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Navidea Biopharmaceuticals Enrolls First Patient in Cervical Cancer Study of Lymphoseek®

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB), today announced that the first patient has been enrolled in a clinical study evaluating Lymphoseek® (technetium Tc 99m tilmanocept) injection in women with known cervical cancer. The study, funded by a Fast-track grant from the National Institutes of Health (NIH), National Cancer Institute (NCI; 1R44CA180390-01) will assess the use of Lymphoseek in sentinel lymph node biopsy (SLNB) during cervical cancer surgery in support of the existing Lymphoseek label in lymphatic mapping. Lymphoseek is designed for the precise identification of lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. Enrollment is currently planned in up to six sites throughout the U.S. The first patient has been enrolled by the principal investigator, Michael M. Frumovitz, M.D., M.P.H., Associate Professor, Department of Gynecologic Oncology and Reproductive Medicine, at The University of Texas MD Anderson Cancer Center.

“This important study could potentially advance the use of SLNB procedures in cervical cancer. Clinical experience and published results using Lymphoseek in other cancer types demonstrate that imaging using Lymphoseek may enable detection of suspicious nodes not previously possible,” said Frederick Cope, Ph.D., M.S., F.A.C.N., C.N.S., Senior Vice President and Chief Scientific Officer of Navidea. “Improving current practice in lymph node mapping and sentinel node detection in cervical cancer surgery may lead to less extensive, more focused surgical procedures. More reliable bilateral SLN identification may decrease the cost and morbidity of complete lymph node dissection in women with early stage cervical cancer.”

“There is currently a growing focus on sentinel lymph node biopsy (SLNB) procedures in gynecologic cancers. Lymphoseek has been safely and efficaciously used in SLNB and mapping procedures in over 50,000 patients to date,” said Rick Gonzalez, President and Chief Executive Officer of Navidea. “With Lymphoseek’s immunodiagnostic properties of selective receptor targeting and improved patient experience, we believe that this study and others like it may accelerate the adoption of lymphatic mapping and SLNB using Lymphoseek in cervical cancer and other solid tumor areas with the intent of improving patient outcomes and reducing post-surgical morbidities in patients undergoing these procedures.”

This multi-center, prospective, open-label study is designed to evaluate Lymphoseek® in patients with known cancer of the cervix. The trial intends to enroll up to 40 women with International Federation of Gynecology and Obstetrics (FIGO) IA2-IIA1 staging. Subjects will receive a single dose of Tc99m tilmanocept administered peritumorally approximately 1-2 hours before surgery. The results will report per-patient false negative rates and compare

the pathology status of Lymphoseek-identified sentinel lymph nodes relative to the pathology status of non-sentinel lymph nodes in nodal staging of patients. Additionally, the study will report sensitivity, negative predictive value, and accuracy. Concordance and reverse concordance of identified nodes will be reported for the cases that use both Lymphoseek and a dye. Information on the protocol for this study (NAV3-19) can be found at: https://www.clinicaltrials.gov/ct2/show/NCT02509585?term=lymphoseek&rank=5.

About Cervical Cancer

Cervical cancer is usually a slow-growing cancer that affects ~12,000 new patients each year in the U.S. Worldwide, the World Health Organization notes that cervical cancer is both the fourth most common cause of cancer and the fourth most common cause of death from cancer in women. Globally in 2012, it was estimated that there were 528,000 new cases of cervical cancer, and 266,000 deaths.

About Sentinel Lymph Node Biopsy[1]

A sentinel lymph node is defined as the first lymph node to which cancer cells are most likely to spread from a primary tumor. Sometimes, there can be more than one sentinel lymph node. A sentinel lymph node biopsy (SLNB) is a procedure in which the sentinel lymph node is identified using an imaging agent such as Lymphoseek, removed, and examined to determine whether cancer cells are present. A negative SLNB result suggests that cancer has not developed the ability to spread to nearby lymph nodes or other organs. A positive SLNB result indicates that cancer is present in the sentinel lymph node and may be present in other nearby lymph nodes or organs. This information helps a doctor determine the stage of the cancer and develop an appropriate treatment plan. SLNB may also help some patients avoid more extensive lymph node surgery and post-surgical complications such as lymphedema, or tissue swelling. SLNB is most commonly used to help stage breast cancer, melanoma and head and neck cancers. SLNB is also being evaluated along with lymphatic mapping in other cancer types, including cervical, endometrial, anal, colorectal, gastric, esophageal, thyroid, and non-small cell lung cancer.

Source: [1]National Cancer Institute. http://www.cancer.gov/about-cancer/diagnosis-staging/staging/sentinel-node-biopsy-fact-sheet#q3; *accessed February 10, 2016.*

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 results guide therapy decisions and determine 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 600,000 new cases of breast cancer, 160,000 new cases of melanoma and 100,000 new cases of head and neck/oral cancer diagnosed 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

Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB) is a biopharmaceutical company focused on the development and commercialization of precision immunodiagnostic agents and immunotherapeutics. Navidea is developing multiple precision-targeted products and platforms including Manocept™ and NAV4694 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 in Europe in November 2014. Navidea's strategy is to deliver superior growth and shareholder return by bringing to market novel products and advancing the Company's pipeline through 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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