NEOPROBE CORP
Form 424B3
February 04, 2009

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Registration No. 333-150650

PROSPECTUS

NEOPROBE CORPORATION

20,166,666 Shares of Common Stock

This prospectus relates to the sale of up to 20,166,666 shares of our common stock by a person who has purchased shares of our common stock or who may purchase shares of our common stock through the conversion of debt, the conversion of shares of our preferred stock or the exercise of warrants as more fully described herein. The aforementioned person is sometimes referred to in this prospectus as the selling stockholder. The prices at which the selling stockholder may sell the shares will be determined by the prevailing market price for the shares or in negotiated transactions. We will not receive proceeds from the sale of our shares by the selling stockholder.

Our common stock is quoted on the OTC Bulletin Board under the symbol NEOP. On January 6, 2009, the last reported sale price for our common stock as reported on the OTC Bulletin Board was $0.57 per share.

THE SECURITIES OFFERED IN THIS PROSPECTUS INVOLVE A HIGH DEGREE OF RISK. YOU SHOULD CONSIDER THE RISK FACTORS BEGINNING ON PAGE 5 BEFORE PURCHASING OUR COMMON STOCK.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 9, 2009.

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Unless otherwise specified, the information in this prospectus is set forth as of January 6, 2009, and we anticipate that changes in our affairs will occur after such date. We have not authorized any person to give any information or to make any representations, other than as contained in this prospectus, in connection with the offer contained in this prospectus. If any person gives you any information or makes representations in connection with this offer, do not rely on it as information we have authorized. This prospectus is not an offer to sell our common stock in any state or other jurisdiction to any person to whom it is unlawful to make such offer.

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PROSPECTUS SUMMARY

The following summary highlights selected information from this prospectus and may not contain all the information that is important to you. To understand our business and this offering fully, you should read this entire prospectus carefully, including the financial statements and the related notes beginning on page F-1. When we refer in this prospectus to the company, we, us, and our, we mean Neoprobe Corporation, a Delaware corporation, together with our subsidiaries. This prospectus contains forward-looking statements and information relating to Neoprobe Corporation. See Cautionary Note Regarding Forward Looking Statements on page 16.

Our Company

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

From our inception through 1998, we devoted substantially all of our efforts and resources to the research and clinical development of radiopharmaceutical and medical device technologies related to the intraoperative diagnosis and treatment of cancers, including our proprietary radioimmunoguided surgery (RIGS®) technology. In 1998, U.S. and European regulatory agencies completed an evaluation of the status of the regulatory pathway for our RIGS products, which coupled with our limited financial resources, 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 in 2002 following 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 blood flow measurement devices, we continued to look for other avenues to reinvigorate our radiopharmaceutical development opportunities portfolio. During 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 over the past few years, we now have one radiopharmaceutical product, Lymphoseek®, in the midst of pivotal Phase 3 clinical trials, and a second, RIGScan® CR, with a renewed development promise after recently receiving clarification of the regulatory pathway as we identify potential development sources of funding or collaboration.

We believe that our virtual business model is unique within our industry as it combines revenue generation from medical devices covering our public company overhead while we devote capital raised through financing efforts to the development of products with even greater potential for shareholder return such as Lymphoseek. 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.

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The Offering

On December 26, 2007, we entered into a Securities Purchase Agreement (SPA) with Platinum-Montaur Life Sciences, LLC (Montaur), pursuant to which we issued Montaur a 10% Series A Convertible Senior Secured Promissory Note in the principal amount of $7,000,000, due December 26, 2011 (the Series A Note) and a five-year Series W warrant to purchase 6,000,000 shares of our common stock, $.001 par value per share (Common Stock), at an exercise price of $0.32 per share. Montaur may convert $3.5 million of the Series A Note into shares of Common Stock at the conversion price of $0.26 per share. The SPA also provided for two further tranches of financing, a second tranche of $3 million in exchange for a 10% Series B Convertible Senior Secured Promissory Note along with a five year Series X warrant to purchase shares of our Common Stock, and a third tranche of $3 million in exchange for 3,000 shares of our 8% Series A Cumulative Convertible Preferred Stock and a five-year Series Y warrant to purchase shares of our common stock. Closing of the second and third tranches were subject to the satisfaction by the Company of certain milestones related to the progress of the Company s Phase 3 clinical trials of the Company s Lymphoseek radiopharmaceutical product.

On April 16, 2008, following receipt by the Company of clearance by FDA to commence a Phase 3 clinical trial for Lymphoseek in patients with breast cancer or melanoma, we amended the SPA related to the second tranche and issued Montaur a 10% Series B Convertible Senior Secured Promissory Note in the principal amount of $3,000,000, also due December 26, 2011 (the Series B Note, and hereinafter referred to collectively with the Series A Note as the Montaur Notes), and a five-year Series X warrant to purchase 8,333,333 shares of our Common Stock at an exercise price of $0.46 per share. Montaur may convert the Series B Note into shares of Common Stock at the conversion price of $0.36 per share. Provided we have satisfied certain conditions stated therein, we may elect to make payments of interest due under the Montaur Notes in registered shares of Common Stock. If we choose to make interest payments in shares of Common Stock, the number of shares of Common Stock to be applied against any such interest payment will be determined by reference to the quotient of (a) the applicable interest payment divided by (b) 90% of the average daily volume weighted average price of our Common Stock on the OTC Bulletin Board (or national securities exchange, if applicable) as reported by Bloomberg Financial L.P. for the five days upon which our Common Stock is traded on the OTC Bulletin Board immediately preceding the date of the interest payment.

On December 5, 2008, after the Company obtained 135 vital blue dye lymph nodes from patients who had completed surgery and the injection of the drug in a Phase 3 clinical trial of Lymphoseek in patients with breast cancer or melanoma, we issued Montaur 3,000 shares of our 8% Series A Cumulative Convertible Preferred Stock (the Preferred Stock) and a five-year Series Y warrant (hereinafter referred to collectively with the Series W warrant and Series X warrant as the Montaur Warrants) to purchase 6,000,000 shares of our Common Stock, at an exercise price of $0.575 per share, also for an aggregate purchase price of $3,000,000. Montaur may convert each share of the Preferred Stock into a number of shares of our common stock equal to the quotient of: (1) the Liquidation Preference Amount of the shares of Preferred Stock by; (2) the Conversion Price. The Liquidation Preference Amount for the Preferred Stock is $1,000 and the Conversion Price of the Preferred Stock was set at $0.50 on the date of issuance, thereby making the shares of Preferred Stock convertible into an aggregate 6,000,000 shares of our Common Stock, subject to adjustment as described in the Certificate of Designations, Voting Powers, Preferences, Limitations, Restrictions, and Relative Rights of Series A 8% Cumulative Convertible Preferred Stock. We may elect to pay dividends due to Montaur on the shares of Preferred Stock in registered shares of Common Stock. The number shares of Common Stock to be applied against any such dividend payment will be determined by reference to the quotient of (a) the applicable dividend payment divided by (b) the average daily volume weighted average price of our Common Stock on the OTC Bulletin Board (or national securities exchange, if applicable) as reported by Bloomberg Financial L.P. for the five days upon which our Common Stock is traded on the OTC Bulletin Board immediately preceding the date of the dividend payment.

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Pursuant to the terms of a Registration Rights Agreement, dated December 26, 2007, as amended by the Amendment to Registration Rights Agreement, dated February 7, 2008, Second Amendment to Registration Rights Agreement, dated April 16, 2008, Third Amendment to Registration Rights Agreement, dated July 10, 2008, and Fourth Amendment to Registration Rights Agreement, dated December 5, 2008, we agreed to file a post-effective amendment to this registration statement providing for the: (a) deregistration of shares of Common Stock issuable upon the conversion of the Series B Note and the shares of Common Stock issuable upon the exercise of the Series X Warrant; and (b) registration of the resale of: (i) the shares of Common Stock issuable upon conversion of the Preferred Stock; (ii) the shares of Common Stock issuable upon exercise of the Series Y Warrant; (iii) 3,500,000 shares of Common Stock issuable as interest or dividends on the Montaur Notes and the Preferred Stock; and (iv) up to 4,666,666 shares issuable upon the conversion of the Series B Note, provided that the total number of shares of Common Stock registered would not exceed 20,166,666. Additionally, we agreed that within thirty-five days of receipt from Montaur of written request therefor, we would prepare and file an additional resale registration statement providing for the resale of: (i) the shares of Common Stock issuable upon the conversion of the Series A Note; (ii) the shares of Common Stock issuable upon the exercise of the Series W Warrant; (iii) any unregistered shares of Common Stock issuable upon the conversion of the Series B Note; and (iv) the shares of Common Stock issuable upon the exercise of the Series X Warrant, provided, however, that we are not required to file such additional registration statement, or may exclude shares from such additional registration statement, if we believe in good faith, based upon advice from the Securities and Exchange Commission s Staff, that application of Rule 415 would not permit registration of all or the excluded portion of such shares. This prospectus covers the resale of up to: (i) 6,000,000 shares of our Common Stock issuable upon the conversion of the Preferred Stock; (ii) 6,000,000 shares of our Common Stock issuable upon the exercise of the Series Y Warrant; (iii) 3,500,000 shares of Common Stock issuable as interest and dividends on the Montaur Notes and Preferred Stock; and (iv) 4,666,666 shares of our Common Stock issuable upon the conversion of the Series B Note, for a total of 20,166,666 shares.

An investment in our common stock is highly speculative and involves a high degree of risk. See Risk Factors beginning on page 5.

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RISK FACTORS

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

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

We had an accumulated deficit of approximately $145 million and had an overall deficit in stockholders equity as of September 30, 2008. Although we were profitable in 2000 and in 2001, we incurred substantial losses in the years prior to that, and again in 2002 and subsequent years. The deficit resulted because we expended more money in the course of researching, developing and enhancing our technology and products and establishing our marketing and administrative organizations than we generated in revenues. We expect to continue to incur significant expenses in the foreseeable future, primarily related to the completion of development and commercialization of **Lymphoseek**, but also potentially related to **RIGS** and our device product lines. As a result, we are sustaining substantial operating and net losses, and it is possible that we will never be able to sustain or develop the revenue levels necessary to again attain profitability.

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

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

To date, our efforts to place Cardiosonix Quantix products have met with limited success. The long-term commercial success of the Quantix product line will require much more widespread acceptance of our blood flow measurement products than we have experienced to date. Widespread acceptance of blood flow measurement would represent a significant change in current medical practice patterns. Other cardiac monitoring procedures, such as pulmonary artery catheterization, are generally accepted in the medical community and have a long standard of use. It is possible that the Quantix product line will never achieve the broad market acceptance necessary to become a commercial success.

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

We may have difficulty raising additional capital, which could deprive us of necessary resources.

We expect to continue to devote significant capital resources to fund research and development and to maintain existing and secure new manufacturing capacity. In order to support the initiatives envisioned in our business plan, we may need to raise additional funds through the sale of assets, public or private debt or equity financing, collaborative relationships or other arrangements. Our ability to raise additional financing depends on many factors beyond our control, including the state of capital markets, the market price of our common stock and the development or prospects for development of competitive technology by others. Because our common stock is not listed on a major stock market, many investors may not be willing or allowed to purchase it or may demand steep discounts. Sufficient additional financing may not be available to us or may be available only on terms that would result in further dilution to the current owners of our common stock.

