NEOPROBE CORP
Form 424B3
April 01, 2010

Filed Pursuant to Rule 424(b)(3)
Registration No. 333-164058

PROSPECTUS SUPPLEMENT

Number 1

to

Prospectus dated January 7, 2010,

of

NEOPROBE CORPORATION

15,500,000 Shares of Common Stock

This Prospectus Supplement relates to the sale of up to 15,500,000 shares of Neoprobe Corporation common stock (the "Shares"). The Shares are being registered to permit public secondary trading of the shares that are being offered by the selling stockholder named in the prospectus. We are not selling any of the Shares in this offering and therefore will not receive any proceeds from this offering.

This Prospectus Supplement No. 1 includes the attached Annual Report on Form 10-K (the "Form 10-K") of Neoprobe Corporation (the "Company") for the fiscal year ended December 31, 2009, filed by the Company with the Securities and Exchange Commission on March 31, 2010. The exhibits to the Form 10-K are not included with this Prospectus Supplement No. 1 and are not incorporated by reference herein.

Our common stock is traded on the OTC 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 April 1, 2010.

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

FORM 10-K

(Mark One)
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2009

or

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE EXCHANGE ACT

For the transition period from to _____ to _____

Commission file number 0-26520

NEOPROBE CORPORATION
(Exact name of registrant as specified 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)

Registrant'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)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90

days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 if this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such
files). Yes ¨ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. Yes oNo x

Indicate by check mark whether the registrant is a large accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer ¨	Smaller reporting company x

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

The aggregate market value of shares of common stock held by non-affiliates of the registrant on June 30, 2009 was $66,881,198.

The number of shares of common stock outstanding on March 26, 2010 was 81,890,508.

DOCUMENTS INCORPORATED BY REFERENCE

None.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things:

- general economic and business conditions, both nationally and in our markets,
- our history of losses, negative net worth and uncertainty of future profitability;
- our expectations and estimates concerning future financial performance, financing plans and the impact of competition;
- our ability to implement our growth strategy;
- anticipated trends in our business;
- advances in technologies; and
- other risk factors set forth under “Risk Factors” in this report.

In addition, in this report, we use words such as “anticipate,” “believe,” “plan,” “expect,” “future,” “intend,” and similar expressions to identify forward-looking statements.

We undertake no obligation to update publicly or revise any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this report. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements.

PART I

Item 1. Business

Development of the Business

Neoprobe Corporation (Neoprobe, the company or we) is a biomedical company that develops and commercializes innovative oncology products that enhance patient care and improve patient outcome. 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. In 1998, U.S. and European regulatory agencies completed evaluations and discussions of the status of the regulatory pathway for our RIGS products, which coupled with our limited financial resources at the time, caused us to suspend our radiopharmaceutical development activities and refocus our operating strategy on our medical device business. After achieving profitability in the fourth quarter of 1999 following this retrenchment, we expanded our medical device offerings at the beginning of 2002 through the acquisition of an Israeli company that was developing a line of blood flow measurement devices.

Although we had expanded our strategic focus with the addition of medical devices outside the oncology field, we continued to look for other avenues to reinvigorate our radiopharmaceutical development portfolio. In 2004, our efforts resulted in a number of positive events that caused us to take steps to re-activate our radiopharmaceutical and therapeutic initiatives. As a result of our efforts since 2004, we now have submitted data from a Phase 3 clinical trial of one of our radiopharmaceutical products, Lymphoseek®, to the U.S. Food and Drug Administration (FDA) for review and have held a successful meeting with FDA that has clarified the process for the near-term filing of a new drug application (NDA) to FDA. In addition, we are enrolling patients in a second Phase 3 clinical trial intended to further support and expand our proposed product labeling for Lymphoseek and to support European filing for the product. Interest in, and activity related to, our original radiopharmaceutical product, RIGScanTM CR, has also increased significantly in recent years as we received formal scientific advice in late 2008 from the European Medicinal Evaluation Agency (EMEA) regarding our regulatory and clinical development plans for RIGScan CR. We took steps during the fourth quarter of 2009 to obtain similar feedback from FDA through the submission of a pre-Phase 3 meeting request and Special Protocol Assessment (SPA) request for which we are currently waiting on a response. Our subsidiary, Cira Biosciences, Inc. (Cira Bio), is also evaluating the market opportunities for yet another technology platform, activated cellular therapy (ACT). The success we have been experiencing in recent years related to our drug development activities caused us, during 2009, to re-evaluate our product initiatives and strategies. As a result of this evaluation, we made the decision during the third quarter of 2009 to discontinue the operations of our blood flow measurement device product line and to look for opportunities to divest our Cardiosonix Ltd. subsidiary. We believe this decision will allow us to better focus on our oncology-related development platforms as we approach several key milestones in the coming twelve to eighteen months.

