any additional data. Also, the regulatory bodies will likely require post-marketing reporting and surveillance programs to monitor the side effects of the products. We cannot assure you that any of our potential drug or biologic products will be approved by the regulatory bodies or approved on a timely or accelerated basis, or that any approvals received will not subsequently be revoked or modified.

In addition to regulations enforced by FDA, the manufacture, distribution, and use of radioactive targeting agents, if developed, are also subject to regulation by the Nuclear Regulatory Commission (NRC), the Department of Transportation and other federal, state, and local government authorities. We, or our manufacturer of the radiolabeled antibodies, must obtain a specific license from the NRC to manufacture and distribute radiolabeled antibodies, as well as comply with all applicable regulations. We must also comply with Department of Transportation regulations on the labeling and packaging requirements for shipment of radiolabeled antibodies to licensed clinics, and must comply with federal, state, and local governmental laws regarding the disposal of radioactive waste. We cannot assure you that we will be able to obtain all necessary licenses and permits and be able to comply with all applicable laws. The failure to obtain such licenses and permits or to comply with applicable laws would have a materially adverse effect on our business, financial condition, and results of operations.

Employees

As of March 14, 2007, we had 22 full-time employees. We consider our relations with our employees to be good.

Risk Factors

An investment in our common stock is highly speculative, involves a high degree of risk, and should be made only by investors who can afford a complete loss. You should carefully consider the following risk factors, together with the other information in this report, including our financial statements and the related notes, before you decide to buy or continue to hold our common stock. Our most significant risks and uncertainties are described below; however, they are not the only risks we face. If any of the following risks actually occur, our business, financial condition, or results of operations could be materially adversely affected, the trading of our common stock could decline, and you may lose all or part of your investment therein.

We have suffered significant operating losses for several years in our history and we may not be able to again achieve profitability.

We had an accumulated deficit of approximately $136 million and have an overall deficit in stockholders' equity as of December 31, 2006. Although we were profitable in 2000 and in 2001, we incurred substantial losses in the years

prior to that, and again in 2002 through 2006. The deficit resulted because we expended more money in the course of researching, developing and enhancing our technology and products and establishing our marketing and administrative organizations than we generated in revenues. We expect to continue to incur significant expenses in the foreseeable future, primarily related to the completion of development and commercialization of **Lymphoseek**, but also potentially related to **RIGS** and the **Quantix** product line. As a result, we are sustaining substantial operating and net losses, and it is possible that we will never be able to sustain or develop the revenue levels necessary to again attain profitability.

Our products and product candidates may not achieve the broad market acceptance they need in order to be a commercial success.

Widespread use of our handheld gamma detection devices is currently limited to one surgical procedure, SLNB, used in the diagnosis and treatment of two primary types of cancer: melanoma and breast cancer. While the adoption of SLNB within the breast and melanoma indications appears to be widespread, expansion of SLNB to other indications such as colorectal and prostate cancers is likely dependent on a better lymphatic tissue targeting agent than is currently available. Without expanded indications in which to apply SLNB, it is likely that gamma detection devices will reach market saturation. Our efforts and those of our marketing and distribution partners may not result in significant demand for our products, and the current demand for our products may decline.

Our future success will also be affected by the success of the Cardiosonix product line. To date, our efforts to place Cardiosonix's products have met with limited success. The long-term commercial success of the Cardiosonix product line will require widespread acceptance of our products as safe, efficient and cost-effective in the treatment of the cardiac and vascular indications for which they are intended. Widespread acceptance of blood flow measurement would represent a significant change in current medical practice patterns. Other cardiac monitoring procedures, such as pulmonary artery catheterization, are generally accepted in the medical community and have a long standard of use. It is possible that the Cardiosonix product line will never achieve the broad market acceptance necessary to become a commercial success.

Our radiopharmaceutical product candidates, **Lymphoseek** and **RIGScan** CR, are still in the process of development, and even if we are successful in commercializing them, we cannot assure you that they will obtain significant market acceptance.

Clinical trials for our radiopharmaceutical product candidates will be lengthy and expensive and their outcome is uncertain.

Before obtaining regulatory approval for the commercial sale of any product candidates, we must demonstrate through preclinical testing and clinical trials that our product candidates are safe and effective for use in humans. Conducting clinical trials is a time consuming, expensive and uncertain process and may take years to complete. We only recently commenced a Phase 2 clinical trial for our most advanced radiopharmaceutical product candidate, **Lymphoseek**, and we are taking steps to evaluate commencement of a Phase 3 clinical trial for our next radiopharmaceutical candidate, **RIGScan** CR. Historically, the results from preclinical testing and early clinical trials have often not been predictive of results obtained in later clinical trials. Frequently, drugs that have shown promising results in preclinical or early clinical trials subsequently fail to establish sufficient safety and efficacy data necessary to obtain regulatory approval. At any time during the clinical trials, we, the participating institutions or FDA might delay or halt any clinical trials for our product candidates for various reasons, including:

- ineffectiveness of the product candidate;
- discovery of unacceptable toxicities or side effects;
- development of disease resistance or other physiological factors;
- delays in patient enrollment; or
- other reasons that are internal to the businesses of our potential collaborative partners, which reasons they may not share with us.

The results of the clinical trials may fail to demonstrate the safety or effectiveness of our product candidates to the extent necessary to obtain regulatory approval or such that commercialization of our product candidates is worthwhile. Any failure or substantial delay in successfully completing clinical trials and obtaining regulatory approval for our product candidates could severely harm our business.