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We believe that we have access to sufficient financial resources with which to fund our operations or those of our subsidiaries for the foreseeable future. We expect to raise additional capital during 2009 through existing financing facilities already available to us in order to continue executing on our current business plan. However, if we are unsuccessful in raising additional capital, closing on financing under already agreed to terms, or the terms of raising such capital are unacceptable, we may have to modify our business plan and/or significantly curtail our planned development activities and other operations.

In December 2006, we entered into a common stock purchase agreement with Fusion Capital Fund II, LLC (Fusion) that allowed us to sell shares of common stock for up to $6.0 million in proceeds. Through December 2008, $4,050,000.73 of proceeds were unused under the agreement. On December 24, 2008, we entered into an amendment to the agreement which increased by $6.0 million the amount of proceeds available to an aggregate remaining available amount of $10,050,000.73. We have authorized up to a total of 18,222,671 shares of our common stock for sale to Fusion under the agreement which includes 7,568,671 shares already purchased by Fusion. We issued 720,000 shares as a commitment fee at the inception of the original agreement in 2006, and issued an additional 360,000 shares in consideration for Fusion s agreement to enter into the amendment. We have issued 234,000 shares of our common stock as an additional commitment fee as shares were sold to Fusion, and up to an additional 486,000 shares of our common stock may be issued to Fusion as additional commitment fee shares as we draw on the $10 million available under the agreement. Our right to make sales under the amended agreement is limited to $50,000 every two business days, unless our stock price equals or exceeds $0.30 per share, in which case we can sell greater amounts to Fusion as the price of our common stock increases. Fusion does not have the right or the obligation to purchase any shares on any business day that the market price of our common stock is less than $0.20 per share. Through December 31, 2008, we have sold Fusion 7,568,671 million shares of common stock and issued 1,314,000 shares of stock as commitment fees to Fusion, resulting in gross proceeds of $1.95 million. Assuming the remaining 10,654,000 shares are sold, the selling price per share would have to average at least $0.94 for us to receive the maximum proceeds from this offering of $12 million. Assuming a purchase price of $0.57 per share (the closing sale price of the common stock on January 6, 2009), the remaining proceeds from this offering would be $6,072,780.

The extent to which we rely on Fusion as a source of funding will depend on a number of factors, including the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources, such as through the sale of our products. Specifically, Fusion does not have the right or the obligation to purchase any shares of our common stock on any business day that the market price of our common stock is less than $0.20 per share. To the extent that we are unable to make sales to Fusion to meet our capital needs, or to the extent that we decide not to make such sales because of excessive dilution or other reasons, and if we are unable to generate sufficient revenues from sales of our products, we will need to secure another source of funding in order to satisfy our working capital needs. Even if we are able to access the full $10,050,000.73 million potentially remaining under the agreement with Fusion, we may still need additional capital to fully implement our business, operating and development plans. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

On December 26, 2007, we entered into a Securities Purchase Agreement (SPA) with Platinum-Montaur Life Sciences, LLC (Montaur), pursuant to which we issued Montaur a 10% Series A Convertible Senior Secured Promissory Note in the principal amount of $7,000,000, due December 26, 2011 (the Series A Note) and a five-year Series W warrant to purchase 6,000,000 shares of our common stock, $.001 par value per share (Common Stock), at an exercise price of $0.32 per share. On April 16, 2008, following receipt by the Company of clearance by FDA to commence a Phase 3 clinical trial for Lymphoseek in patients with breast cancer or melanoma, we amended the SPA and issued Montaur a 10% Series B Convertible Senior Secured Promissory Note in the principal amount of $3,000,000, also due December 26, 2011 (the Series B Note, and hereinafter referred to collectively with the Series A Note as the Montaur Notes), and a five-year Series X warrant to purchase 8,333,333 shares of our Common Stock at an exercise price of $0.46 per share. Montaur may convert the Series B Note into shares of Common Stock at the conversion price of $0.36 per share. On December 5, 2008, after the Company had obtained 135 vital blue dye lymph nodes from patients who had completed surgery and the injection of the drug in the Phase 3 clinical trial of

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3,000 shares of our 8% Series A Cumulative Convertible Preferred Stock (the Preferred Stock) and a five-year Series Y warrant (hereinafter referred to collectively with the Series W warrant and Series X warrant as the Montaur Warrants) to purchase 6,000,000 shares of our Common Stock, at an exercise price of $0.575 per share, also for an aggregate purchase price of $3,000,000.

The Series A Note bears interest at a rate per annum equal to 10%, and is partially convertible at the option of Montaur into Common Stock at a price of $0.26 per share. The Series B Note also bears interest at a rate per annum equal to 10%, and is convertible into shares of Common Stock at the conversion price of $0.36 per share. Pursuant to the provisions of the Certificate of Designations, Voting Powers, Preferences, Limitations, Restrictions, and Relative Rights of Series A 8% Cumulative Convertible Preferred Stock, Montaur may convert all or any portion of the shares of the Preferred Stock into an aggregate 6,000,000 shares of our Common Stock, subject to adjustment as described in the Certificate of Designations.

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

Before obtaining regulatory approval for the commercial sale of any product candidates, we must demonstrate through preclinical testing and clinical trials that our product candidates are safe and effective for use in humans. Conducting clinical trials is a time consuming, expensive and uncertain process and may take years to complete. We recently successfully completed a Phase 2 clinical trial for our most advanced radiopharmaceutical product candidate, **Lymphoseek**, are in the midst of the first of two pivotal Phase 3 trials for this product in breast cancer or melanoma and have a second trial pending in head and neck squamous cell carcinoma. We have recently obtained approval from the EMEA of a Phase 3 clinical protocol for our next radiopharmaceutical candidate, **RIGScan** CR and are preparing to approach FDA to obtain similar clearance. Historically, the results from preclinical testing and early clinical trials have often not been predictive of results obtained in later clinical trials. Frequently, drugs that have shown promising results in preclinical or early clinical trials subsequently fail to establish sufficient safety and efficacy data necessary to obtain regulatory approval. At any time during the clinical trials, we, the participating institutions, FDA or EMEA might delay or halt any clinical trials for our product candidates for various reasons, including:

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

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

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

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

- generate cash flow and revenue;
- offset some of the costs associated with our internal research and development, preclinical testing, clinical trials and manufacturing;

seek and obtain regulatory approvals faster than we could on our own; and,

successfully commercialize existing and future product candidates.

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

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

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

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

We may not receive the regulatory approvals necessary to commercialize our **Lymphoseek** and **RIGScan** product candidates, which could cause our business to be severely harmed. Our product candidates are subject to extensive and rigorous government regulation. FDA regulates, among other things, the development, testing, manufacture, safety, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products. If our potential products are marketed abroad, they will also be subject to extensive regulation by foreign governments. None of our product candidates has been approved for sale in the United States or in any foreign market. The regulatory review and approval process, which includes preclinical studies and clinical trials of each product candidate, is lengthy, complex, expensive and uncertain. Securing FDA clearance to market requires the submission of extensive preclinical and clinical data and supporting information to FDA for each indication to establish the product candidate s safety and efficacy. Data obtained from preclinical and clinical trials are susceptible to varying interpretation, which may delay, limit or prevent regulatory approval. The approval process may take many years to complete and may involve ongoing requirements for post-marketing studies. In light of the limited regulatory history of monoclonal antibody-based therapeutics, regulatory approvals for our products may not be obtained without lengthy delays, if at all. Any FDA or other regulatory approvals of our product candidates, once obtained, may be withdrawn. The effect of government regulation may be to:

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

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

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

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

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

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import bans;
- voluntary or mandatory product recalls and publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications.

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

FDA regulates our gamma detection and blood flow measurement products in the United States. Foreign countries also subject these products to varying government regulations. In addition, these regulatory authorities may impose limitations on the use of our products. FDA enforcement policy strictly prohibits the marketing of FDA cleared

medical devices for unapproved uses. Within the European Union, our products are required to display the CE Mark in order to be sold. We have obtained FDA clearance to market and European certification to display the CE Mark on our current line of gamma detection systems and on initial blood flow product, the **Quantix/OR**. We may not be able to obtain clearance to market any new products in a timely manner, or at all. Failure to comply with these and other current and emerging regulatory requirements in the global markets in which our products are sold could result in, among other things, warning letters, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, refusal of the government to grant pre-market clearance for devices, withdrawal of clearances, and criminal prosecution.

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We rely on third parties to manufacture our products and our business will suffer if they do not perform.

We rely on independent contract manufacturers for the manufacture of our current **neoprobe® GDS** line of gamma detection systems and for our **Quantix** line of blood flow monitoring products. Our business will suffer if our contract manufacturers have production delays or quality problems. Furthermore, medical device manufacturers are subject to the QSR of FDA, international quality standards, and other regulatory requirements. If our contractors do not operate in accordance with regulatory requirements and quality standards, our business will suffer. We use or rely on components and services used in our devices that are provided by sole source suppliers. The qualification of additional or replacement vendors is time consuming and costly. If a sole source supplier has significant problems supplying our products, our sales and revenues will be hurt until we find a new source of supply. In addition, our distribution agreement with Ethicon Endo-Surgery, Inc. (EES) for gamma detection devices contains failure to supply provisions, which, if triggered, could have a significant negative impact on our business.

We may be unable to establish the pharmaceutical manufacturing capabilities necessary to develop and commercialize our potential products.

We do not have our own manufacturing facility for the manufacture of the radiopharmaceutical compounds necessary for clinical testing or commercial sale. We intend to rely in part on third-party contract manufacturers to produce sufficiently large quantities of drug materials that are and will be needed for clinical trials and commercialization of our potential products. Third-party manufacturers may not be able to meet our needs with respect to timing, quantity or quality of materials. If we are unable to contract for a sufficient supply of needed materials on acceptable terms, or if we should encounter delays or difficulties in our relationships with manufacturers, our clinical trials may be delayed, thereby delaying the submission of product candidates for regulatory approval and the market introduction and subsequent commercialization of our potential products. Any such delays may lower our revenues and potential profitability.

We may develop our manufacturing capacity in part by expanding our current facilities or building new facilities. Either of these activities would require substantial additional funds and we would need to hire and train significant numbers of employees to staff these facilities. We may not be able to develop manufacturing facilities that are sufficient to produce drug materials for clinical trials or commercial use. We and any third-party manufacturers that we may use must continually adhere to current Good Manufacturing Practices regulations enforced by FDA through its facilities inspection program. If our facilities or the facilities of third-party manufacturers cannot pass a pre-approval plant inspection, FDA will not grant approval to our product candidates. In complying with these regulations and foreign regulatory requirements, we and any of our third-party manufacturers will be obligated to expend time, money and effort on production, record-keeping and quality control to assure that our potential products meet applicable specifications and other requirements. If we or any third-party manufacturer with whom we may contract fail to maintain regulatory compliance, we or the third party may be subject to fines and/or manufacturing operations may be suspended.

Unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives applicable to our radiopharmaceutical products and product candidates could limit our potential product revenue.

The regulations governing drug pricing and reimbursement vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed and, in many of these countries, the pricing review period begins only after approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we monitor these regulations, our product candidates are currently in the development stage and we will not be able to assess the impact of price regulations for at least several years. As a result, we may obtain regulatory approval for a product in a particular country, but then be subject to price regulations that may delay the commercial launch of the product and may negatively impact the revenues we are able to derive from sales in that country.