We believe that our virtual business model is unique within our industry as we combine revenue generation from medical devices to cover our public company overhead while we devote capital raised through financing efforts to the development of products such as Lymphoseek which possess even greater potential for shareholder return. In addition, we have sought to maintain a development pipeline with additional longer-term return potential such as RIGScan CR and ACT that provide the opportunity for incremental return on the achievement of key development and funding milestones.

Our Technology

Gamma Detection Devices

Through 2009, our line of gamma radiation detection devices has generated substantially all of our revenue. Our gamma detection systems are 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 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 mounted 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 pen flashlight. The neoprobe® GDS gamma detection system, originally released in 1998 under the name neo2000®, is the fourth generation of our gamma detection products. The neoprobe GDS is designed as a platform for future growth of our instrument business. The neoprobe GDS is software upgradeable and is designed to support future surgical targeting probes without the necessity of costly factory remanufacture. Our most recent software release enables our entire installed base of neoprobe GDS and neo2000 users to use our wireless gamma detection probes, based on Bluetooth® wireless technology, that have been commercially launched over the last few years. During 2009, we also introduced a new gamma detection probe capable of detecting higher energy isotopes such as Fludeoxyglucose 18F (FDG or F18) that are frequently used in connection with Positron Emission Tomography (PET) scans.

Surgeons are using our gamma detection devices in a surgical application referred to as intraoperative lymphatic mapping (ILM or lymphatic mapping) or sentinel lymph node biopsy (SLNB). ILM helps trace the lymphatic drainage 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. ILM 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 have 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.

The application of ILM to solid tumor cancer treatment has been most widely developed in the breast cancer and melanoma indications. Numerous clinical studies, involving thousands of patients and published in peer-reviewed medical journals as far back 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 ILM or 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 four years ago. While we are not aware of the exact timing of publication or presentation of results from these trials, it is possible that such data may be available sometime later in 2010. Accrual on the second trial was halted early (in 2007), 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 widely 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 continue to approach 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, we believe we are beginning to see the development of a replacement device market in the gamma detection device sector, aided in part by new offerings such as our wireless probes, as devices purchased over ten years ago during the early years of lymphatic mapping begin to be retired.

Although lymphatic mapping has found its greatest acceptance thus far in breast cancer and melanoma, we believe that Lymphoseek may be instrumental in extending ILM into other solid tumor cancers in which surgeons are currently investigating such as prostate, gastric, colon, head and neck, and non-small cell lung cancers. Investigations in these other cancer types have thus far met with mixed levels of success due, we believe, to limitations associated with currently available radioactive tracing agents; however, we believe our development of Lymphoseek may positively impact the effectiveness of ILM in such indications. Surgeons have also been using our devices for other gamma-guided surgery applications, such as evaluating the thyroid function and conducting parathyroid surgery, and in determining the state of disease in patients with vulvar and penile cancers. Expanding the application of ILM beyond the current primary uses in the treatment of breast cancer and melanoma is a primary focus of our strategy regarding our gamma-guided surgery products and is consistent with our Phase 3 Lymphoseek clinical trial strategy. To support that expansion, we continue to work with our marketing and distribution partners to develop additional enhancements to the neoprobe GDS platform such as the wireless probes that were introduced over the last few years and the new F18 probe we launched at the Society of Surgical Oncology (SSO) 62nd Annual Cancer Symposium held in March of 2009. We believe the market for the intraoperative detection of higher energy isotope detection is just beginning to develop and may not significantly impact our sales for some time.

