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Results of Lymphoseek® Phase 3 Clinical Trials in Breast Cancer Published in Annals of Surgical Oncology

- Lymphoseek Meets Primary Efficacy Endpoint in Assessment of Lymphatic Mapping Performance in Patients with Breast Cancer -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB), a biopharmaceutical company focused on the development and commercialization of precision diagnostic radiopharmaceuticals, today announced the peer-reviewed publication of results from two Phase 3 clinical trials of Lymphoseek® (technetium 99m tilmanocept) Injection in patients with breast cancer. The trials assessed the performance of Lymphoseek against the standard of care, vital blue dye (VBD), in lymphatic mapping. Results demonstrated that Lymphoseek met its primary efficacy endpoint of rate of agreement, or concordance, with VBD. The study, *"Comparative Evaluation of [^{99m}Tc]Tilmanocept for Sentinel Lymph Node Mapping in Breast Cancer Patients: Results of Two Phase 3 Trials,"* was published in the current online edition of the journal *Annals of Surgical Oncology* [DOI 10.1245/s10434-013-2887-8].

Lymphoseek is a receptor-targeted radiopharmaceutical recently approved by the U.S. Food and Drug Administration and indicated for use in lymphatic mapping for breast cancer and melanoma. In this procedure key lymph nodes adjacent to a primary tumor, that may contain tumor metastases, are identified and biopsied to determine if cancer has spread to these lymph nodes.

"Lymphoseek was specifically designed to provide clinicians who perform lymphatic mapping procedures with actionable information, and we believe that the data reported in this publication demonstrate its utility and safety in identifying tumor-draining lymph nodes," said Frederick Cope, Ph.D., Senior Vice President, Pharmaceutical Research and Clinical Development of Navidea. "These data from breast cancer patients, in conjunction with previously published data from our Phase 3 clinical trials in melanoma, comprise part of our NDA registration package for Lymphoseek with the FDA. We are confident that Lymphoseek may hold significant improvement for patients who undergo lymphatic mapping procedures."

"Tilmanocept was originally developed at UCSD as a targeted molecular approach to help stage breast cancer and melanoma patients, and we advanced the agent through Phase 1 clinical trials with funding provided by Susan G. Komen Breast Cancer Foundation and the American Cancer Society," said Anne Wallace, M.D., Chief, Division of Plastic Surgery; Professor of Surgery, UC San Diego School of Medicine; Director of the Breast Care Unit; UC San Diego Moores Cancer Center; and a Principal Investigator in the Lymphoseek Phase 3 clinical trials. "The results from these Phase 3 clinical trials in breast cancer demonstrate the potential that specifically-designed imaging agents may have an important

role in reliably localizing tumor-draining lymph nodes and in optimizing patient management post-surgery. Appropriate lymphatic mapping and sentinel node biopsy can benefit certain patients by sparing them removal of unnecessary lymphoid tissue and preventing side effects such as lymphedema or swelling, pain and sensory changes, scarring or disfigurement, and extended recovery times."

Completed Lymphoseek Phase 3 Clinical Trials in Breast Cancer

Two Phase 3 non-randomized trials were conducted in patients with breast cancer undergoing lymphatic mapping. The primary endpoint was the rate of agreement (concordance) between [^{99m}Tc]tilmanocept and vital blue dye, which was defined as the proportion of lymph nodes identified by VBD that were also identified by Lymphoseek. A pre-specified minimum rate of agreement of 90% had been established in the trials' statistical plan. In the trials, a total of 148 patients with breast cancer from 13 centers received [^{99m}Tc]tilmanocept followed by vital blue dye and then underwent sentinel lymph node mapping. Lymph nodes that demonstrated [^{99m}Tc]tilmanocept uptake and/or the presence of blue dye were removed and examined for the presence of tumor. Of the 209 blue-dyed lymph nodes removed from the patients, 207 (99.04%) demonstrated [^{99m}Tc]tilmanocept uptake ($p<0.0001$).

In assessing reverse concordance (the proportion of blue-dyed nodes relative to all nodes with [^{99m}Tc]tilmanocept uptake) according to the protocol, Lymphoseek detected 320 lymph nodes. Of these nodes, VBD detected 207 (64.69%).

Lymph node identification

The performance of [^{99m}Tc]tilmanocept in intraoperative lymph node identification was also assessed. Of the patients injected with both [^{99m}Tc]tilmanocept and vital blue dye who underwent surgical removal of the lymph nodes, 146 patients had at least one radioactive node, due to [^{99m}Tc]tilmanocept uptake, and 131 patients had at least one blue node. This difference was statistically significant ($p<0.0001$).

Pathology

Of 33 pathology-positive lymph nodes (18.2% patient pathology rate), [^{99m}Tc]tilmanocept detected 31 of 33 positive lymph nodes found in the patients. Blue dye detected 25 of the 33 positive lymph nodes, but no positive lymph nodes were detected exclusively by vital blue dye.