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The healthcare industry is undergoing fundamental changes resulting from political, economic and regulatory influences. In the United States, comprehensive programs have been proposed that seek to increase access to healthcare for the uninsured, control the escalation of healthcare expenditures within the economy and use healthcare reimbursement policies to balance the federal budget.

We expect that Congress and state legislatures will continue to review and assess healthcare proposals, and public debate of these issues will likely continue. We cannot predict which, if any, of such reform proposals will be adopted and when they might be adopted. Other countries also are considering healthcare reform. Significant changes in healthcare systems could have a substantial impact on the manner in which we conduct our business and could require us to revise our strategies.

The sale of our common stock to Fusion may cause dilution and the sale of common stock acquired by Fusion could cause the price of our common stock to decline.

In connection with our agreement with Fusion, we have authorized the sale of up to 18,222,671 shares of our common stock and the issuance of 1,800,000 shares in commitment fees, and we are required to file a registration statement with the SEC for the sale to the public of 11,500,000 shares issuable to Fusion pursuant to the agreement. Through December 31, 2008, we have sold Fusion 7,568,671 shares of common stock and issued 1,314,000 shares of stock as commitment fees to Fusion. The number of shares ultimately offered for sale to the public will be dependent upon the number of shares purchased by Fusion under the agreement. It is anticipated that these shares will be sold over a period of up to 26 months from the date of the December 24, 2008 amendment to the agreement, at prices that will fluctuate based on changes in the market price of our common stock over that period. Depending upon market liquidity at the times sales are made, these sales could cause the market price of our common stock to decline. Consequently, sales to Fusion may result in substantial dilution to the interests of other holders of our common stock. The sale of a substantial number of shares of our common stock by Fusion, or anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales. However, we have the right to control the timing and amount of any sales of our shares to Fusion and the agreement may be terminated by us at any time at our discretion without any cost to us.

The sale of the shares of common stock acquired in private placements could cause the price of our common stock to decline.

During 2003 and 2007, we completed financings in which we issued common stock, convertible notes, warrants and other securities convertible into common stock to certain private investors. The terms of these transactions require that we file registration statements with the Securities and Exchange Commission (SEC) under which the investors may resell to the public common stock acquired in these transactions, as well as common stock acquired on the exercise of the warrants and convertible securities held by them.

The selling stockholders under these registration statements may sell none, some or all of the shares of common stock acquired from us, as well as common stock acquired on the exercise of the warrants and convertible securities held by them. We have no way of knowing whether or when the selling stockholders will sell the shares covered by these registration statements. Depending upon market liquidity at the time, a sale of shares covered by these registration statements at any given time could cause the trading price of our common stock to decline. The sale of a substantial number of shares of our common stock under these registration statements, or anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

We may lose out to larger and better-established competitors.

The medical device and biotechnology industries are intensely competitive. Some of our competitors have significantly greater financial, technical, manufacturing, marketing and distribution resources as well as greater experience in the medical device industry than we have. The particular medical conditions our product lines address can also be addressed by other medical devices, procedures or drugs. Many of these alternatives are widely accepted by physicians and have a long history of use. Physicians may use

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our competitors products and/or our products may not be competitive with other technologies. If these things happen, our sales and revenues will decline. In addition, our current and potential competitors may establish cooperative relationships with large medical equipment companies to gain access to greater research and development or marketing resources. Competition may result in price reductions, reduced gross margins and loss of market share.

Our products may be displaced by newer technology.

The medical device and biotechnology industries are undergoing rapid and significant technological change. Third parties may succeed in developing or marketing technologies and products that are more effective than those developed or marketed by us, or that would make our technology and products obsolete or non-competitive. Additionally, researchers could develop new surgical procedures and medications that replace or reduce the importance of the procedures that use our products. Accordingly, our success will depend, in part, on our ability to respond quickly to medical and technological changes through the development and introduction of new products. We may not have the resources to do this. If our products become obsolete and our efforts to develop new products do not result in any commercially successful products, our sales and revenues will decline.

We may not have sufficient legal protection against infringement or loss of our intellectual property, and we may lose rights to our licensed intellectual property if diligence requirements are not met.

Our success depends, in part, on our ability to secure and maintain patent protection, to preserve our trade secrets, and to operate without infringing on the patents of third parties. While we seek to protect our proprietary positions by filing United States and foreign patent applications for our important inventions and improvements, domestic and foreign patent offices may not issue these patents. Third parties may challenge, invalidate, or circumvent our patents or patent applications in the future. Competitors, many of which have significantly more resources than we have and have made substantial investments in competing technologies, may apply for and obtain patents that will prevent, limit, or interfere with our ability to make, use, or sell our products either in the United States or abroad.

In the United States, patent applications are secret until patents are issued, and in foreign countries, patent applications are secret for a time after filing. Publications of discoveries tend to significantly lag the actual discoveries and the filing of related patent applications. Third parties may have already filed applications for patents for products or processes that will make our products obsolete or will limit our patents or invalidate our patent applications.

We typically require our employees, consultants, advisers and suppliers to execute confidentiality and assignment of invention agreements in connection with their employment, consulting, advisory, or supply relationships with us. They may breach these agreements and we may not obtain an adequate remedy for breach. Further, third parties may gain access to our trade secrets or independently develop or acquire the same or equivalent information.

Agencies of the United States government conducted some of the research activities that led to the development of antibody technology that some of our proposed antibody-based surgical cancer detection products use. When the United States government participates in research activities, it retains rights that include the right to use the technology for governmental purposes under a royalty-free license, as well as rights to use and disclose technical data that could preclude us from asserting trade secret rights in that data and software.

The patents underlying our radiopharmaceutical products and ACT technology are exclusively licensed to us by third parties. The relevant license agreements require us to be current in exercising diligence in the development and commercialization of products using the licensed patents. While we believe our efforts demonstrate adequate current diligence, failure to meet the diligence requirements in any license agreements to the satisfaction of the licensors, if not cured on a timely basis, may result in our loss of some or all of our license rights to the patents licensed thereunder.

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The government grants Cardiosonix has received for research and development expenditures restrict our ability to manufacture blood flow monitoring products and transfer technologies outside of Israel and require us to satisfy specified conditions. If we fail to satisfy these conditions, we may be required to refund grants previously received together with interest and penalties, and may be subject to criminal charges.

Cardiosonix received grants from the government of Israel through the Office of the Chief Scientist (OCS) of the Ministry of Industry and Trade for the financing of a portion of its research and development expenditures associated with our blood flow monitoring products. From 1998 to 2001, Cardiosonix received grants totaling $775,000 from the OCS. The terms of the OCS grants may affect our efforts to transfer manufacturing of products developed using these grants outside of Israel without special approvals. In January 2006, the OCS consented to the transfer of manufacturing as long as Neoprobe complies with the terms of the OCS statutes under Israeli law. As long as we maintain at least 10% Israeli content in our blood flow devices, we will pay a royalty rate of 4% on sales of applicable blood flow devices and must repay the OCS a total of $1.2 million in royalties. However, should the amount of Israeli content of our blood flow device products decrease below 10%, the royalty rate could increase to 5% and the total royalty payments due could increase to $2.3 million. This may impair our ability to effectively outsource manufacturing or engage in similar arrangements for those products or technologies. In addition, if we fail to comply with any of the conditions imposed by the OCS, we may be required to refund any grants previously received together with interest and penalties, and may be subject to criminal charges. In recent years, the government of Israel has accelerated the rate of repayment of OCS grants related to other grantees and may further accelerate them in the future.

We may lose the license rights to certain in-licensed products if we do not exercise adequate diligence.

Our license agreements for **Lymphoseek**, **RIGS**, and ACT contain provisions that require that we demonstrate ongoing diligence in the continuing research and development of these potential products. Cira Bio s rights to certain applications of the ACT technology may be affected by its failure to achieve certain capital raising milestones although no such notices to that effect have been received to date. We have provided information, as required or requested, to the licensors of our technology indicating the steps we have taken to demonstrate our diligence and believe we are adequately doing so to meet the terms and/or intent of our license agreements. However, it is possible that the licensors may not consider our actions adequate in demonstrating such diligence. Should we fail to demonstrate the requisite diligence required by any such agreements or as interpreted by the respective licensors, we may lose our development and commercialization rights for the associated product.

We could be damaged by product liability claims.

Our products are used or intended to be used in various clinical or surgical procedures. If one of our products malfunctions or a physician misuses it and injury results to a patient or operator, the injured party could assert a product liability claim against our company. We currently have product liability insurance with a $10 million per occurrence limit, which we believe is adequate for our current activities. However, we may not be able to continue to obtain insurance at a reasonable cost. Furthermore, insurance may not be sufficient to cover all of the liabilities resulting from a product liability claim, and we might not have sufficient funds available to pay any claims over the limits of our insurance. Because personal injury claims based on product liability in a medical setting may be very large, an underinsured or an uninsured claim could financially damage our company.

We may have difficulty attracting and retaining qualified personnel and our business may suffer if we do not.

Our business has experienced challenges the past two years that have resulted in several significant changes in our strategy and business plan, including the shifting of resources to support our current product initiatives and downsizings to what we consider to be the minimal support structure necessary to operate a publicly traded company. Our management will need to remain flexible to support our business model over the next few years. However, losing members of the Neoprobe management team could have an adverse effect on our operations. Our success depends on our ability to attract and retain technical and management personnel with expertise and experience in the medical device business. The

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competition for qualified personnel in the medical device industry is intense and we may not be successful in hiring or retaining the requisite personnel. If we are unable to attract and retain qualified technical and management personnel, we will suffer diminished chances of future success.

Our secured indebtedness imposes significant restrictions on us, and a default could cause us to cease operations.

All of our material assets have been pledged as collateral for the $10 million in principal amount of our Series A and Series B Convertible Notes issued to Montaur, and a $1 million in principal amount Series B Convertible Note issued to our CEO and members of his family dated July 3, 2007, as amended December 26, 2007 (collectively, the Notes). In addition to the security interest in our assets, the Notes carry substantial covenants that impose significant requirements on us, including, among others, requirements that:

- we pay all principal by December 26, 2011;
- we use the proceeds from the sale of the Notes only for permitted purposes, such as **Lymphoseek** development and general corporate purposes;
- we keep reserved out of our authorized shares of common stock sufficient shares to satisfy our obligation to issue shares on conversion of the Notes and the exercise of the warrants issued in connection with the sale of the Notes; and
- we indemnify the purchasers of the Notes against certain liabilities.

Additionally, with certain exceptions, the Notes prohibit us from:

- amending our organizational or governing agreements and documents, entering into any merger or consolidation, dissolving the company or liquidating its assets, or acquiring all or any substantial part of the business or assets of any other person;
- engaging in transactions with any affiliate;
- entering into any agreement inconsistent with our obligations under the Notes and related agreements;
- incurring any indebtedness, capital leases, or contingent obligations outside the ordinary course of business;
- granting or permitting liens against or security interests in our assets;
- making any material dispositions of our assets outside the ordinary course of business;
- declaring or paying any dividends or making any other restricted payments; or
- making any loans to or investments in other persons outside of the ordinary course of business.

Our ability to comply with these provisions may be affected by changes in our business condition or results of our operations, or other events beyond our control. The breach of any of these covenants would result in a default under the Notes, permitting the holders of the Notes to accelerate their maturity and to sell the assets securing them. Such actions by the holders of the Notes could cause us to cease operations or seek bankruptcy protection.

