NEOPROBE CORP
Form 10-K
March 16, 2011

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, 2010

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:

Common Stock, par value $.001 per share	NYSE Amex Equities
(Title of Class)	(Name of Each Exchange on Which Registered)

Securities registered pursuant to Section 12(g) of the Act: None

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 of 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 ¨ No 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 x
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, 2010 was $142,554,910.

The number of shares of common stock outstanding on March 11, 2011 was 88,175,675.

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 benefit. 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 RIGScanTM product 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. As a result of our efforts over the last several years we have successfully re-established our core competency regarding

radiopharmaceutical development. We recently announced that we had enrolled an adequate number of subjects to enable us to meet the lymph node accrual goal for the second Phase 3 clinical trial for our lead radiopharmaceutical product candidate, Lymphoseek®, and as a result, we are now preparing to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA). Interest in, and activity related to, our original radiopharmaceutical initiative, RIGS, has also increased significantly in recent years following the receipt of formal scientific advice in late 2008 from the European Medicines Agency (EMA). We recently held a meeting with FDA that has clarified the regulatory and development process related to our RIGScan product. As a result of this meeting, we intend to implement additional manufacturing activities through 2011 as a first step to recommencing human clinical study of the technology in 2012 and beyond. 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 re-evaluation, we made the decision during the third quarter of 2009 to discontinue the operations of our blood flow measurement device product line. To date, we have been unsuccessful in our attempts to sell our Cardiosonix Ltd. subsidiary. As a result, we are taking additional steps to complete the shutdown of our blood flow measurement device business. We believe this decision will allow us to better focus on our pipeline development opportunities that better leverage our core competencies. We expect to continue utilizing a virtual business model to further our product and pipeline development that provides the opportunity for incremental return on the achievement of key development and funding milestones.

Our Technology

Gamma Detection Devices

Through 2010, 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 F-18 fluorodeoxyglucose (18F FDG) that are frequently used in connection with Positron Emission Tomography (PET) scans. During early March of 2011, we introduced a 9mm wireless gamma detection probe further expanding our family of wireless probes to enable surgeons to address a broader range of surgical challenges. In addition, in February 2011 we licensed intellectual property that may be used to develop an intraoperative hand-held miniature gamma camera to be used in combination with either Lymphoseek or RIGScan products.

Surgeons use 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. These 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, with or without a blue dye. 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 radiotracer 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 for our neoprobe GDS 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. Recently, important data regarding lymph node dissections were published in the Journal of the American Medical Association (JAMA, February 9, 2011) and in the New England Journal of Medicine (NEJM, January 19, 2011). We believe the information published in both articles continues to underscore the importance of effective SLNB in the staging and treatment of patients with solid tumor cancers. 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 that a replacement device market in the gamma detection device sector is beginning to develop, 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 9mm wireless probe introduced at the Society of Surgical Oncology (SSO) 64th Annual Cancer Symposium held in March 2011.

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.

4

Lymphoseek (Tilmanocept) is a diagnostic imaging agent designed for radiolabeling and subsequent administration in radiodetection and visualization of the lymphatic system draining the region of injection for delineation of the lymphatic tissue. Lymphoseek is designed to accumulate in lymphatic tissue by specifically binding to mannose binding receptor (MBR; CD206) proteins that reside on the surface of resident dendritic cells and macrophages. Lymphoseek is a macromolecule consisting of multiple units of diethylene triamine pentaacetic acid (DTPA) and mannose, each synthetically attached to a 10 kDa dextran backbone. The mannose acts as a substrate for the receptor, and the DTPA serves as a chelating agent for labeling with Technetium Tc 99m.

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, one multi-center Phase 2 trial and three 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	Completed
Prostate	1	14	Closed
Colon	1	6	Closed
Breast or Melanoma	2	80	Completed
Breast or Melanoma	3	179	Completed
Breast or Melanoma	3	150	Node accrual target reached
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 supported in part 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 two Phase 1 studies in prostate and colon cancers were closed prior to planned target completion due in part to our determination that the planned product labeling for Lymphoseek, based on our dialogue with FDA, would be as a general lymphatic tissue tracing agent rather than as a disease-specific agent. The ongoing Phase 3 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.

