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Navidea Biopharmaceuticals' Lymphoseek® (technetium Tc 99m tilmanocept) Injection Demonstrates Preferential Accumulation in Tumor-Positive Sentinel Lymph Nodes in Post-Hoc Analysis

- Ability of receptor-targeted Lymphoseek to accurately target appropriate lymph nodes may lessen patient morbidity from extensive oral cavity surgery -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB), a biopharmaceutical company focused on precision diagnostic radiopharmaceuticals, today announced results from a post-hoc analysis of patient data from the Company's Phase 3 clinical trial (NEO3-06) of Lymphoseek in head and neck cancer. The ability of Lymphoseek to localize in sentinel lymph nodes is based on its ability to target specific CD206 mannose receptor sites in macrophages, a type of immune cell which resides in high concentration in lymph nodes. In the NEO3-06 Phase 3 study, Lymphoseek localization to lymph nodes showed a strong correlation with a full regional lymph node dissection and pathology analysis with a low false negative rate, a priority in identifying sentinel nodes. Lymphoseek was also observed to home preferentially to pathology-positive nodes at a higher rate than pathology-negative nodes. These results suggest that Lymphoseek not only effectively targets sentinel lymph nodes, but further that its ability to highlight tumor-positive lymph nodes may be augmented mechanistically by the recruitment of macrophages to cancer-harboring lymph nodes.

"The accurate detection of tumor-draining lymph nodes is fundamental for effective lymphatic mapping, to minimize lymph tissue removal, and to provide clinically useful information regarding potential cancer metastasis," said Francisco J. Civantos, M.D., FCS, University of Miami School of Medicine, Miami, Fla. "Approximately 75% of patients with stage 1 and 2 oral cavity head and neck cancer may be substantially over-treated if they are subjected to elective neck dissection, which involves surgical removal of a regional lymph node chain involving 30 to 45 lymph nodes. Receptor-targeted radiopharmaceuticals such as Lymphoseek, that are designed to facilitate accurate and reliable diagnostic evaluation of specific sentinel lymph nodes, can help spare patients morbidity that may result from elective neck dissection procedures."

"As a purpose-built, receptor-targeted radiopharmaceutical, Lymphoseek is designed to target and accumulate in macrophages present in tumor-draining lymphatic tissue," said Frederick Cope, Ph.D., Senior Vice President and Chief Scientific Officer of Navidea.

“Tumor-positive lymph nodes recruit cells called Tumor-Associated Macrophages, or TAM’s, which are rich in CD206 receptors. The ability of Lymphoseek to specifically target and accumulate in macrophages demonstrated in this study led to localization of the product in tumor-draining pathology-positive lymph nodes that was 18 times higher than in all disease-negative lymph nodes. In the clinic, this reliable uptake of Lymphoseek into appropriate tissue allows for accurate removal and assessment of lymph nodes at highest risk of harboring occult metastases.”

The analysis, based on data from the Phase 3 clinical trial for Lymphoseek in head and neck cancer (NEO3-06), evaluated 83 patients to determine whether Lymphoseek localization in pathology-positive lymph nodes was higher than its localization in pathology-negative nodes, and if those results were consistent with the overall sentinel lymph node population. Sentinel lymph nodes and/or non-sentinel lymph nodes (nodes removed in elective neck dissection, or END) were removed from patients undergoing sentinel lymph node biopsy for head and neck squamous cell carcinoma, and all lymph nodes were assessed for the presence of tumor. Intraoperative counts were obtained for all lymph nodes removed including END nodes. Average in vivo gamma counts for all lymph nodes removed indicated that the count ratio of pathology-positive nodes to pathology negative nodes was approximately 18:1 ($p<0.0001$). For sentinel lymph nodes only, the ratio was >2.5:1 ($p<0.016$). The results were presented in an oral session by Frederick Cope of Navidea Biopharmaceuticals, at the 2014 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in St. Louis, Mo.

About the Lymphoseek Phase 3 Clinical Trial (NEO3-06) in Head and Neck Cancer (Oral Cavity)

Navidea’s Phase 3 clinical trial (NEO3-06) of Lymphoseek was a prospective, open-label, multicenter, within-patient study of Lymphoseek® (technetium Tc 99m tilmanocept) Injection. It was designed to identify sentinel lymph nodes (SLNs) and determine the false negative rate (FNR) associated with Lymphoseek-identified SLNs relative to the pathological status of non-SLNs in head and neck and intraoral squamous cell carcinoma, which is the current “gold standard.” The findings indicate that Lymphoseek accurately identified SLNs in the trial subjects for assessment, and that it is likely to be predictive of overall node pathology status. Moreover, multiple level nodal dissections of patients in the trial with cancer-positive lymph nodes led to an average removal of 38 lymph nodes per patient, whereas Lymphoseek on average would have led to the removal of approximately 4 lymph nodes, representing a substantial reduction in potential morbidity for patients with head and neck cancer undergoing sentinel lymph node biopsy.

About Lymphoseek®

Lymphoseek® (technetium Tc 99m tilmanocept) Injection is a novel, receptor-targeted, small-molecule radiopharmaceutical used in lymphatic mapping procedures that are performed to help in the diagnostic evaluation of potential cancer spread for patients with 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. Lymphoseek was approved by the U.S. Food and Drug Administration (FDA) in March, 2013 for use in lymphatic mapping to assist in the localization of lymph nodes draining a primary tumor in patients with breast cancer or melanoma. The Company anticipates continuing

development of Lymphoseek into other solid tumor areas that may include other head and neck cancers such as thyroid cancer, prostate cancer and cancers of the female reproductive system (e.g., cervix, endometrial and vulva cancer). Lymphoseek was granted Fast Track and Priority Review designation for its sNDA for sentinel lymph node detection in patients with head and neck cancer and is currently in review with the FDA.

Accurate diagnostic evaluation of cancer is critical, as it guides therapy decisions and determines patient prognosis and risk of recurrence. According to publicly available information, approximately 235,000 new cases of breast cancer, 76,000 new cases of melanoma and 69,500 new cases of head and neck/oral cancer are expected to be diagnosed in the United States in 2014, and approximately 367,000 new cases of breast cancer, 83,000 new cases of melanoma and 137,000 new cases of head and neck/oral cancer diagnosed in Europe annually.

U.S. Indication and Important Safety Information About Lymphoseek

Indication

Lymphoseek (technetium Tc 99m tilmanocept) Injection is a lymphatic mapping agent indicated for use 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

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 developing multiple precision diagnostic products and platforms, including NAV4694, NAV5001, Manocept™ and NAV1800 (RIGScan™), to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making 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. 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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