Our common stock is traded over the counter, which may deprive stockholders of the full value of their shares.

Our common stock is quoted via the OTC Bulletin Board. As such, our common stock may have fewer market makers, lower trading volumes and larger spreads between bid and asked prices than securities listed on an exchange such as the New York Stock Exchange or the NASDAQ Stock Market. These factors may result in higher price volatility and less market liquidity for the common stock.

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A low market price may severely limit the potential market for our common stock.

Our common stock is currently trading at a price substantially below $5.00 per share, subjecting trading in the stock to certain SEC rules requiring additional disclosures by broker-dealers. These rules generally apply to any non-NASDAQ equity security that has a market price share of less than $5.00 per share, subject to certain exceptions (a penny stock). Such rules require the delivery, prior to any penny stock transaction, of a disclosure schedule explaining the penny stock market and the risks associated therewith and impose various sales practice requirements on broker-dealers who sell penny stocks to persons other than established customers and institutional or wealthy investors. For these types of transactions, the broker-dealer must make a special suitability determination for the purchaser and have received the purchaser s written consent to the transaction prior to the sale. The broker-dealer also must disclose the commissions payable to the broker-dealer, current bid and offer quotations for the penny stock and, if the broker-dealer is the sole market maker, the broker-dealer must disclose this fact and the broker-dealer s presumed control over the market. Such information must be provided to the customer orally or in writing before or with the written confirmation of trade sent to the customer. Monthly statements must be sent disclosing recent price information for the penny stock held in the account and information on the limited market in penny stocks. The additional burdens imposed upon broker-dealers by such requirements could discourage broker-dealers from effecting transactions in our common stock.

The price of our common stock has been highly volatile due to several factors that will continue to affect the price of our stock.

Our common stock traded as low as $0.29 per share and as high as $0.87 per share during the 12-month period ended December 31, 2008. The market price of our common stock has been and is expected to continue to be highly volatile. Factors, including announcements of technological innovations by us or other companies, regulatory matters, new or existing products or procedures, concerns about our financial position, operating results, litigation, government regulation, developments or disputes relating to agreements, patents or proprietary rights, may have a significant impact on the market price of our stock. In addition, potential dilutive effects of future sales of shares of common stock by the company and by stockholders, and subsequent sale of common stock by the holders of warrants and options could have an adverse effect on the market price of our shares.

Some additional factors which could lead to the volatility of our common stock include:

price and volume fluctuations in the stock market at large which do not relate to our operating performance;

financing arrangements we may enter that require the issuance of a significant number of shares in relation to the number of shares currently outstanding;

public concern as to the safety of products that we or others develop; and

fluctuations in market demand for and supply of our products.

An investor s ability to trade our common stock may be limited by trading volume.

Generally, the trading volume for our common stock has been relatively limited. A consistently active trading market for our common stock may not occur on the OTCBB. The average daily trading volume for our common stock on the OTCBB for the 12-month period ended December 31, 2008, was approximately 123,000 shares.

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Some provisions of our organizational and governing documents may have the effect of deterring third parties from making takeover bids for control of our company or may be used to hinder or delay a takeover bid.

Our certificate of incorporation authorizes the creation and issuance of blank check preferred stock. Our Board of Directors may divide this stock into one or more series and set their rights. The Board of Directors may, without prior stockholder approval, issue any of the shares of blank check preferred stock with dividend, liquidation, conversion, voting or other rights, which could adversely affect the relative voting power or other rights of the common stock. Preferred stock could be used as a method of discouraging, delaying, or preventing a take-over of our company. If we issue blank check preferred stock, it could have a dilutive effect upon our common stock. This would decrease the chance that our stockholders would realize a premium over market price for their shares of common stock as a result of a takeover bid.

Because we will not pay dividends in the foreseeable future, stockholders will only benefit from owning common stock if it appreciates.

We have never paid dividends on our common stock and we do not intend to do so in the foreseeable future. We intend to retain any future earnings to finance our growth. Accordingly, any potential investor who anticipates the need for current dividends from his investment should not purchase our common stock.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus 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 prospectus.

In addition, in this prospectus, we use words such as anticipate, believe, plan, expect, future, intend, and simi 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 prospectus. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements.

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USE OF PROCEEDS

This prospectus relates to shares of our common stock that may be offered and sold from time to time by the selling stockholder. We will receive no proceeds from the sale of shares of common stock in this offering.

CAPITALIZATION

The following table sets forth our cash, other current assets, debt and capitalization as of September 30, 2008, as follows:

- on an actual basis; and
- on a pro forma basis to give effect to the issuance of the Series A Preferred Stock and the Series Y Warrant, and the issuance of shares of common stock to Fusion as commitment shares.

The table does not include the effect of the shares registered in this Registration Statement as the shares registered are for a secondary offering by selling shareholders.

	September 30, 2008 Actual (Unaudited)	Adjustments	September 30, 2008 Pro Forma
Cash	$ 2,599,816	2,820,000(1)	$ 5,419,816
Other current assets	2,308,067	216,000(2)	2,524,067
Current liabilities	2,115,209		2,115,209
Long-term liabilities	6,949,400	238,819(1)	7,188,219
Preferred stock		3,000,000(1)	3,000,000
Stockholders (deficit) equity:			
Common stock	69,787	360(2)	70,147
Additional paid-in capital	142,927,031	2,716,897(1)(2)	145,643,928
Accumulated deficit	(144,711,971)	(2,920,076)(1)	(147,632,047)
Total stockholders (deficit) equity	(1,715,153)	(202,819)	(1,917,972)
Total capitalization	$ 7,349,456		$ 10,385,456

(1) As a result of issuance of the Series A Preferred Stock with the Series Y Warrant in December 2008, the Company increased cash by $2,820,000, long term liabilities by $238,819, additional paid-in capital related to the beneficial conversion

feature and the warrant, net of placement agent fees of $180,000, by $2,501,257 and accumulated deficit by $2,920,076.

(2) As a result of the issuance of 360,000 shares of common stock to Fusion in exchange for their commitment to provide the Company funding, other current assets increased by $216,000, common stock increased by $360 and additional paid-in capital increased by $215,640.

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MARKET FOR COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Our common stock trades on the OTCBB under the trading symbol NEOP. The prices set forth below reflect the quarterly high, low and closing sales prices for shares of our common stock during the last two fiscal years, and the current fiscal year through January 6, 2009, as reported by Reuters Limited. These quotations reflect inter-dealer prices, without retail markup, markdown or commission, and may not represent actual transactions.

	High	***Low***	***Close***
Fiscal Year 2009			
First Quarter through January 6, 2009	$0.59	$0.56	$0.57
Fiscal Year 2008			
First Quarter	$0.42	$0.29	$0.35
Second Quarter	0.87	0.34	0.68
Third Quarter	0.75	0.42	0.57
Fourth Quarter	0.68	0.45	0.57
Fiscal Year 2007:			
First Quarter	$0.27	$0.20	$0.24
Second Quarter	0.32	0.19	0.31
Third Quarter	0.50	0.23	0.31
Fourth Quarter	0.35	0.25	0.29

As of December 31, 2008, we had approximately 794 holders of common stock of record. On January 6, 2009, the last reported sale price for our common stock as reported on the OTC Bulletin Board was $0.57 per share.

We have not paid any dividends on our common stock and do not anticipate paying cash dividends in the foreseeable future. We intend to retain any earnings to finance the growth of our business. We cannot assure you that we will ever pay cash dividends. Whether we pay cash dividends in the future will be at the discretion of our Board of Directors and will depend upon our financial condition, results of operations, capital requirements and any other factors that the Board of Directors decides are relevant. See Management s Discussion and Analysis of Financial Condition and Results of Operations.

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DESCRIPTION OF BUSINESS

Development of the Business

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

From our inception through 1998, we devoted substantially all of our efforts and resources to the research and clinical development of radiopharmaceutical and medical device technologies related to the intraoperative diagnosis and treatment of cancers, including our proprietary radioimmunoguided surgery (**RIGS**®) technology. In 1998, U.S. and European regulatory agencies completed an evaluation of the status of the regulatory pathway for our **RIGS** products, which coupled with our limited financial resources, 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 in 2002 following 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 blood flow measurement devices, we continued to look for other avenues to reinvigorate our radiopharmaceutical development portfolio. During 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 over the past few years, we now have one radiopharmaceutical product, Lymphoseek®, on the verge of commencing two pivotal Phase 3 clinical trials, and a second, RIGScan® CR, nearing a greater level of activity as we seek to clarify the regulatory pathway and identify potential development sources of funding or collaboration. Our subsidiary, Cira Biosciences, Inc. (Cira Bio), also took steps in early 2008 to identify funding sources to assist it in evaluating the market opportunities for yet another technology platform, activated cellular therapy (ACT).

We believe that our virtual business model is unique within our industry as it combines revenue generation from medical devices covering our public company overhead while we devote capital raised through financing efforts to the development of products with even greater potential for shareholder return such as Lymphoseek. 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 2008, 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 the U.S. Food and Drug Administration (FDA) and other international regulatory agencies for marketing and commercial distribution throughout most major global markets.

Our patented gamma detection device systems consist of hand-held detector probes and a control unit. The critical detection component is a highly radiosensitive crystal contained in the tip of the probe that relays a signal through a preamplifier to the control unit to produce both a digital readout and an audible signal. The detector element fits into a housing approximately the size of a pen flashlight. The **neoprobe GDS** gamma detection system, originally released in 1998 under the name **neo2000**®, is the fourth generation of our gamma detection systems. 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 remanufacture. Since 1998, we have developed and released four major software upgrades for customer units designed to improve the

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utility of the system and/or offer the users additional features, including our most recent release that enables our entire installed base of **neoprobe GDS** users to use our wireless gamma detection probes based on Bluetooth® technology which were commercially launched in late 2006. Generally, these software upgrades have been included in new units offered for sale but have also been offered for sale separately.

Surgeons are using our gamma detection devices in a surgical application referred to as sentinel lymph node biopsy (SLNB) or intraoperative lymphatic mapping (ILM or lymphatic mapping). SLNB 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. SLNB begins when a patient is injected at the site of the main tumor with a commercially available radioactive tracing agent. The agent is intended to follow the same lymphatic flow as the cancer would 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.

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

Hundreds of articles have been published in recent years in peer-reviewed journals on the topic of SLNB. Furthermore, a number of thought leaders and cancer treatment institutions have recognized and embraced the technology as standard of care for melanoma and for breast cancer. Our marketing partner continues to see strong sales, especially for use in breast cancer treatment. SLNB in breast cancer has been the subject of national and international clinical trials, including one major study sponsored by the U.S. Department of Defense and the National Cancer Institute (NCI) and one sponsored by the American College of Surgeons. The first of these trials completed accrual approximately three years ago and preliminary results may be available sometime in 2009. Accrual on the second trial was halted early, due, we believe, to the overwhelming desire of patients to be treated with SLNB rather than be randomized in a trial whereby they might receive a full axillary dissection. We believe that once data from these trials are published there may be an additional demand for our devices from those surgeons who have not yet adopted the SLNB procedure. We also believe, based on an estimate of the total number of operating rooms in medical centers that are capable of performing the types of procedures in which our gamma detection devices are used, that while we are potentially reaching saturation at the major cancer centers and teaching institutions, a significant portion of the global market for gamma detection devices such as ours remains untapped. We also 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 probe, 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 SLNB 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. 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 SLNB 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 software-based enhancements to the **neoprobe GDS** platform as well as our new wireless probes introduced in late 2006.