Safety

[^{99m}Tc]tilmanocept was well tolerated in the trials, with no serious adverse reactions ascribed to the radiopharmaceutical.

About Lymphoseek®

Indication and Important Safety Information About Lymphoseek

Indication

Lymphoseek (technetium Tc 99m tilmanocept) Injection is indicated for lymphatic mapping with a hand-held gamma counter to assist in the localization of lymph nodes draining a primary tumor site in patients with breast cancer or melanoma.

Important Safety Information

In clinical trials with Lymphoseek, no serious hypersensitivity reactions were reported, however Lymphoseek may pose a risk of such reactions due to its chemical similarity to dextran. Serious hypersensitivity reactions have been associated with dextran and modified forms of dextran (such as iron dextran drugs).

Prior to the administration of Lymphoseek, patients should be asked about previous hypersensitivity reactions to drugs, in particular dextran and modified forms of dextran. Resuscitation equipment and trained personnel should be available at the time of Lymphoseek administration, and patients observed for signs or symptoms of hypersensitivity following injection.

The most common adverse reactions are injection site irritation and/or pain (<1%).

FULL LYMPHOSEEK PRESCRIBING INFORMATION CAN BE FOUND AT: WWW.LYMPHOSEEK.COM

Lymphoseek® (technetium Tc 99m tilmanocept) Injection is a novel, receptor-targeted, small-molecule radiopharmaceutical used in lymphatic mapping procedures that are performed to help stage breast cancer and melanoma. Lymphoseek is designed to identify the lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer, in patients with breast cancer or melanoma. Lymphoseek was approved for use by the U.S. Food and Drug Administration in March, 2013.

Lymphatic mapping is a procedure in which lymph nodes that may contain tumor metastases are identified and biopsied to determine if cancer has spread beyond the primary tumor. Accurate staging of cancer is critical, as it guides therapy decisions and determines patient prognosis and risk of recurrence. According to the American Cancer Society, approximately 232,000 new cases of breast cancer and 77,000 new cases of melanoma are expected to be diagnosed in the United States in 2013.[1]

About Lymphatic Mapping

Lymphatic mapping is a procedure designed to guide lymph node dissection and biopsy procedures. It consists of Intraoperative Lymphatic Mapping (ILM) often accompanied by lymphoscintigraphy. Lymphoscintigraphy is an imaging procedure routinely performed pre-operatively to provide guidance on the location of lymph nodes to be biopsied. ILM is a surgical procedure in which lymph nodes draining the area around a tumor are identified and biopsied to determine if cancer has spread to the lymph nodes. These nodes, medically referred to as “Sentinel Lymph Nodes,” are removed and analyzed for the presence of malignant cells. Lymphatic Mapping provides an accurate staging procedure that can help ensure optimal surgical and therapeutic choices, including the avoidance of the morbidity of a complete lymph node dissection for patients in whom the Sentinel Lymph Nodes were found to be free of cancer.

About Navidea Biopharmaceuticals, Inc.

Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB) is a biopharmaceutical company focused on the development and commercialization of precision diagnostics and radiopharmaceutical agents. Navidea is actively developing four radiopharmaceutical agent platforms – Lymphoseek®, NAV4694, NAV5001 and RIGScan™ – to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making and, ultimately, patient care. Navidea's strategy is to deliver superior growth and shareholder return by bringing to market novel radiopharmaceutical agents and advancing the Company's pipeline through selective acquisitions, global partnering and commercialization efforts. For more information, please visit www.navidea.com.

The Private Securities Litigation Reform Act of 1995 (the Act) provides a safe harbor for forward-looking statements made by or on behalf of the Company. Statements in this news release, which relate to other than strictly historical facts, such as statements about the Company's plans and strategies, expectations for future financial performance, new and existing products and technologies, anticipated clinical and regulatory pathways, and markets for the Company's products are forward-looking statements within the meaning of the Act. The words "believe," "expect," "anticipate," "estimate," "project," and similar expressions identify forward-looking statements that speak only as of the date hereof. Investors are cautioned that such statements involve risks and uncertainties that could cause actual results to differ materially from historical or anticipated results due to many factors, including, but not limited to, the Company's continuing operating losses, uncertainty of market acceptance of its products, reliance on third-party manufacturers, accumulated deficit, future capital needs, uncertainty of capital funding, dependence on limited product line and distribution channels, competition, limited marketing and manufacturing experience, risks of development of new products, regulatory risks and other risks detailed in the Company's most recent Annual Report on Form 10-K and other Securities and Exchange Commission filings. The Company undertakes no obligation to publicly update or revise any forward-looking statements.

[1] ***Source:*** ACS Cancer Facts & Figures, 2013

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