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 are used. The product we are developing with the greatest near-term potential in this area is Lymphoseek, a proprietary drug compound under exclusive worldwide license from the Regents of the University of California through their UC, San Diego affiliate (UCSD). 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 product specifically designed and labeled for the targeting of sentinel lymph nodes.

The initial pre-clinical evaluations of Lymphoseek were completed in 2001. Since that time, Neoprobe, in cooperation with UCSD, has completed or initiated five Phase 1 clinical trials, a multi-center Phase 2 trial and multi-center Phase 3 trials involving Lymphoseek. The status of these trials is listed below:

Indication	Phase	Number of Patients	Status
Breast (peritumoral injection)	1	24	Completed
Melanoma	1	24	Completed
Breast (intradermal injection, next day surgery)	1	31	Ongoing
Prostate	1	20	Ongoing
Colon	1	20	Ongoing
Breast or Melanoma	2	80	Completed
Breast or Melanoma	3	179	Completed
Head and Neck Squamous Cell Carcinoma (“Sentinel”)	3	196*	Ongoing

*estimated number based upon interim analysis; actual number is dependent on statistical analysis at potential stoppage points

The Phase 1 studies to date have been substantially supported through research grants from 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 some of these clinical evaluations of Lymphoseek have been presented at meetings of the Society of Nuclear Medicine, the Society of Surgical Oncology and the World Sentinel Node Congress. The ongoing breast, 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, 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 early 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 additional non-clinical testing was successfully completed in late 2005 and the reports were filed with FDA in December 2005. 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.

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 characterization. Neoprobe began the transfer of bulk drug manufacturing to Reliable Biopharmaceutical Corporation (Reliable) early in 2005 and engaged OSO BioPharmaceuticals Manufacturing LLC (OSO Bio, formerly Cardinal Health PTS) 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 2006.

We received clearance from FDA in May 2006 to move forward with patient enrollment for a multi-center 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 2006 and completed enrollment of the 80 patients in June 2007. We announced positive preliminary efficacy results from our Phase 2 Lymphoseek trial in June 2007 and final results in December 2007. Localization of Lymphoseek to lymphoid tissue was confirmed by pathology in over 99% of the lymph node tissue samples removed during the Phase 2 trial. We held an end of Phase 2 meeting with FDA during late October 2007 during which the final results were reviewed. The Phase 2 study was conducted at five of the leading cancer centers in the U.S.: John Wayne Cancer Center; University of California, San Francisco; MD Anderson Cancer Center; University Hospital Cleveland (Case Western Reserve); and the University of Louisville.

Based on dialogue with FDA through 2007, we proposed to FDA a plan for conducting Phase 3 studies to support an NDA for marketing clearance of Lymphoseek. During 2008, we initiated patient enrollment in the first Phase 3 clinical study in patients with either breast cancer or melanoma (NEO3-05). In March 2009, we announced that this study had reached the accrual of 203 lymph nodes, the study's primary accrual objective. The NEO3-05 Phase 3 clinical trial was designed to provide, and achieved its primary endpoint of, the evaluation of the efficacy of Lymphoseek in anatomically delineating lymph nodes in both breast cancer and melanoma patients that may be predictive of determining whether cancer has spread into the lymphatic system. Final data from the trial in patients with breast cancer and melanoma has now been reviewed and audited. The NEO3-05 study has also been closed on the national clinical trials website, www.clinicaltrials.gov. In December 2009, Neoprobe submitted an end-of-Phase 3 meeting request to FDA to discuss the results of the clinical trial as part of our continuing preparation of a NDA In March 2010, Neoprobe met with FDA regarding NEO3-05. The FDA review included the efficacy and safety results of the NEO3-05 study and Neoprobe's plans for the submission of a NDA for Lymphoseek. The NDA submission will be based on the clinical results of NEO3-05 and other already completed clinical evaluations of Lymphoseek. FDA encouraged Neoprobe to request a series of pre-NDA meetings in the coming months to review the components of the NDA prior to its formal submission. Neoprobe indicated to FDA that the Company plans to submit the NDA following satisfactory completion of these meetings.

