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Navidea Announces Data Demonstrating Potential of Manocept™ Platform to Diagnose Rheumatoid Arthritis and Kaposi's Sarcoma

– Data from three proof-of-concept studies reported at the Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) –

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAV), a biopharmaceutical company focused on precision diagnostic radiopharmaceuticals, today announced results from three research studies performed with collaborators that demonstrate the potential for the Company's Manocept™ platform imaging agents to diagnose and stage rheumatoid arthritis (RA) and Kaposi's Sarcoma (KS). The data were presented by scientific collaborators at the 2014 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in St. Louis, MO.

"These data reinforce the potential for our macrophage-targeting Manocept platform, from which our FDA-approved product Lymphoseek® (technetium 99m tilmanocept) Injection is derived, to significantly expand our commercial opportunities by addressing immuno-inflammatory disorders," commented Frederick Cope, Ph.D., Senior Vice President and Chief Scientific Officer of Navidea. "The core mechanism of the Manocept platform is its ability to bind to the mannose receptor (CD206), enabling Manocept-derived molecules to uniquely seek out, identify and accumulate in macrophages, which are an emerging marker of disease-associated inflammation. By targeting macrophages, Manocept-derived agents represent a potentially powerful approach to helping physicians diagnose, treat and monitor patients with inflammation-based disorders such as RA and KS."

Experimental Preclinical Results

The results of two studies conducted at The Ohio State University Wexner Medical Center indicated that CD206-targeted imaging agents based on the Manocept platform show strong potential as *in vivo* imaging agents to detect immune-mediated inflammation with possible use in early diagnosis and monitoring of therapeutic efficacy in RA. Wael Jarjour, M.D., Associate Professor and Director, Division of Rheumatology & Immunology, presented data using the CD206-targeted fluorescent imaging agent *Cy3-tilmanocept*, demonstrating that archival synovial tissue and synovial fluid obtained from patients diagnosed with RA contain a significant population of macrophages that express high-levels of the CD206 receptor. It was shown that these macrophages strongly co-localize *Cy3-tilmanocept* and CD206 receptors. The degree of macrophage infiltration in tissue from healthy or osteoarthritic patients was significantly lower than in RA tissues.

Thomas Rosol, D.V.M., Ph.D., Professor, Department of Veterinary Biosciences, presented data evaluating intravenous administration of *Cy3-tilmanocept* in mice with induced RA to determine joint localization and specificity. *Cy3-tilmanocept* was demonstrated to preferentially localize to macrophages in affected joints with little to no localization in unaffected joints.

Results from studies at University of California San Francisco in Kaposi's Sarcoma confirmed findings in a previous macrophage expression study that Manocept-based agents represent an opportunity for dynamic imaging, local staging and a potential ability to detect and monitor for visceral KS metastasis. Michael S. McGrath, M.D., Ph.D., Professor, Departments of Laboratory Medicine, Pathology, and Medicine presented data compiled from 66 KS cases and controls which validate previous research observations that both tumor associated macrophages (TAMs) and KS tumor cells express CD206 mannose receptors. Immuno-histochemistry analysis of the KS samples showed that expression of CD206 macrophage antigens, found to be the most prevalent for both KS tumor spindle cells and TAMs, was similar across all tissue forms of KS including plaque, oral and visceral.

The poster presentations can be found on the Navidea website in the [Publications](http://www.navidea.com/development-programs/publications/bibliography.html) (<http://www.navidea.com/development-programs/publications/bibliography.html>) section:

- *"Fluorescent CD206-targeted Manocept-Cy3 (Mano-Cy3) specifically localizes on macrophages (MPs) derived from rheumatoid arthritis (RA) patients' synovial fluid & is quantitatively greater than that from non-RA patients";*
- *"Intravenous administration (IV) of the CD206-targeted Manocept-Cy3 (Mano-Cy3) to mice with induced rheumatoid arthritis (RA) results in heterogeneous localization of Mano-Cy3 with strong specificity for RA-expressing joints"; and*
- *"CD206-targeted Cy3-Manocept (Mano-Cy3) localizes in nearly all cells present in Kaposi's sarcoma representing an opportunity for dynamic imaging, local staging and a potential for visceral metastasis imaging"*

About the Manocept™ Platform

Navidea's Manocept platform is predicated on the ability to specifically target the CD206 mannose receptor expressed on macrophages. Macrophages play important roles in many disease states and are an emerging target in many disorders where diagnostic uncertainty exists. This flexible and versatile platform acts as an engine for purpose-built molecules that may enhance diagnostic accuracy, clinical decision-making and ultimately patient care, while offering the potential to utilize a breadth of diagnostic imaging modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection. The Company's FDA-approved precision diagnostic lymphatic mapping agent, Lymphoseek® (technetium 99m tilmanocept) Injection, is representative of the ability to successfully exploit this mechanism to develop powerful, new diagnostic agents.

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 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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