If we fail to obtain collaborative partners, or those we obtain fail to perform their obligations or discontinue clinical trials for particular product candidates, our ability to develop and market potential products could be severely limited.

Our strategy for the development and commercialization of our product candidates depends, in large part, upon the formation of collaborative arrangements. Collaborations may allow us to:

- generate cash flow and revenue;
- offset some of the costs associated with our internal research and development, preclinical testing, clinical trials and manufacturing;
- seek and obtain regulatory approvals faster than we could on our own; and
- successfully commercialize existing and future product candidates.

We do not currently have collaborative agreements covering **Lymphoseek, RIGScan** CR or ACT. We cannot assure you that we will be successful in securing collaborative partners, or that we will be able to negotiate acceptable terms for such arrangements. The development, regulatory approval and commercialization of our product candidates will depend substantially on the efforts of collaborative partners, and if we fail to secure or maintain successful collaborative arrangements, or if our partners fail to perform their obligations, our development, regulatory, manufacturing and marketing activities may be delayed, scaled back or suspended.

We rely on third parties for the worldwide marketing and distribution of our gamma detection and blood flow measurement devices, who may not be successful in selling our products.

We currently distribute our gamma detection devices in most global markets through two partners who are solely responsible for marketing and distributing these products. The partners assume direct responsibility for business risks related to credit, currency exchange, foreign tax laws or tariff and trade regulation. Our blood flow products are marketed and sold in the U.S. and a number of foreign markets through other distribution partners specific to those markets. Further, we have had only limited success to date in marketing or selling our **Quantix** line of blood flow products. While we believe that our distribution partners intend to continue to aggressively market our products, we cannot assure you that the distribution partners will succeed in marketing our products on a global basis. We may not be able to maintain satisfactory arrangements with our marketing and distribution partners, who may not devote adequate resources to selling our products. If this happens, we may not be able to successfully market our products, which would decrease our revenues.

Our radiopharmaceutical product candidates are subject to extensive government regulations and we may not be able to obtain necessary regulatory approvals.

We may not receive the regulatory approvals necessary to commercialize our **Lymphoseek** and **RIGScan** product candidates, which could cause our business to be severely harmed. Our product candidates are subject to extensive and rigorous government regulation. FDA regulates, among other things, the development, testing, manufacture, safety, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products. If our potential products are marketed abroad, they will also be subject to extensive regulation by foreign governments. None of our product candidates has been approved for sale in the United States or in any foreign market. The regulatory review and approval process, which includes preclinical studies and clinical trials of each product candidate, is lengthy, complex, expensive and uncertain. Securing FDA clearance to market requires the submission of extensive preclinical and clinical data and supporting information to FDA for each indication to establish the product candidate's safety and efficacy. Data obtained from preclinical and clinical trials are susceptible to varying

interpretation, which may delay, limit or prevent regulatory approval. The approval process may take many years to complete and may involve ongoing requirements for post-marketing studies. In light of the limited regulatory history of monoclonal antibody-based therapeutics, regulatory approvals for our products may not be obtained without lengthy delays, if at all. Any FDA or other regulatory approvals of our product candidates, once obtained, may be withdrawn. The effect of government regulation may be to:

- delay marketing of potential products for a considerable period of time;

- limit the indicated uses for which potential products may be marketed;
- impose costly requirements on our activities; and
- provide competitive advantage to other pharmaceutical and biotechnology companies.

We may encounter delays or rejections in the regulatory approval process because of additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. Failure to comply with applicable FDA or other regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory action against our product candidates or us. Outside the United States, our ability to market a product is contingent upon receiving clearances from the appropriate regulatory authorities. This foreign regulatory approval process includes risks similar to those associated with FDA approval process.

Our radiopharmaceutical product candidates will remain subject to ongoing regulatory review even if they receive marketing approval. If we fail to comply with continuing regulations, we could lose these approvals and the sale of our products could be suspended.

Even if we receive regulatory clearance to market a particular product candidate, the approval could be conditioned on us conducting additional costly post-approval studies or could limit the indicated uses included in our labeling. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, the manufacturer of the product and its facilities will continue to be subject to FDA review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing clearance, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping related to the product will remain subject to extensive regulatory requirements. We may be slow to adapt, or we may never adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements.

If we fail to comply with the regulatory requirements of FDA and other applicable U.S. and foreign regulatory authorities or previously unknown problems with our products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import bans;
- voluntary or mandatory product recalls and publicity requirements;
- suspension or withdrawal of regulatory approvals;

- total or partial suspension of production; and

- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications.

Our existing products are highly regulated and we could face severe problems if we do not comply with all regulatory requirements in the global markets in which these products are sold.

FDA regulates our gamma detection and blood flow measurement products in the United States. Foreign countries also subject these products to varying government regulations. In addition, these regulatory authorities may impose limitations on the use of our products. FDA enforcement policy strictly prohibits the marketing of FDA cleared medical devices for unapproved uses. Within the European Union, our products are required to display the CE Mark in order to be sold. We have obtained FDA clearance to market and European certification to display the CE Mark on our current line of gamma detection systems and on two blood flow products, the **Quantix/ND** and **Quantix/OR**. We may not be able to obtain clearance to market any new products in a timely manner, or at all. Failure to comply with these and other current and emerging regulatory requirements in the global markets in which our products are sold could result in, among other things, warning letters, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, refusal of the government to grant pre-market clearance for devices, withdrawal of clearances, and criminal prosecution.