5

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, FDA 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 establish the commercial manufacturing process for filling and lyophilization of the drug product. 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. 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. The results of the Phase 2 study were published in the February 2011 online edition of the Annals of Surgical Oncology.

During 2008, we initiated patient enrollment in a Phase 3 clinical study in subjects 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 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 in 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 addition, the secondary endpoint of the study was to pathologically examine lymph nodes identified by either the vital blue dyes or Lymphoseek to determine if cancer was present in the lymph nodes.

In June 2009, we initiated a Phase 3 clinical trial to be conducted in subjects with head and neck squamous cell carcinoma (NEO3-06). The NEO3-06 clinical study was designed to expand the potential labeling for Lymphoseek as a sentinel lymph node targeting agent after the initial marketing clearance for the product. Our discussions with FDA and the European Medicines Agency (EMA) have also suggested that the NEO3-06 clinical 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 will support registration in the European Union (EU). Our plan remains to have approximately 20 participating institutions in the NEO3-06 clinical trial. Subject 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 this trial is slower than the accrual rate for the

NEO3-05 and NEO3-09 trials due in part to the incidence rate for head and neck cancers for subjects eligible to participate in this trial. We do not expect this trial to complete full accrual until sometime in 2012; however, there are opportunities to stop the trial at earlier points in the event we encounter subjects with disease-involved lymph nodes at a higher than historical expected rate.

In March 2010, Neoprobe met with FDA to review the clinical outcomes of NEO3-05. The meeting included a review of the efficacy and safety results of the NEO3-05 clinical study and Neoprobe's plans for the submission of a NDA for Lymphoseek based on the results of NEO3-05 and other previously completed clinical studies. During the meeting, Neoprobe provided FDA with the clinical results of the protocol-compliant clinical sites that participated in the NEO3-05 clinical study that contributed 136 intent-to-treat subjects who provided 215 lymph nodes containing the vital blue dye. 210 of the vital blue dye positive lymph nodes contained Lymphoseek for an overall concordance rate of 98%, achieving a very high level of statistical correlation (p-value = 0.0001) for the primary endpoint of the clinical study. Prior to the meeting, FDA requested that Neoprobe conduct a "reverse concordance" assessment of the clinical study where Lymphoseek might identify lymph nodes missed by the vital blue dyes. This assessment showed that 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 reported safety events related to Lymphoseek. FDA indicated that the clinical data from the NEO3-05 clinical study and other completed clinical evaluations of Lymphoseek would be supportive of a NDA submission for Lymphoseek. FDA also encouraged Neoprobe to request a series of pre-NDA meetings to review the non-clinical and chemistry, manufacturing and control (CMC) components of the NDA prior to its formal submission. Neoprobe completed successful non-clinical and CMC pre-NDA reviews with FDA during the second quarter of 2010.

As a result of the March 2010 meeting, we moved forward with a plan to file the NDA for Lymphoseek later in 2010. A key part of the plan, however, was to ensure that the patient population in the safety database that would be considered in the approval of Lymphoseek would be adequate to meet the expectations of FDA. As such, in July 2010, Neoprobe initiated enrollment in another Phase 3 clinical evaluation of Lymphoseek in subjects with either breast cancer or melanoma (NEO3-09) which we expected would accrue patients, primarily for purposes of augmenting the safety population and to support expanded product labeling claims. Based on guidance received in the March 2010 meeting, we planned to file data related to the NEO3-09 trial as part of a planned major amendment to the primary NDA.

In October 2010, Neoprobe met with FDA for a pre-NDA assessment for Lymphoseek. As a result of the pre-NDA assessment, FDA requested that data from both the completed NEO3-05 study and the NEO3-09 study currently in progress be included in the Company's primary NDA for Lymphoseek rather than submitting the NEO3-09 study safety data as a planned major amendment to the ongoing NDA review, as initially intended. The pre-NDA assessment resulted in no modification to the NEO3-09 trial design or endpoints or to any of the other previously agreed-to clinical or regulatory components of the Lymphoseek NDA. As such, NEO3-09 will now be one of two adequate and well-controlled trials included in the primary NDA submission for a first-cycle review.

