NEOPROBE CORP
Form 424B3
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Registration No. 333-139185

PROSPECTUS SUPPLEMENT

Number 1

to

Prospectus dated December 29, 2006,

of

NEOPROBE CORPORATION

13,440,000 Shares of Common Stock

This Prospectus Supplement relates to the sale of up to 13,440,000 shares of Neoprobe Corporation common stock (the "Shares") by Fusion Capital Fund II, LLC (Fusion Capital). We will not receive proceeds from the sale of the Shares by Fusion Capital.

This Prospectus Supplement No. 1 includes the attached Annual Report on Form 10-KSB (the "Form 10-KSB") of Neoprobe Corporation, for the year ended December 31, 2006. The exhibits to the Form 10-KSB are not included with this Prospectus Supplement No. 1 and are not incorporated by reference herein.

Our common stock is traded on the Over-the-Counter Bulletin Board under the symbol "NEOP."

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS SUPPLEMENT. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this Prospectus Supplement No. 1 is May 3, 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