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Blood Flow Measurement Devices

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

real-time monitoring;

intra-operative quantification;

non-invasive diagnostics; and

evaluation of cardiac function.

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

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

The **Quantix** technology utilizes a special application of the Doppler method through simultaneous projection of a combination of narrow beams with a known angle between them. Thus, based on trigonometric and Doppler considerations, the angle of insonation can be obtained, resulting in accurate, angle-independent blood flow velocity measurements that do not require the use of complicated, expensive imaging systems. In order to obtain high-resolution velocity profiles, the **Quantix** device uses a multi-gated pulse wave Doppler beam. With this method, specific sample volumes along the ultrasound beam can be separately evaluated, and the application of a flow/no flow criterion can be made. The Cardiosonix technology applies a special use of digital Doppler technology, which with the digital signal processing power of the system allows hundreds of sample volumes to be sampled and processed simultaneously, thus providing high resolution velocity profiles for both angle and vascular diameter calculations, and subsequently volume blood flow measurements. Through 2008, we have focused our blood flow measurement efforts on measuring blood flow in cardiac bypass grafts. The technology also has the potential to be applied in other healthcare settings where measurement of blood flow may be beneficial. We have recently begun devoting additional efforts in modifying the device for use in vascular assessment, particularly associated with dialysis applications.

Quantix/OR™ is designed to permit cardiovascular surgeons to obtain intraoperative volume blood flow readings in various targeted blood vessels within seconds. The system consists of an insonation angle-independent ultrasound probe and digital numerical displays of blood flow rate. Thus, the surgeon obtains immediate, real-time and quantitative readings while focused on the target vessel. Quantifying blood flow can be very beneficial during anastomostic or other bypass graft procedures to determine adequate blood flow. While measurement is advisable whenever a blood vessel is exposed and manipulated intra-operatively, generally this is not the current practice. Ultimately, in practice, the surgeon typically resorts to using his or her eyes and fingers in a process called finger palpation to qualitatively assess vessel flow. The **Quantix/OR** offers the surgeon immediate and simple quantitative assessment of blood flow in multiple blood vessels and grafts. The primary advantage of finger palpation is that it is fast, simple and low cost; the disadvantages are that it requires a good deal of experience, it is difficult to perform in vessels embedded in tissue, it can become difficult to interpret in large vessels, and it permits only a very qualitative and subjective assessment. A significant partial occlusion (or even a total occlusion) will result in significant vessel distention and strong pulse that may mislead the surgeon. Rather than rely on such a subjective clinical practice, which is highly experience-dependent, the **Quantix/OR** is designed to allow the surgeon to rely on more quantifiable and objective information. We believe that **Quantix/OR** represents a measurable improvement over existing technologies to directly measure blood flow intraoperatively. Other technologies that attempt to measure intraoperative blood flow directly are generally more invasive and are impractical when non-skeletonized vessel measurements are required. As a result, a majority of surgeons generally resort to finger palpation to qualitatively, rather than quantitatively, measure vessel perfusion.

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

Our strategy related to the Quantix/OR for 2009 is to identify pathways to support the greater penetration of the **Quantix/OR** in cardiovascular and vascular applications. However, given our limited success in achieving market penetration to-date and the minimal support activities we are currently devoting to the product line, we cannot assure you that any of Cardiosonix s products will achieve market acceptance. As a result, we may be forced to consider other strategic alternatives. See Risk Factors.

Lymphoseek

Our gamma detection devices are primarily capital in nature; as such, they generate revenue only on the initial sale. To complement the one-time revenue stream related to capital products, we are working on developing recurring revenue or procedural products that would generate revenue based on each procedure in which they were used. The product we are working on with the greatest near-term potential in this area involves a proprietary drug compound under exclusive worldwide license from the University of California, San Diego (UCSD) that we refer to as **Lymphoseek**. The UCSD license grants Neoprobe the commercialization rights to **Lymphoseek** for diagnostic imaging and intraoperative detection applications. If proven effective and cleared for commercial sale, **Lymphoseek** would be the first radiopharmaceutical product specifically designed and labeled for the targeting of sentinel lymph nodes. Neoprobe and UCSD completed the initial pre-clinical evaluations of **Lymphoseek** in 2001. Since that time, UCSD has completed or initiated five Phase 1 clinical 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	60	Ongoing
Prostate	1	20	Ongoing
Colon	1	20	Ongoing
Breast and Melanoma	2	80	Completed
Breast and Melanoma	3	150*	Ongoing
Head and Neck Squamous Cell Carcinoma	3	180	Pending

* Patient number is approximate and is based on an estimated average number of lymph nodes expected to be removed from each patient. The trial size is based on extracting a total of 203 lymph nodes from the

patients
enrolled.

The Phase 1 studies were or are being supported, including being substantially funded through research grants, by a number of organizations such as the Susan G. Komen Breast Cancer Research Foundation, the American Cancer Society (ACS) and the NCI. Research data from some of these clinical evaluations of **Lymphoseek** have been presented at recent meetings of the Society of Nuclear Medicine, the Society of Surgical Oncology and the World Sentinel Node Congress. The 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.

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In November 2003, we met with the Interagency Council on Biomedical Imaging in Oncology (Interagency Council), an organization representing FDA, the NCI and the Centers for Medicare and Medicaid Services, to discuss the regulatory approval process and to determine the objectives for the next clinical trial involving **Lymphoseek**. During 2004, we prepared and submitted an IND application to FDA to support the marketing clearance of **Lymphoseek**. In the first quarter of 2005, we announced that FDA had accepted our application to establish a corporate IND for **Lymphoseek**. With the transfer of the UCSD physician IND to Neoprobe, we assumed full clinical and commercial responsibility for the development of **Lymphoseek**. Following the establishment of the corporate IND, Neoprobe s clinical and regulatory personnel began discussions with FDA regarding the clinical development program for **Lymphoseek**.

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

Upon the submission of the IND and draft Phase 2 protocol, FDA advised Neoprobe that commercially produced **Lymphoseek** would need to be used in the Phase 2 clinical study, as opposed to using drug previously manufactured in laboratories at UCSD. Also, the regulatory agencies raised a number of Chemistry, Manufacturing and Control (CMC) questions regarding the drug compound and its complete characterization. Neoprobe began the transfer of bulk drug manufacturing to Reliable Biopharmaceutical Corporation (Reliable) early in 2005 and engaged Cardinal Health, Inc. (Cardinal Health) to develop and validate procedures and assays to establish commercial standards for the formulation, filling and lyophilization of the drug compound. We submitted an initial CMC response to FDA in April 2006.

We 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 recent discussions and correspondence with FDA, we proposed to FDA that we conduct two separate Phase 3 studies. During 2008, we initiated patient enrollment in the first of the two phase 3 clinical studies. The first study is expected to involve approximately 150 evaluable patients with either melanoma or breast cancer although the patient number is an estimate as the trial is based on the evaluation of 203 lymph nodes from enrolled patients and the average number of lymph nodes per patient may vary. Patients in this trial are receiving both **Lymphoseek** and a non-radiopharmaceutical agent (i.e., a vital blue dye) that is currently used as a marker in lymphatic mapping procedures. The endpoint of this trial is to show concordance of **Lymphoseek** to the vital blue dye of 94% or more. During the Phase 2 trial, we noted a concordance rate of approximately 97% in the 56 patients who received both **Lymphoseek** and the blue dye.

We have provided FDA and the centralized European Medicinal Evaluation Agency (EMEA) with the full protocol and associated materials for a second Phase 3 study to be conducted in patients with head and neck squamous cell carcinoma. This second Phase 3 study is designed to validate Lymphoseek as a sentinel lymph node targeting agent. Our discussions with FDA and EMEA have also suggested that the Phase 3 trials will support an intended use of Lymphoseek in sentinel lymph node biopsy procedures. We believe such an indication would be beneficial to the marketing and commercial adoption of

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Lymphoseek in the U.S. and EU. Finally, we are harmonizing the second Phase 3 protocol in head and neck tumors for Lymphoseek based upon input from both FDA and EMEA. We expect this process to be concluded in the near future. We plan to have approximately 15 to 20 participating institutions in the trial, which we hope will enable us to enroll patients at a fairly rapid rate. We have commenced institutional preparatory activities to initiate the study after the appropriate regulatory clearances have been obtained.

Our goal is to file the new drug application for Lymphoseek in the second half of 2009, which will be dependent upon our ability to commence and successfully conclude the Phase 3 clinical studies in a timely fashion. Depending on the timing and outcome of the FDA regulatory review cycle, we believe that Lymphoseek can be commercialized in late 2010. In addition, Neoprobe has had advanced discussions regarding the drug approval and registration process under the centralized European drug evaluation procedures with EMEA in London. 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. We cannot assure you, however, that this product will achieve regulatory approval, or if approved, that it will achieve market acceptance.

We expect to incur approximately $4 million in out-of-pocket development costs in 2009 related to the clinical and regulatory development of Lymphoseek. We cannot assure you, however, that this product will achieve regulatory approval, or if approved, that it will achieve market acceptance. See Risk Factors.

RIGS

From inception until 1998, Neoprobe devoted significant efforts and resources to the development of its proprietary **RIGS** technology. The **RIGS** system combines a patented hand-held gamma radiation detection probe, proprietary radiolabeled cancer-specific targeting agents, and patented surgical methods to provide surgeons with real-time information to locate tumor deposits not detectable by conventional methods. The **RIGS** system is designed to assist the surgeon in the more thorough removal of the cancer, thereby leading to improved surgical treatment of the patient. The targeting agents used in the **RIGS** process are monoclonal antibodies, labeled with a radioactive isotope that emits low energy gamma rays. The device used is a very sensitive radiation detection instrument that is capable of detecting small amounts of radiation bound to the targeting agent. Before surgery, a cancer patient is injected with one of the targeting agents which circulates throughout the patient s body and binds specifically to cancer cell antigens or receptors. Concentrations of the targeting agent are then located during surgery by Neoprobe s gamma detection device, which emits an audible tone to direct the surgeon to targeted tissue.

RIGScan CR is an intraoperative agent consisting of a radiolabeled murine monoclonal antibody (MAb CC49). The radiolabel used is ^{125}I, a 27 35 KeV emitting isotope. The 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.

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

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

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

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

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

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

In recent years, we have obtained access to survival analyses of patients treated with **RIGScan** CR which have been prepared by third parties, indicating that **RIGScan** CR may be predictive of, or actually contribute to, a positive outcome when measuring survival of the patients that participated in our original BLA studies. The data or its possible significance was unknown at the time of the BLA review given the limited maturity of the follow-up experience. The data includes publication by some of the primary

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investigators involved in the Phase 3 **RIGS** trials who have independently conducted survival follow-up analyses to their own institution s **RIGS** trial patients with apparently favorable results relating to the long-term survival prognosis of patients who were treated with **RIGS**. In addition, we learned that FDA has held the BLA originally filed with FDA in 1996 open. Based primarily on these pieces of information, we requested a meeting with FDA to discuss the possible next steps for evaluating the survival related to our previous Phase 3 clinical trials as well as the possible submission of this data, if acceptable, as a prospective analysis in response to questions originally asked by FDA in response to our original BLA.