In February 2011, we announced that we had enrolled an adequate number of subjects to enable us to meet the lymph node accrual goal for the NEO3-09 clinical trial. Preliminary top-line data are expected to be announced in the second quarter of 2011. In addition, the results of the NEO3-09 clinical study may support the inclusion of enhanced product claims for Lymphoseek in the primary NDA submission.

The Lymphoseek NDA submission will be based on the clinical results of the Phase 3 clinical studies NEO3-05 and NEO3-09, and other already completed clinical evaluations of Lymphoseek. The request for the total data package from two Phase 3 clinical trials is consistent with FDA's ongoing initiative to push for more complete primary submissions and to limit major amendments made to NDAs. This ongoing initiative to shorten drug review cycle times was re-emphasized by FDA's Office of New Drug Development in late 2009 and enables more successful first-cycle reviews which ultimately shortens overall drug approval timelines. We believe inclusion of the NEO3-09 study data in the primary NDA submission may support stronger product labeling as an outcome of a first-cycle review of the Lymphoseek NDA and may also positively impact market adoption.

We plan to use the safety and efficacy results from the NEO3-06 Phase 3 clinical evaluations of Lymphoseek, which will include sites in the EU, to support the drug registration application process in the EU through the centralized drug authority EMA as well as to amend the filing in the U.S. for expanded product labeling. Neoprobe expects to submit the NDA for Lymphoseek during the first half of 2011. Depending on the timing and the outcome of the FDA regulatory review cycle, we believe that Lymphoseek could be commercialized in early 2012. 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 radiopharmaceutical agents used in the RIGS process are monoclonal antibodies that are specific for cancer markers, or antigens, 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 is an intraoperative biologic targeting agent consisting of a radiolabeled murine monoclonal antibody (CC49 MAb, Minretumomab). Various potential radioisotopes can be used as the radiolabel. 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.

The RIGS system was conceived to be a diagnostic aid in the intraoperative detection of clinically occult disease in patients with colon or rectal cancer. RIGScan CR is intended to be used in conjunction with other diagnostic methods for the detection of the extent and location of occult tumor and tumor metastases 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 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 EMA 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.

8

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 EMA. Both FDA and EMA 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 enhancing patient outcomes 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 EMA 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 guidance and pathways for approval that existed at that time, we determined that we did not have sufficient financial resources to conduct the additional studies requested.

In 2004, we obtained access to survival analyses of patients treated with RIGScan CR which have been prepared by third parties, indicating that RIGScan status was correlated with patient survival trends and 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. These data and its possible significance were unknown at the time of the BLA review given the limited maturity of the follow-up experience. The data include 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 these 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 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. 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 that a potential sample size of 2,400 to 2,800 patients would be required in clinical studies to get RIGScan CR registered, 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 held a pre-submission meeting with EMA and received positive feedback to the clinical trial design which involved approximately 400 patients. EMA subsequently indicated preliminary concurrence with a plan to harmonize the U.S. and EU regulatory pathways.

Our desire has been, and continues to be, to develop a clinical development plan which is harmonized between the U.S. and the EU in order to fully engage potential development partners. To that end, during December 2009 we submitted an IND amendment to FDA which included the design of a proposed Phase 3 clinical trial of RIGScan CR. Since filing the IND amendment, we have determined that due to differences in the current manufacturing process from the process used in the 1990's, a further amendment to the IND should be filed addressing the differences. In addition, in October 2010, we filed a response letter to FDA related to the Agency's complete response letter to the open BLA from 1997. The review responsibility for the RIGS BLA was recently transferred from CBER to the Division of Medical Imaging Products in CDER at FDA. The submission of the BLA response letter was the first of several near-term activities that Neoprobe intends to complete with FDA to reactivate the development of the RIGS technology. We have since filed a new IND request for the biologic component of the RIGS technology and held a pre-IND meeting with FDA to discuss the clinical development and regulatory plans for RIGScan.

