July 23, 2015

Verification of Lymphoseek® Mechanism of Action Published in Journal of Immunology

– Direct evidence demonstrates that CD206 is major binding receptor for tilmanocept -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB), today announced the peer-reviewed publication of data verifying the Lymphoseek® (technetium Tc 99m tilmanocept) injection CD206-binding mechanism of action in the *Journal of Immunology*. Strong evidence-based studies demonstrate macrophages are the major target cell and identify CD206, the mannose receptor, as the tilmanocept-binding receptor. CD206 is highly expressed on the surface of tissue macrophages that are known to reside in the sentinel lymph nodes (SLN) draining a primary tumor. Lymphoseek was specifically designed to provide clinicians with a tool to reliably and accurately locate the SLNs which have the highest likelihood of containing metastasized cancer cells and to aid effective cancer staging and inform post-surgical treatment.

"In our studies, we provide evidence that tilmanocept is the first receptor-targeted cancer prognostic agent which is bound by the mannose receptor as well as evidence of the potential mechanism underlying the utility of tilmanocept. In particular we demonstrate the specificity of binding, the tightness of binding and the strong correlation of tilmanocept-binding to macrophages found in sentinel lymph node tissue," said Larry S. Schlesinger M.D. with the Center for Microbial Interface Biology, Department of Microbial Infection and Immunity at The Ohio State University Wexner Medical Center and PI of the study. “In practice this means the molecular nature of tilmanocept allows it to rapidly enter into lymphatic channels, localize in tumor-draining lymph nodes and bind to target receptor(s) for longer retention in these SLNs giving it the required characteristics for a potentially ideal agent for SLN mapping.”

“This publication highlights data from rather elegant experiments which confirm our belief that tilmanocept binds primarily to macrophages found in the sentinel lymph nodes of cancer patients and demonstrating its utility in identifying these SLNs,” said Frederick O. Cope, Ph.D. FACN, Navidea’s Chief Scientific Officer. “These results provide Lymphoseek with a clear clinical differentiation from other non-targeted procedures and enable additional opportunities for designing receptor-targeted, advanced imaging agents and future potential for the delivery of therapeutics for cancer and other macrophage-dependent diseases.”

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 squamous cell carcinoma of the oral cavity 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.

Summary of Results

A series of studies examined the receptor(s) for tilmanocept. Using complementary approaches including competitive binding, siRNA, Sentinel Lymph Node histochemistry and flow cytometry, the data show that tilmanocept binds predominantly to human macrophages and that the mannose receptor (CD206) is the major receptor for its recognition. The authors conclude that this provides evidence for a potential mechanism underlying the utility of tilmanocept as a sensitive detector of lymph nodes that have the highest likelihood of containing cancer cells if metastasis has occurred. For complete details of the studies, findings and results, "γ-Tilmanocept, a New Radiopharmaceutical Tracer for Cancer Sentinel Lymph Nodes, Binds to the Mannose Receptor (CD206)" is published as an online article in the Journal of Immunology's "Next in the JI". *(J Immunol 140200; published ahead of print July 22, 2015, doi:10.4049/jimmunol.14020050)*

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

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™ 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 radiopharmaceutical agents and therapeutics, 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.

View source version on businesswire.com:
http://www.businesswire.com/news/home/20150723005761/en/

Navidea Biopharmaceuticals
Tom Baker, 617-532-0624
tbaker@navidea.com
or
Sharon Correia, 978-655-2686
Associate Director, Corporate Communications

Source: Navidea Biopharmaceuticals, Inc.