The April 2004 meeting with FDA was an important event in the re-activation of the **RIGS** program. The meeting was very helpful from a number of aspects: we confirmed that the **RIGS** BLA remains active and open. We believe this will improve both the cost effectiveness and timeliness of future regulatory submissions for **RIGScan** CR. Additionally, FDA preliminarily confirmed that the BLA may be applicable to the general colorectal population; and not just the recurrent colorectal market as applied for in 1996. Applicability to a general colorectal population could result in a greater market potential for the product than if applicable to just the recurrent population. During the meeting, FDA 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.

It should be noted, however, that the **RIGScan** CR biologic drug has not been produced for several years and based on the feedback we recently received from EMEA, 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. We have initiated discussions with established biologic manufacturing organizations to determine the costs and timelines associated with the production of commercial quantities of the CC49 antibody. In addition, we will need tore- establish radiolabeling capabilities for the CC49 antibody in order to meet the regulatory needs for the **RIGScan** CR product.

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

In November 2005, Neoprobe submitted a corporate IND application for the modified humanized version of **RIGScan** CR. With the establishment of the corporate IND, responsibility for the clinical and commercial development of the humanized version of **RIGScan** CR was officially transferred from a physician sponsored IND to Neoprobe. Prior to the evaluation of the modified antibody in a Phase 1 clinical trial, all clinical development of **RIGScan** CR had been conducted with a murine (i.e., mouse DNA-based) version of a monoclonal antibody. The Phase 1 trial was the first test in human patients using a modified version of the antibody from which the prominent parts of the mouse DNA chain had been removed. In early 2006, we filed an IND amendment that included a final report to FDA of the Phase 1 study.

Over the past few years, we have made progress in advancing our RIGScan CR development program while incurring little in the way of research expenses. Our RIGS technology, which had been essentially inactive since failing to gain approval following our original license application in 1997, has been the subject of renewed interest due primarily to the analysis of survival data related to patients who participated in the original Phase 3 clinical studies that were completed in 1996. After a successful pre-submission meeting with EMEA in July, we submitted a plan during the third quarter of 2008 on how we would propose to complete clinical development plan for RIGScan CR. The clinical protocol we submitted to EMEA involves 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.

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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 the EMEA will assist us in those efforts. 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.

Activated Cellular Therapy

Through various research collaborations, we performed early-stage research on another technology platform, ACT, based on work originally done in conjunction with the **RIGS** technology. ACT is intended to boost the patient s own immune system by removing lymph nodes identified during surgery and then, in a cell processing technique, activating and expanding helper T-cells found in the nodes. Within 10 to 14 days, the patient s own immune cells, activated and numbering more than 20 billion, are infused into the patient in an attempt to trigger a more effective immune response to the cancer.

In the course of our research into ACT performed with **RIGS**, we learned that these lymph node lymphocytes containing helper T-cells could be activated and expanded to treat patients afflicted with viral and autoimmune disease as well as oncology patients. We have seen promising efficacy of this technology demonstrated from six Phase 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. In addition, a scientific advisory group is being formed to develop a clinical and regulatory approach for the Cira Bio technology. Following the completion of these assessments and the formation of a commercialization strategy, Cira Bio intends to raise the necessary capital to move this technology platform forward. 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 in connection with the successful completion of a financing transaction by Cira Bio. In the first quarter of 2008, we also entered into discussions with an investment banking firm to help us gauge the interest of potential investment in the ACT technology. We still hope to raise funds through Cira Bio to support the continued development of ACT; however, our fundraising efforts have thus far not been successful and our option to purchase the remaining 10% interest in Cira Bio expired on June 30, 2008. If we are successful in identifying a funding source, we expect that any funding would likely be accomplished by an investment directly into Cira Bio, so that the funds raised would not dilute current Neoprobe shareholders. Obtaining this funding would likely dilute Neoprobe s ownership interest in Cira Bio; however, we believe that moving forward such a promising technology will only yield positive results for the Neoprobe stockholders and the patients who could benefit from these treatments. However, we do not know if we will be successful in obtaining 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.

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Market Overviews

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

Cancer Market Overview

Cancer is the second leading cause of death in the U.S. and Western Europe and is estimated to be responsible for over 560,000 deaths annually in 2008 in the U.S. alone. The NIH estimates the overall annual costs for cancer (the primary focus of our gamma detection and pharmaceutical products) for the U.S. in the year 2007 at $219.2 billion: $89.0 billion for direct medical costs, $18.2 billion for indirect morbidity, and $112.0 billion for indirect mortality. Our line of gamma detection systems is currently used primarily in the application of SLNB in breast cancer and melanoma which, according the ACS, are estimated to account for 13% and 4%, respectively, of new cancer cases in the U.S. in 2008.

The NIH has estimated that breast cancer will annually affect half a million women in North America, Western Europe, and other major economic markets. Breast cancer is the second leading cause of death from cancer among all women in the U.S. The incidence of breast cancer, while starting to show minor declines in the past year or so, generally increases with age, rising from about 100 cases per 100,000 women at age 40 to about 400 cases per 100,000 women at age 65. 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 182,000 new cases of invasive breast cancer are expected to be diagnosed and approximately 41,000 women are estimated to die from the disease during 2008 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.

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 estimated that nearly 148,000 new incidences of colon and rectal cancers were expected to occur in the U.S. in 2008. 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 $2 billion annually, depending on the level of reimbursement allowed. However, we cannot assure you that **RIGScan** CR will be cleared to market, or if cleared to market, that it will receive the reimbursement or achieve the level of sales we have currently estimated.

Blood Flow Measurement Market Overview

Cardiovascular disease is the number one killer of men and women in the U.S. and in a majority of countries in the rest of the world that track such statistics. The National Center for Healthcare Services (NCHS) registered nearly 7 million inpatient cardiovascular procedures in the U.S. during 2005 with a

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primary diagnosis of cardiovascular disease. In the U.S. in 2005, the NCHS estimates that there were 469,000 coronary artery bypass surgeries performed on 261,000 patients. We, as well as our competitors and other industry analysts, generally estimate the rest of the world s incidence of such modalities at approximately equal to as much as two time U.S. estimates.

The American Heart Association (AHA) estimated the total cost of cardiovascular diseases and stroke in the United States would exceed $448 billion in 2008. A substantial portion of these expenditures is expected to be for non-invasive image and intravascular examination.

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

Industry analysts have estimated the potential market for blood flow measurement devices will exceed $240 million annually by 2010. However, at the present state of market development and acceptance of blood flow measurement within the medical community, the penetrable market is likely significantly less. At present, we would estimate that less than 25% of by-pass procedures involve blood flow measurement. We believe that gaining a modest share of the potential penetrable market could result in meaningful supplemental annual revenues for our company. We cannot assure you, however, that Cardiosonix products will achieve market acceptance and generate the level of sales or prices anticipated.

Marketing and Distribution

Gamma Detection Devices

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

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

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

We entered into 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. Under this agreement, we manufacture and sell our SLNB products almost exclusively to EES, who distributes the products globally (except for Japan). EES has no ongoing purchase or reimbursement commitments to us other than the rolling four-month binding purchase commitment for gamma detection devices 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 EES also contains certain termination provisions and licenses to our intellectual property that take effect only in the event we fail to supply product, or for other reasons such as a change of control. See Risk Factors.

Gamma Detection Radiopharmaceuticals

During the fourth quarter of 2007, we executed an agreement with 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 share of each patient dose sold. In addition, Neoprobe will receive up to $3 million in payments upon the achievement of certain sales milestones by Cardinal Health. We do not currently have collaborative agreements covering **Lymphoseek** in other areas of the world 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 believe there are development milestones that can be achieved prior to the need for significant capital investment in **RIGScan** CR such as preparing the request for a SPA and completing a final protocol review. However, we continue to believe it will be necessary for us to identify a development partner or an alternative funding source in order to prepare for and to fund the pivotal clinical testing that will be necessary to gain marketing clearance for **RIGScan** CR. At the present time, while we have parties who have indicated an interest in entering into a development relationship, we do not believe these efforts will result in a definitive partnership at least until a regulatory and development pathway is obtained. We anticipate continuing discussions for **RIGScan** CR as we move forward with the clinical development of the product; however, 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.

Blood Flow Measurement Devices

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

Our time and effort in the marketing and sales of blood flow devices through 2008 has been to improve market penetration for the **Quantix/OR** through working with third party distributors. Sales in the cardiovascular market, particularly in the U.S., continue to disappoint us. As a result, we intend to re-evaluate our current distribution relationships and are investigating alternative sales and distribution channels for the **Quantix** devices. We continue to evaluate our outlook for our blood flow measurement business and believe the outcome of our work in the dialysis/vascular assessment arena is critical in demonstrating the ultimate viability of this product line.

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Manufacturing

Gamma Detection Devices

We rely on independent contract manufacturers, some of which are single-source suppliers, for the manufacture of the principal components of our current line of gamma detection system products. See Risk Factors. We have devoted significant resources to develop production capability for our gamma detection systems at qualified contract manufacturers. Production of the **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 Products, a division of II-VI Corporation (eV), and TriVirix International, Inc. (TriVirix). We also purchase certain accessories for our line of gamma detection systems from other qualified manufacturers.

We purchase certain solid-state crystals and associated electronics to be used in the manufacture of our proprietary line of hand-held gamma detection probes from eV Products, a subsidiary of II-VI Corporation; however, we do not currently have a supply agreement with eV. The number of potential suppliers of such solid-state crystals is limited. In the event we were unable to secure a viable alternative source of supply should we become unable to obtain crystals from eV, any prolonged interruption of this source could restrict the availability of our probe products, which would adversely affect our operating results.

In February 2004, we executed a Product Supply Agreement with TriVirix for the manufacture of the **neoprobe GDS**, 14mm probe and 11mm laparoscopic probe. The term of this agreement expired in February 2008 but was automatically extended through February 2009. The Agreement is automatically extended for successive one-year periods unless six months notice is provided by either party.

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

Gamma Detection Radiopharmaceuticals

In preparation for the commencement of a multi-center clinical evaluation of **Lymphoseek**, Neoprobe engaged drug manufacturing organizations to produce the drug that was used in the Phase 2 trial and is expected to be used in the pivotal (i.e., Phase 3) clinical trials. Reliable has produced the active chemical compound and OSO BioPharmaceuticals Manufacturing LLC (OSO Bio), formerly Cardinal Health Pharmaceutical Technology and Services, has performed final product manufacturing including final drug formulation, lyophilization (i.e., freeze-drying) and packaging processes. Once packaged, the vialed drug can then be shipped to a hospital or regional commercial radiopharmacy where it can be made radioactive (i.e., radiolabeled) with Tc99m to become **Lymphoseek**. The commercial manufacturing processes at Reliable and OSO Bio have been validated and both organizations have assisted Neoprobe in the preparation of the chemistry, manufacturing and control sections of our submissions to FDA. Both Reliable and OSO Bio are registered manufacturers with FDA. At this point, drug product produced by Reliable and OSO Bio has been produced under clinical development agreements. Commercial supply and distribution agreements are being negotiated with both Reliable and OSO Bio. We cannot assure you that we will be successful in reaching such agreements with Reliable or OSO Bio on terms satisfactory to us or at all.

In preparation for the initiation of the next phase of clinical evaluation of **RIGScan** CR, we have also initiated discussions with potential biologic manufacturers and radiolabeling organizations. We have held discussions with parties who may assist in the manufacturing validation and radiolabeling of the **RIGScan** CR product; however, we have not yet finalized agreements with these entities. We anticipate finalizing these discussions following securing a development partner in order to accommodate the

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commencement of future **RIGScan** CR clinical trials. We cannot assure you that we will be successful in securing and/or maintaining the necessary biologic, product and/or radiolabeling capabilities. See Risk Factors.

