January 29, 2015

Lymphoseek® Performance vs. Sulfur Colloid in Breast Cancer Patients Published in Annals of Surgical Oncology; Fewer Nodal Dissections Required

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB) today announced that an analysis comparing sentinel lymph node (SLN) biopsy procedures using Lymphoseek® (technetium Tc 99m tilmanocept) injection (TcTM) + vital blue dye (VDB) to filtered [^{99m}Tc] sulfur colloid (fTcSC) + VBD in breast cancer patients was published in the *Annals of Surgical Oncology*. Results demonstrated the following:

- Lymphoseek patients had significantly fewer SLNs removed per procedure (mean TcTM: 1.85 vs. fTcSC: 3.24, $p < 0.0001$)
- Proportionally fewer nodes were necessary to detect cancer spread; and
- Nodes removed using Lymphoseek held greater predictive value for diagnosing spread of breast cancer to lymph nodes.

The study, *"Comparison of [^{99m}Tc]Tilmanocept and Filtered [^{99m}Tc]Sulfur Colloid for Identification of SLNs in Breast Cancer Patients,"* authored by Anne Wallace, M.D., *et. al.,* at the UC San Diego School of Medicine was published in the January print issue of the journal, *Annals of Surgical Oncology* [DOI 10.1245/s10434-014-3892-2.]

"We recommend sentinel node biopsy for patients with early stage breast cancer and in select cases of ductal carcinoma in situ," said Anne Wallace, M.D., Professor of Surgery, UC San Diego School of Medicine; Director of the Comprehensive Breast Health Center; UC San Diego Moores Cancer Center, primary author of this study. "The results of this comparative analysis in breast cancer patients demonstrate that specific, receptor-targeted imaging agents may play an important role in improved targeting of clinically relevant nodes, excision of fewer tumor-draining lymph nodes and in optimizing patient management post-surgery. Appropriate sentinel node biopsy may benefit breast cancer 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."

Lymphoseek is a receptor-targeted imaging agent that was approved by the U.S. Food and Drug Administration (FDA) for guiding sentinel lymph node biopsy in patients with clinically node negative breast cancer, melanoma and certain oral cancers as well as for lymphatic mapping in patients with solid tumors for which this procedure is a component of intraoperative management. In these procedures, 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.

“Surgical staging of regional lymph nodes with intraoperative lymphatic mapping and sentinel node biopsy has emerged as the worldwide standard of care for patients with many types of cancer,” commented Michael Tomblyn M.D., M.S., Navidea’s Executive Medical Director. “This study further supports previous findings and reinforces our belief in the clinical benefit that Lymphoseek may provide patients and clinicians. As this analysis indicates, it appears that Lymphoseek produces better targeting of primary SLNs resulting in removal of fewer SLNs. The significantly lower proportion of patients with ‘4 or more SLNs removed’ with Lymphoseek versus fTcSC (4% vs. 33%) could result in reduced morbidity for breast cancer patients. Based on the strong signal from this retrospective analysis, we are excited about the current prospective, randomized, investigator-initiated studies that we expect will confirm these promising data.”

About Lymphoseek

Lymphoseek® (technetium Tc 99m tilmanocept) injection is the first and only FDA-approved receptor-targeted lymphatic mapping agent. It is a novel, receptor-targeted, small-molecule radiopharmaceutical used in the evaluation of lymphatic basins that may have cancer involvement in patients. Lymphoseek is designed for the precise identification of lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. Lymphoseek is approved by the U.S. Food and Drug Administration (FDA) for use in solid tumor cancers where lymphatic mapping is a component of surgical management and for guiding sentinel lymph node biopsy in patients with clinically node negative breast cancer, melanoma or squamous cell carcinoma of the oral cavity. Lymphoseek has also received European approval in imaging and intraoperative detection of sentinel lymph nodes in patients with melanoma, breast cancer or localized squamous cell carcinoma of the oral cavity.

Accurate diagnostic evaluation of cancer is critical, as it guides therapy decisions and determines patient prognosis and risk of recurrence. Overall in the U.S., solid tumor cancers may represent up to 1.2 million cases per year. The sentinel node label in the U.S. and Europe may address approximately 235,000 new cases of breast cancer, 76,000 new cases of melanoma and 45,000 new cases of head and neck/oral cancer in the U.S., and approximately 367,000 new cases of breast cancer, 83,000 new cases of melanoma and 55,000 new cases of head and neck/oral cancer diagnosed in Europe annually.

Lymphoseek Indication and Important Safety Information

Lymphoseek is a radioactive diagnostic agent indicated with or without scintigraphic imaging for:

- Lymphatic mapping using a handheld gamma counter to locate lymph nodes draining a primary tumor site in patients with solid tumors for which this procedure is a component of intraoperative management.
- Guiding sentinel lymph node biopsy using a handheld gamma counter in patients with clinically node negative squamous cell carcinoma of the oral cavity, 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.

Any radiation-emitting product may increase the risk for cancer. Adhere to dose recommendations and ensure safe handling to minimize the risk for excessive radiation exposure to patients or health care workers.

In clinical trials, no patients experienced serious adverse reactions and the most common adverse reactions were injection site irritation and/or pain (<1%).

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

About Navidea Biopharmaceuticals Inc.

Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB) is a biopharmaceutical company focused on the development and commercialization of precision diagnostics, therapeutics and radiopharmaceutical agents. Navidea is developing multiple precision-targeted products and platforms including Manocept™, NAV4694, and NAV5001, to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making, targeted treatment and, ultimately, patient care. Lymphoseek® (technetium Tc 99m tilmanocept) injection, Navidea's first commercial product from the Manocept platform, was approved by the FDA in March 2013 and by the EMA in November 2014. 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.

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Source: Navidea Biopharmaceuticals, Inc.