The NEO3-05 Phase 3 study was an open label trial of node-negative subjects with either breast cancer or melanoma. It was designed to evaluate the safety and the accuracy of Lymphoseek while identifying the lymph nodes draining from the subject's tumor site. To demonstrate the accuracy of Lymphoseek, each subject consenting to participate in the study was injected in proximity to the tumor with Lymphoseek and one of the vital blue dyes that are commonly used in lymphatic mapping procedures. The primary efficacy objective of the study was to identify lymph nodes that contained the vital blue dye and to demonstrate a statistically acceptable concordance rate between the identification of lymph nodes with the vital blue dye and Lymphoseek. To be successful, the study needed to achieve a statistical p-value of at least 0.05.

In this review meeting with FDA, the full analysis of the NEO3-5 clinical data was discussed. The protocol compliant clinical sites that participated in the NEO3-05 study contributed 136 Intent-To-Treat (ITT) subjects who provided 215

lymph nodes that contained the vital blue dye. 210 of the vital blue dye positive lymph nodes contained Lymphoseek for an overall concordance rate of 98% achieving a statistical p-value of 0.0001. In addition to the nodes identified by vital blue dye and Lymphoseek, Lymphoseek was able to identify 85 additional lymph nodes that did not contain the vital blue dye, and 18% of these nodes were found by pathology to contain cancer. There were no significant safety events related to Lymphoseek. The FDA indicated that the clinical data would be supportive of a NDA submission for Lymphoseek.

In future pre-NDA meetings, Neoprobe will continue discussions with the FDA reviewers regarding the pre-clinical and chemistry, manufacturing and control quality data modules that will be part of the NDA submission. Neoprobe will be discussing elements of the statistical analysis plan that would support the NDA, including the design of any prospective clinical evaluations to support the primary indication, and to potentially expand the future indications for Lymphoseek.

A second Phase 3 study is also underway to further validate Lymphoseek as a sentinel lymph node targeting agent. This second trial, NEO3-06 or the “Sentinel” trial, is being conducted in patients with head and neck squamous cell carcinoma. The Sentinel study is designed to validate Lymphoseek as a sentinel lymph node targeting agent. Our discussions with FDA and EMEA have also suggested that the Sentinel trial will further support the use of Lymphoseek in sentinel lymph node biopsy procedures. We believe the outcome of the trial will be beneficial to the marketing and commercial adoption of Lymphoseek in the U.S. and European Union (EU). We plan to have approximately 20 participating institutions in the Sentinel trial. Patient recruitment and enrollment is actively underway at a number of institutions and the trial protocol is currently under review at several other institutions. The accrual rate for trials of this nature is highly dependent on the timing of IRB approvals of the NEO3-06 protocol. Our experience in the NEO3-05 trial has shown that this process may be lengthening due to risk management concerns on the part of hospitals participating in clinical trials and other factors.

We plan to use the safety and efficacy results from the Phase 3 clinical evaluations of Lymphoseek, which will include sites in the EU, to support the drug registration application process in the EU as well as to amend the filing in the U.S. for expanded product labeling. Based on the positive outcome of the recent meeting regarding NEO3-05, Neoprobe expects to submit the NDA for Lymphoseek later in the summer of 2010. Depending on the timing of the planned pre-NDA meetings with FDA and the outcome of the FDA regulatory review cycle, we believe that Lymphoseek could be commercialized in mid-2011. 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 with proprietary radiolabeled cancer-specific targeting agents to provide surgeons with real-time information to locate tumor deposits generally 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.