Blood Flow Measurement Devices

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

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

Competition

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

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

Gamma Detection Devices

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

It is often difficult to glean accurate competitive information within the lymphatic mapping field, primarily because most of our competitors are either subsidiaries or divisions of large corporations or privately held corporations, whose sales revenue or volume data is not readily available or determinable. In addition,

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lymphatic mapping does not currently have a separate reimbursement code in most healthcare systems. As such, determining trends in the actual number of procedures being performed using lymphatic mapping is difficult. We believe, based on our understanding of EES success rate in competitive bid situations, that our market share has remained relatively constant or increased slightly in light of changes in the competitive landscape over the past few years. As we have discussed, we believe that current sales levels indicate that some prospective customers may be waiting on the results of important international clinical trials prior to adoption the SLNB procedure and purchasing a gamma detection device. We expect the results from these trials, when announced, will likely have a positive impact on sales volumes. We believe our intellectual property portfolio will be a barrier to competitive products; however, we cannot assure you that competitive products will not be developed, be successful in eroding our market share or affect the prices we receive for our gamma detection devices. See Risk Factors.

Gamma Detection Radiopharmaceuticals

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

Surgeons who practice the lymphatic mapping procedure that **Lymphoseek** is intended for currently use other radiopharmaceuticals such as a sulphur-colloid compound in the U.S. and other colloidal compounds in other markets. However, these drugs are being used off-label in most major global markets (i.e., they are not specifically indicated for use as a lymphatic targeting agent). As such, we believe that **Lymphoseek**, if ultimately approved, would be the first drug specifically labeled for use as a sentinel lymph node targeting agent.

Blood Flow Measurement Devices

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

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

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

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

Patents and Proprietary Rights

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

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

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

We continue to maintain proprietary protection for the products related to **RIGS** and ACT in major global markets such as the U.S. and the EU, which although not currently integral to our near-term business plans, may be important to a potential **RIGS** or ACT development partner. The original methodology aspects of our **RIGS** technology are claimed in the United States in U.S. Patent No. 4,782,840, which expired in August 2005. However, Neoprobe has recently gained access to additional methodology applications related to our **RIGS** technology that are covered by patents that provide additional patent coverage through 2018, unless extended. In addition to the **RIGS** methodology patents, composition of matter patents have been issued in the U.S. and EU that cover the antibodies used in clinical studies. The most recent of these patents was issued in 2004 and additional patent applications are pending.

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

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

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

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

Government Regulation

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

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

For some products, and in some countries, government regulation is significant and, in general, there is a trend toward more stringent regulation. In recent years, FDA and certain foreign regulatory bodies have pursued a more rigorous enforcement program to ensure that regulated businesses like ours comply with applicable laws and regulations. We devote significant time, effort and expense addressing the extensive governmental regulatory requirements applicable to our business. To date, we have not received any notifications or warning letters from FDA or any other regulatory bodies of alleged deficiencies in our

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compliance with the relevant requirements, nor have we recalled or issued safety alerts on any of our products. However, we cannot assure you that a warning letter, recall or safety alert, if it occurred, would not have a material adverse effect on our company.

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

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

Gamma Detection and Blood Flow Measurement Devices

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

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

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

Gamma Detection Radiopharmaceuticals (Lymphoseek and RIGScan)

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

The process of completing pre-clinical and clinical testing, manufacturing validation and submission of a marketing application to the appropriate regulatory bodies usually takes a number of years and requires the expenditure of substantial resources, and we cannot assure you that any approval will be granted on a timely basis, if at all. Additionally, the length of time it takes for the various regulatory bodies to evaluate an application for marketing approval varies considerably, as does the amount of preclinical and clinical data required to demonstrate the safety and efficacy of a specific product. The regulatory bodies may require additional clinical studies that may take several years to perform. The length of the review period may vary widely depending upon the nature and indications of the proposed product and whether the regulatory body has any further questions or requests any additional data. Also, the regulatory bodies

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will likely require post-marketing reporting and surveillance programs to monitor the side effects of the products. We cannot assure you that any of our potential drug or biologic products will be approved by the regulatory bodies or approved on a timely or accelerated basis, or that any approvals received will not subsequently be revoked or modified.

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

Research and Development

We spent approximately $4.7 million and $2.9 million on research and development activities in the fiscal years ended December 31, 2008, and December 31, 2007, respectively.

Employees

As of Janaury 7, 2009, we had 24 full-time employees. We consider our relations with our employees to be good.

DESCRIPTION OF PROPERTY

We currently lease approximately 11,300 square feet of office space at 425 Metro Place North, Dublin, Ohio, as our principal offices. The current lease term is from June 1, 2007 and ending on January 31, 2013, at a monthly base rent of approximately $8,200 during 2009. We must also pay a pro-rata portion of the operating expenses and real estate taxes of the building. We believe these facilities are in good condition, but that we may need to expand our leased space related to our radiopharmaceutical activities depending on the level of activities performed internally versus by third parties.

MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion should be read together with our Financial Statements and the Notes related to those statements, as well as the other financial information included in this Registration Statement on Form S-1, of which this prospectus is a part. Some of our discussion is forward-looking and involves risks and uncertainties. For information regarding risk factors that could have a material adverse effect on our business, refer to the Risk Factors section of this prospectus beginning on page 5.

The Company

Neoprobe Corporation is a biomedical technology company that provides innovative surgical and diagnostic products that enhance patient care. We currently market two lines of medical devices; our **neoprobe GDS** gamma detection systems and the **Quantix** line of blood flow measurement devices of our subsidiary, Cardiosonix. In addition to our medical device products, we have two radiopharmaceutical products, **Lymphoseek** and **RIGScan®** CR, in advanced phases of clinical development. We are also exploring the development of our activated cellular therapy (ACT) technology for patient-specific disease treatment through our majority-owned subsidiary, Cira Biosciences, Inc. (Cira Bio).

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YEARS ENDED DECEMBER 31, 2007 AND 2006

Results of Operations

Revenue for 2007 increased to $7.1 million from $6.1 million in the prior year. The increase was primarily due to sales of our wireless probes which were initially launched in December 2006, offset by decreases in unit sales and pricing of our base gamma detection systems. In addition, sales of **Quantix** products in 2007 decreased by $253,000 compared to 2006.

Gross margins for 2007 decreased to 55% as compared to 57% in 2006. The decrease in gross margins on net product sales was primarily due to a combination of factors including lower margins on sales of demonstration units during 2007 as EES outfitted its entire U.S. sales force with both the angled and straight versions of the wireless probes, higher than expected production costs on our initial production runs of wireless probes, increased estimated warranty costs following the commercial launch of the wireless probe products which we consider normal for a new product, and a 1% price decline on base gamma detection systems sold by EES. Gross margins in 2007 and 2006 were also adversely affected by inventory impairments of $105,000 and $125,000, respectively, related to our **Quantix** products.

Results for 2007 also reflect a decrease in research and development expenditures of $938,000 to $2.9 million from $3.8 million in 2006. The decrease was primarily due to lower **Lymphoseek** development expenses resulting from the reduction in preclinical testing and drug development costs offset by the costs associated with our Phase 2 clinical trials. Research and development costs were further reduced by savings related to curtailing our activities associated with the blood flow measurement and decreasing activities related to gamma detection device lines after launching the wireless probes. Consolidated selling, general and administrative expenses decreased to $2.8 million in 2007 from $3.1 million in 2006.

Net Sales and Margins. Net sales, comprised primarily of our gamma detection systems, increased $1.1 million, or 18%, to $7.1 million in 2007 from $6.1 million in 2006. Gross margins on net sales decreased to 55% of net sales for 2007 compared to 57% of net sales for 2006.

The increase in net sales was the result of increased gamma detection device sales of $1.3 million and increased gamma detection device extended service contract revenue of $68,000, offset by decreases of $253,000 in blood flow measurement device sales and $9,000 in gamma detection device service-related revenue. Revenue from our new wireless probes more than offset declines in unit sales and pricing on our control units and corded probes. The price at which we sell our gamma detection products to EES is based on a percentage of the global average selling price received by EES on sales of Neoprobe products to end customers, subject to a minimum floor price. The base system price at which we sold **neo2000** systems to EES decreased approximately 1% during 2007 compared to 2006.

The decrease in gross margins on net product sales was primarily due to a combination of factors including lower margins on sales of wireless probe demonstration units during 2007, higher than expected production costs on our initial production runs of wireless probes, increased estimated warranty costs following the commercial launch of our new wireless probe products, and a minor price decline on control units and corded probes sold by EES. Gross margins in 2007 and 2006 were also adversely affected by inventory impairments of $105,000 and $125,000, respectively, related to our **Quantix** products.

Research and Development Expenses. Research and development expenses decreased $938,000 or 25% to $2.9 million during 2007 from $3.8 million in 2006. Research and development expenses in 2007 included approximately $1.8 million in drug and therapy product development costs, $680,000 in gamma detection device development costs and $359,000 in product design activities for the **Quantix** products. This compares to expenses of $2.1 million, $952,000 and $708,000 in these segment categories during 2006. The changes in each category were primarily due to (i) lower costs related to the Phase 2 **Lymphoseek** clinical activities in 2007 than the non-clinical expenses and trial preparation costs incurred in 2006, (ii) decreased product development activities related to our wireless gamma detection probes, and (iii) decreased product refinement activities related to the **Quantix/OR**, respectively.

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Selling, General and Administrative Expenses. Selling, general and administrative expenses decreased $239,000 or 8% to $2.8 million during 2007 from $3.1 million in 2006. The net difference was due primarily to decreases in marketing, facilities expenses, insurance, and other personnel-related expenses that were partially offset by increases in compensation and professional services.

Other Income (Expenses). Other expenses, net increased $2.0 million to $3.3 million during 2007 from $1.3 million in 2006. Interest expense related to the convertible debt agreements we completed in December 2004, July 2007 and December 2007 increased $788,000 to $2.3 million during 2007 from $1.5 million in 2006. Of this interest expense, $1.4 million and $809,000 in 2007 and 2006, respectively, was non-cash in nature related to the amortization of debt issuance costs and discounts resulting from the warrants and beneficial conversion features of the convertible debt. The increase in non-cash interest was primarily due to the impact of the acceleration of principal repayments on the effective interest method of calculating the discount amortization which the company adjusted during the third quarter of 2007. During the fourth quarter of 2007, we also recorded debt extinguishment charges of $860,000 related to modification of the terms of a convertible debt agreement with our CEO. In addition, we recorded a $248,000 increase in derivative liabilities resulting from the accounting treatment for the convertible note agreement we executed in December 2007 and the related warrants to purchase our common stock, which contained certain provisions that resulted in their being treated as derivative instruments. We recorded a decrease of $154,000 in interest income related to lower balances of cash and investments during 2007 compared to 2006.

Liquidity and Capital Resources

Cash balances decreased to $1.5 million at December 31, 2007 from $2.5 million at December 31, 2006. The net decrease primarily resulted from cash used to repay and service our outstanding debt, and to fund our operations, mainly for research and development activities, but was substantially offset by proceeds from new convertible notes and the issuance of common stock during 2007. The current ratio increased to 2.1:1 at December 31, 2007 from 1.6:1 at December 31, 2006. The increase in the current ratio was primarily due to the replacement of convertible debt instruments which had significant payments due within the next year by convertible debt with a longer term.