The focus of Neoprobe's February 2011 pre-IND meeting with FDA was to first define the basic CMC requirements needed to resume clinical development efforts on RIGScan. FDA reviewed Neoprobe's comprehensive pre-IND package, including key aspects of the clinical development and drug development plans, and provided clear direction to the Company on its clinical and manufacturing activities going forward. As an outcome of the pre-IND meeting, we have clarified the path to reinitiate RIGScan development and the requirements for resuming development activities and moving toward clinical trials, FDA's guidance has provided direction to enhance our manufacturing platform, including process improvements to increase manufacturing efficiency and the quality of the underlying biologic antibody. We can now begin to implement our manufacturing plans through 2011 as a first step to recommencing clinical study of the technology in 2012 and beyond.

It should also be noted that the RIGScan biologic drug has not been produced for several years. We have successfully completed the initial steps in re-characterizing the drug cell line and believe, based on work done to date, that the cell line is still viable. We plan to submit these data to EMA and 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 Biopharmaceutical Services, Inc. (Laureate Biopharma). 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. Laureate Biopharma has made progress in the re-validation of the manufacturing process and has completed preliminary biologic characterization activities. They are expected to provide Neoprobe with cGMP-produced material to support non-clinical and clinical evaluation within the next few months. Our development plans for RIGScan include the consideration of alternative radiolabeling processes. Depending on the outcome of our evaluation, we will need to establish radiolabeling capabilities for the CC49 antibody in order to meet the regulatory needs for the RIGScan product. We have already begun discussions with parties capable of supporting such activities.

We believe it will likely be necessary and beneficial for us to identify a development partner to prepare for the pivotal clinical testing that will be necessary to gain marketing clearance for RIGScan. Such a partner may or may not be involved in funding future RIGS development. In the past, we have engaged in discussions with various parties regarding potential partnerships. We believe the recently clarified regulatory pathway with FDA is very valuable, and we believe re-approaching the EMA through the scientific advice process will be helpful in clarifying the regulatory

pathway in the EU and will be helpful for us and our potential partners in assessing the full potential for RIGScan. 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 EMA 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 expanded, 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-derived 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 during 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. Espicom Business Intelligence estimated in 2010 an annual medical device market of $95 billion in the U.S. and $230 billion internationally.

Cancer Market Overview

Cancer is the second leading cause of death in the U.S. and Western Europe and was estimated by the ACS to be responsible for over 569,000 deaths annually in 2010 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 2010 at $263.8 billion: $102.8 billion for direct medical costs, $20.9 billion for indirect morbidity, and $140.1 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 14% and 4%, respectively, of new cancer cases which occurred in the U.S. in 2010.

The NIH has estimated that 1.4 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 207,000 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 2010 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 may address not only the current breast and melanoma markets on a procedural basis, but also to assist in the clinical evaluation and staging of solid tumor cancers and expanding SLNB to additional indications, such as gastric, non-small cell lung and other solid tumor cancers.

We estimate the total market potential for Lymphoseek, if ultimately approved for all of these indications, could exceed $450 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. See Risk Factors.

The ACS has also estimated that nearly 143,000 new incidences of colon and rectal cancers were expected to occur in the U.S. in 2010. Based on an assumed recurrence rate of 40%, this would translate into total potential surgical procedures of approximately 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. See Risk Factors.

12

Marketing and Distribution

Gamma Detection Devices

We began marketing the neo2000 gamma detection system in October 1998. From October 1999 through July 2010, our gamma detection systems have been marketed and distributed throughout most of the world through Ethicon Endo-Surgery, Inc. (EES), a Johnson & Johnson company. We entered into a distribution agreement with EES effective October 1, 1999 for an initial five-year term with options to extend for two successive two-year terms. In March 2004, EES exercised its first two-year extension option, and in March 2006 EES exercised its option for the second and final two-year term extension, thus extending the term of our the agreement through the end of 2008. In December 2007, Neoprobe and EES executed an amendment to the distribution agreement which extended the agreement through the end of 2013. In July 2010, EES sold its breast care franchise to Devicor Medical Products, LLC (Devicor). As a part of the acquisition, Devicor took on EES' sales and marketing resources in the U.S. and certain rest-of-world markets. In connection with their acquisition of EES' breast care franchise, Devicor assumed all of EES' rights and responsibilities related to the sales, marketing and distribution of our gamma detection products. Under this agreement, we manufacture and sell our gamma detection medical devices on an exclusive basis to Devicor. Devicor has no ongoing purchase or reimbursement commitments to us other than the rolling four-month binding purchase commitment for gamma detection devices and certain annual minimum sales levels in order to maintain their exclusivity in distribution in most global markets. In addition, the economic terms of the revenue sharing from the end customer sale of our gamma detection devices increased commencing in January 2009. Our agreement with Devicor also contains certain termination provisions and licenses to our intellectual property that take effect only in the event we fail to supply product, or for other reasons such as a change of control. 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 Devicor 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. See Risk Factors.