RIGScanTM CR is an intraoperative targeting agent consisting of a radiolabeled murine monoclonal antibody (CC49 MAb). The radiolabel used is 125I, a 27 - 35 KeV emitting isotope. The CC49 MAb was developed by the NCI and is 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 antigen 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 U.S., Israel, and the EU. 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 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 EMEA. Both FDA and 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 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 2004, we 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. Based primarily on this survival-related information, we requested a meeting with FDA in 2004 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 also 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.

Our statistical analyses following the 2004 meeting with FDA indicated a potential trial size of 2,400 to 2,800 patients, which proved cost prohibitive to us and our potential development partners in evaluating continued development for RIGScan CR. However, during 2008 we developed a protocol design which we believe could support our desired clinical endpoints but in a much smaller patient population. We made the decision to initially approach the EMEA with this trial design under their formal process for seeking scientific advice. After holding a successful pre-submission meeting with EMEA in July 2008, we received positive feedback in October 1998 to the clinical trial design which involved approximately 400 patients in a randomized trial of patients with colorectal cancer. The participants in the trial would be randomized to either a control or RIGS treatment arm. Patients randomized to the RIGS arm would have their disease status evaluated at the end of their cancer surgery to determine the presence or absence of RIGS-positive tissue. Patients in both randomized arms would be followed to determine if patients with RIGS-positive status have a lower overall survival rate and/or a higher occurrence of disease recurrence. The hypothesis for the trial is based upon the data from the earlier NEO2-13 and NEO2-14 trial results.

Our desire has been, and continues to be, to develop a clinical development plan which is harmonized between the U.S. and the EU. To that end, during December 2009 we submitted an investigational new drug (IND) amendment to the United States FDA which includes the design of a proposed Phase 3 clinical trial of RIGScan CR. The IND amendment includes a Special Protocol Assessment (SPA) in accordance with the Prescription Drug User Fee Act of 1992 (PDUFA) and current regulatory guidelines, and will be registered on the clinicaltrials.gov website following discussions with FDA regarding the SPA, which we expect will take place sometime in the second quarter of 2010.

The Phase 3 clinical study as currently designed would be a randomized clinical study that would evaluate the ability of RIGScan CR to identify tumor-associated tissue in a group of patients as compared to a group of patients provided with traditional surgical care. Based on our current statistical analysis, we now believe the sample size for the

proposed Phase 3 clinical study may be as few as 300 patients including both the RIGScan CR and traditional treatment groups. In addition to assessing the ability of RIGScan CR to identify tumor-associated tissue, the survival rate of the RIGScan CR treated patients will be compared to the patients treated with conventional treatment modalities.

It should also be noted that the RIGScan CR biologic drug has not been produced for several years. We would have to perform some additional work related to ensuring the drug cell line is still viable and submit this data to EMEA and possibly FDA for their evaluation in connection with preparations to restart pivotal clinical trials. During the third quarter of 2009, we announced that we had executed a Biopharmaceutical Development and Supply Agreement with Laureate Pharma, Inc. This agreement will support the initial evaluation of the viability of the CC49 master working cell bank as well as the initial steps in re-validating the commercial production process for the biologic agent used in RIGScan CR. In addition, we will need to re-establish radiolabeling capabilities for the CC49 antibody in order to meet the regulatory needs for the RIGScan CR product. We have also begun discussions with parties capable of supporting such activities.

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 fund the pivotal clinical testing that will be necessary to gain marketing clearance for RIGScan CR. In the past, we have engaged in discussions with various parties regarding such a partnership. We believe the recently clarified regulatory pathway approved by EMEA is very valuable, but we believe clarifying the regulatory pathway in the U.S. is important for us and our potential partners in assessing the full potential for RIGScan CR. 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 or obtain financing to fund development of the RIGS technology and do not know if such arrangements could be obtained on a timely basis on terms acceptable to us, or at all. We also cannot assure you that FDA or 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 during the late 1990’s 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 1 clinical trials covering the oncology, viral and autoimmune applications.