Operating Activities. Cash used in operations decreased $2.3 million to $1.3 million during 2007 compared to $3.6 million in 2006.

Accounts receivable increased to $1.6 million at December 31, 2007 from $1.2 million at December 31, 2006. The increase was primarily a result of normal fluctuations in timing of purchases and payments by EES, including a pronounced increase in sales of extended warranty contracts during the fourth quarter of 2007 and better than expected pricing related to our wireless probe as compared to the provisional price, offset by credits related to wireless probes sold to EES as demonstration units. We expect overall receivable levels will continue to fluctuate during 2008 depending on the timing of purchases and payments by EES.

Inventory levels remained steady at $1.2 million at December 31, 2007 and 2006. Gamma detection device materials decreased and work-in-process inventories decreased as we completed and sold the initial production runs of wireless probes, while finished device inventories increased due to normal fluctuations in timing of production runs and sales to EES. Blood flow measurement device materials and finished device inventories increased in anticipation of increased activity in the vascular assessment market. Drug materials decreased and work-in-process inventories increased as we completed the second commercial production run of **Lymphoseek**. We expect overall inventory levels to remain relatively steady during 2008.

Investing Activities. Investing activities used $48,000 during 2007 versus $1.4 million provided during 2006. We received $1.5 million from maturities of available-for-sale securities during 2006. Capital expenditures during 2007 and 2006 were primarily for production tools and equipment and software.

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Financing Activities. Cash provided by financing activities increased to $351,000 during 2007 from $240,000 used in 2006. Proceeds from the issuance of common stock were $1.9 million during 2007. Proceeds from the issuance of new notes payable were $8.0 million during the same period. Payments of notes payable were $8.3 million and $235,000 during 2007 and 2006, respectively. Payments of debt issuance costs were $565,000 during 2007. Payments for the repurchase of warrants related to debt extinguished in 2007 totaled $675,000.

THREE AND NINE MONTH PERIODS ENDED SEPTEMBER 30, 2008 AND 2007

Overview

This Overview section contains a number of forward-looking statements, all of which are based on current expectations. Actual results may differ materially. Our financial performance is highly dependent on our ability to continue to generate income and cash flow from our medical device product lines. We cannot assure you that we will achieve the volume of sales anticipated, or if achieved, that the margin on such sales will be adequate to produce positive operating cash flow.

We believe that the future prospects for Neoprobe continue to improve as we make progress in all of our key growth areas. We continue to expect revenue from our gamma device line to continue to provide a strong revenue base during 2008 and to exceed 2007. We also expect that sales of our blood flow measurement devices will be lower for 2008 than 2007 levels; however, due to the reduction in investment in this product line, the potential negative cash flow impact of the blood flow line on our ongoing business has been minimized. Our primary development efforts over the last few years have been focused on our oncology drug development initiatives; Lymphoseek and RIGScan CR. We continue to make progress with both initiatives; however, neither Lymphoseek nor RIGS are anticipated to generate any significant revenue for us during 2009.

Our operating expenses during 2008 were focused primarily on support of Lymphoseek product development. In addition, we continued to modestly invest in our gamma detection device line related to product line expansion and innovation. We expect our drug-related development expenses to increase significantly for 2008 over 2007 as we continue the multi-center Phase 3 clinical evaluations of Lymphoseek that were initiated during the second quarter of 2008 and support the other drug stability and production validation activities related to supporting the potential marketing registration of Lymphoseek. We expect to continue to incur modest development expenses to support our device product lines as well as we work with our marketing partners to expand our product offerings in the gamma device arena. During 2008, we significantly curtailed our financial support for our blood flow measurement products. We expect to continue to limit such expenditures in 2009.

Our efforts during 2008 resulted in the following research and development milestone achievements:

Obtained clearance from FDA to commence patient enrollment in a Phase 3 clinical study to evaluate the efficacy of Lymphoseek in patients with breast cancer or melanoma.

Submitted a protocol design for a second Phase 3 clinical study to evaluate the efficacy of Lymphoseek as a sentinel lymph node tracing agent in patients with head and neck squamous cell carcinoma.

Completed $6 million in investment from Montaur. The closing represents the second and third tranches received from Montaur bringing their investment to $13 million completing the commitment made in December of last year.

Initiated the formalized scientific advice review process for Lymphoseek in the European Union (EU).

Commenced a Phase 3 multi-center clinical trial for Lymphoseek in patients with breast cancer and melanoma.

Introduced the neoprobe GDS enhanced gamma detection system.

Introduced a wireless version of our laparoscopic gamma detection probe based on Bluetooth® technology.

Received a positive response on a regulatory pathway and a Phase 3 clinical trial design for RIGScan® CR with regulatory authorities in the EU under the scientific review process.

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In April 2008, we received clearance from FDA to commence patient enrollment in the first Lymphoseek Phase 3 study, which is being conducted in approximately 150 patients with either breast cancer or melanoma. The trial design is similar to the successfully conducted Phase 2 study, except that we will be monitoring the concordance of Lymphoseek uptake in lymph nodes with the uptake of vital blue dye in the same lymph nodes. We initiated the first of the Phase 3 study sites in June 2008. To-date, we have initiated a total of 12 sites and believe this trial will be done by or near the end of 2008.

In addition, we have provided FDA and the centralized European Medicinal Evaluation Agency (EMEA) with the full protocol and associated materials for a second Phase 3 study to be conducted in patients with head and neck squamous cell carcinoma. This second Phase 3 study is designed to validate Lymphoseek as a sentinel lymph node targeting agent. Our discussions with FDA and EMEA have also suggested that the Phase 3 trials will support an intended use of Lymphoseek in sentinel lymph node biopsy procedures. We believe such an indication would be beneficial to the marketing and commercial adoption of Lymphoseek in the U.S. and EU. 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 in the U.S. We expect the harmonization process to be concluded in the near future and for the study to be commenced shortly thereafter. We plan to have approximately 25 participating institutions in the trial, which we hope will enable us to enroll patients at a fairly rapid rate. We have commenced some of the preliminary activities to initiate the study after the appropriate regulatory clearances have been obtained. Our goal is to file the new drug application for Lymphoseek near the end of 2009; however, this will be dependent upon our ability to commence and successfully conclude the Phase 3 clinical studies in a timely fashion. Depending on the timing and outcome of the FDA regulatory review cycle, we believe that Lymphoseek may still be commercialized during 2010. We cannot assure you, however, that this product will achieve regulatory approval, or if approved, that it will achieve market acceptance.

Over the past few years, we have made progress in advancing our RIGScan CR development program while incurring minimal research expenses. Our RIGS technology, which had been essentially inactive since failing to gain approval following our original license application in 1997, has been the subject of renewed interest due primarily to the analysis of survival data related to patients who participated in the original Phase 3 clinical studies that were completed in 1996. Earlier in 2008, we initiated a scientific review of a Phase 3 trial design for RIGScan CR with the EMEA and completed a very positive pre-submission meeting in July 2008; we received their decision on the scientific review of the RIGScan clinical program in October 2008.

The scientific advice review process and the EMEA response yielded a number of positive outcomes. First, we were able to present and to have accepted a proposal for the reactivation of the manufacturing of the biologic used in RIGScan CR and the radiolabeling of the product. Second, EMEA indicated all of the safety data previously generated in the RIGScan clinical trials was accepted by opinion; further, the opinion indicated that the historical safety data coupled with any prospective data would be sufficient to establish the safety parameters for RIGScan CR. Thirdly, the scientific advice opinion agreed with our assessment that RIGScan CR could be assessed in a mixed population of primary and recurrent/metastatic colorectal patients. This resulted in a proposed trial design involving approximately 380 patients in total with equal control and RIGS treatment groups. This number of patients is significantly less than had been considered previously. 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. Finally, the advice opinion provided Neoprobe with the opportunity to seek a conditional marketing authorization (CMA) for RIGScan CR in the European Union at various points in the development process, although there can be no assurance that if such a request is submitted, it would receive a favorable response. CMA procedures were established by the EMEA in 2007 CMAs provide a time specific marketing authorization for a product treating a life-threatening illness while additional development work is being completed. A CMA is subject to annual review by the EMEA s governing body which ratified the RIGScan scientific advice.

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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. We believe the recent positive feedback from the EMEA adequately clarifies the regulatory pathway in a fashion that will allow us to re-approach parties that we have talked to in the past as well as potential new parties. The development timeline for RIGScan CR is highly dependent on securing adequate financial support to move the project forward in a timely fashion in order to satisfy potential development diligence requirements. However, even if we are able to make development partnership or funding arrangements on satisfactory terms, we believe it would take a minimum of 12 15 months following the restart of biologic production activities before a pivotal clinical trial could commence. Excluding the potential opportunity to seek a CMA, 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.

In early 2005, we formed a new subsidiary, Cira Bio, to raise the capital necessary to further 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 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 licenses to several pending patent applications covering oncology and viral disease applications of the ACT technology.

In August 2007 we entered into an option agreement whereby Neoprobe could purchase the remaining 10% interest in Cira Bio from Cira LLC for $250,000 in connection with the successful completion of a financing transaction by Cira Bio. In the first quarter of 2008, we also entered into discussions with an investment banking firm to help us gauge the interest of potential investment in the ACT technology. We still hope to raise funds through Cira Bio to support the continued development of ACT; however, our fundraising efforts have thus far not been successful and our option to purchase the remaining 10% interest in Cira Bio expired on June 30, 2008. If we are successful in identifying a funding source, we expect that any funding would likely be accomplished by an investment directly into Cira Bio, so that the funds raised would not dilute current Neoprobe shareholders. Obtaining this funding would likely dilute Neoprobe s ownership interest in Cira Bio; however, we believe that moving forward such a promising technology will only yield positive results for the Neoprobe stockholders and the patients who could benefit from these treatments. However, we do not know if we will be successful in obtaining 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.

We anticipate generating total revenues from our medical device businesses for 2008 of approximately $8 million. We expect that these sales levels will result in a net profit from the sale of our gamma detection devices in 2008, excluding the allocation of any corporate general and administrative costs. We expect to show a loss for our blood flow measurement device product line for 2008 due to ongoing development and marketing support that is required to expand market acceptance for the product line. However, we have limited our investment in the blood flow line significantly over the past year and believe, given some incremental amount of sales success, that we are not far from a breakeven point for the blood flow line. We will continue to monitor the state of market development and success for our blood flow measurement business and adjust our business plans accordingly. Our overall operating results for 2008 will also be greatly affected by the amount of development of our radiopharmaceutical products. If we are unsuccessful in achieving adequate commercial sales of the Quantix products, or if we modify our business plan, our medical device profitability estimates will be adversely affected and our business plan will likely need to be modified.

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Primarily as a result of the significant development costs we expect to incur related to the continued clinical development of Lymphoseek, we do not expect to achieve operating profit during 2008. In addition, our net loss and loss per share will likely be significantly impacted by the non-cash interest expense we expect to record due to the accounting treatment for the derivative liabilities related to the convertible debt we issued in December 2007 and the beneficial conversion feature and warrants related to the convertible debt we issued in April 2008. We cannot assure you that our current or potential new products will be successfully commercialized, that we will achieve significant product revenues, or that we will achieve or be able to sustain profitabilit