Gamma Detection Radiopharmaceuticals

During the fourth quarter of 2007, we executed an agreement with Cardinal Health, Inc.'s radiopharmaceutical distribution division (Cardinal Health) for the exclusive distribution of Lymphoseek in the United States. The agreement is for a term of five years from the date of marketing clearance of a NDA from FDA. Under the terms of our agreement with Cardinal Health, Neoprobe will receive a significant share of the revenue from each patient dose of Lymphoseek sold. In addition, Neoprobe will receive up to $3 million in payments upon the achievement of certain sales milestones by Cardinal Health. We have had preliminary discussions with potential marketing and distribution partners in the EU and other major world markets; however, we do not currently have collaborative agreements covering Lymphoseek in areas of the world other than the U.S. or for RIGScan CR or ACT. We cannot assure you that we will be successful in securing collaborative partners for other global markets or radiopharmaceutical products, or that we will be able to negotiate acceptable terms for such arrangements. We believe the most preferable and likely

distribution partners for Lymphoseek would be entities with established radiopharmaceutical distribution channels, although it is possible that other entities with more traditional oncology pharmaceutical portfolios may also have interest.

With respect to RIGScan CR, we continue to believe it will be necessary for us to identify a development partner or an alternative funding source in order to prepare for and to fund further clinical testing that will be necessary to gain marketing clearance for RIGScan CR. We are aware of potential development partners who have previously indicated an interest in entering into a development relationship and expect to have ongoing discussions with such parties in the coming months; however, we do not expect to enter into any definitive partnership at least until we have further advanced the clinical testing for RIGScan CR. We cannot assure you that we will be able to secure marketing and distribution partners for the product, or if secured, that such arrangements will result in significant sales of RIGScan CR.

Manufacturing

Gamma Detection Devices

As part of our virtual business model, we rely on independent contract manufacturers, some of which are single-source suppliers, for the manufacture of the principal components of our current line of gamma detection system products. See Risk Factors. We have devoted significant resources to develop production capability of our gamma detection systems at qualified contract manufacturers. Production of the neoprobe GDS control unit, the 14mm probe, the 11mm laparoscopic probe, and the wireless probes involve the manufacture of components by a combination of subcontractors, including but not limited to, eV Microelectronics, a division of Endicott Interconnect Technologies, Inc. (eV), Redlen Technologies (Redlen) and Nortech Systems, Inc. (Nortech). We also purchase certain accessories for our line of gamma detection systems from other qualified manufacturers.

We purchase certain solid-state crystals used in the manufacture of our proprietary line of hand-held gamma detection probes from eV and Redlen. We do not currently have a supply agreement with either eV or Redlen, however we currently purchase from both under extended blanket purchase orders. The number of potential suppliers of such solid-state crystals is limited. However, we believe our relationships with eV and Redlen mitigate the risk of prolonged interruption of supply of crystals that could negatively impact the availability of our probe gamma detection device products, which would accordingly adversely affect our operating results.

In February 2004, we executed a Product Supply Agreement with TriVirix International, Inc. (TriVirix) for the manufacture and/or final assembly of our gamma detection products, including probes and control units. This agreement was assigned to Nortech in connection with Nortech’s acquisition of TriVirix during 2010. The original term of this agreement expired in February 2007 but has been extended under the automatic renewal terms of the agreement through February 2012. The agreement will continue to be automatically extended for successive one-year periods unless six months notice is provided by either party.