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.

In 2006, Cira Bio engaged the Battelle Memorial Institute to complete a technology and manufacturing process assessment of the cellular therapy approach. Cira Bio has attempted over the past few years to raise the necessary capital to move this technology platform forward. In August 2007 we entered into a Stock and Technology Option Agreement whereby Neoprobe gained the option to purchase the remaining 10% of Cira Bio from Cira LLC for $250,000; however, this option expired in 2008. The prospects for the ACT technology were buoyed during the fourth quarter of 2009 as a result of the publication of the discovery of a retrovirus linked to chronic fatigue syndrome, an autoimmune dysfunction the treatment of which showed promise the early clinical trials for ACT. Scientists are continuing to evaluate the data regarding the linkage. Should the link to the retrovirus be further substantiated, the development prospects for ACT will likely improve. We do not know if our assessment of the technology's prospects will ultimately yield positive results or if we will be successful in obtaining funding on terms acceptable to us, or at all. In the event we fail to obtain financing for Cira Bio, the technology rights for the oncology applications of ACT may revert back to Neoprobe and the technology rights for the viral and autoimmune applications may revert back to Cira LLC upon notice by either party. See Risk Factors.

Market Overviews

The medical device marketplace is a fast growing market. Epsicom Business Intelligence estimated in 2009 an annual medical device market of $91 billion in the U.S. and $131 billion internationally.

Cancer Market Overview

Cancer is the second leading cause of death in the U.S. and Western Europe and has been estimated to be responsible for over 562,000 deaths annually in 2009 in the U.S. alone. The NIH has estimated the overall annual costs for cancer (the primary focus of our gamma detection and pharmaceutical products) for the U.S. for 2008 at $228.1 billion: $93.2 billion for direct medical costs, $18.8 billion for indirect morbidity, and $116.1 billion for indirect mortality. Our line of gamma detection systems is currently used primarily in the application of ILM in breast cancer and melanoma which, according to the ACS, have been estimated to account for 13% and 5%, respectively, of new cancer cases which occurred in the U.S. in 2009.

The NIH has estimated that 1.3 million new cases of invasive breast cancer are expected to occur annually among women worldwide. Breast cancer is the second leading cause of death from cancer among all women in the U.S. The incidence of breast cancer, while starting to show minor declines in the past few years, generally increases with age, rising from about 120 cases per 100,000 women at age 40 to about 400 cases per 100,000 women at age 65. While the incidence rate for breast cancer appears to be decreasing, the overall number of new cases of breast cancer is still increasing. According to the ACS, over 192,000 new cases of invasive breast cancer are expected to be diagnosed and approximately 40,000 women are estimated to have died from the disease during 2009 in the U.S. alone. Thus, we believe that the significant aging of the population, combined with improved education and awareness of breast cancer and diagnostic methods, will continue to 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 continue to treat the majority of breast cancer patients. Over 10,000 hospitals are located in the markets targeted for our gamma detection SLNB products. We believe a significant portion of the potential market for gamma detection devices remains unpenetrated and that a replacement market is beginning to develop as units placed in the early years of SLNB begin to exceed over ten years of use. In addition, 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.

11

We estimate the total market potential for Lymphoseek, if ultimately approved for all of these indications, could exceed $250 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 has also estimated that nearly 147,000 new incidences of colon and rectal cancers were expected to occur in the U.S. in 2009. 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.

Marketing and Distribution

Gamma Detection Devices

We began marketing the neo2000 gamma detection system 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 our gamma detection product line, the neoprobe GDS, is a control unit that is software-upgradeable, permitting product enhancements without costly remanufacturing. Since the original launch of the GDS' predecessor platform, the neo2000 (in 1998), we have also introduced a number of enhanced radiation detection probes optimized for lymphatic mapping procedures, including three wireless probes, as well as a new probe optimized for the detection of high energy radioisotopes. We have also developed four major software 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 gamma detection 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 a distribution agree