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Immunotherapeutic Potential of Manocept™ Platform Reviewed in the Journal Nuclear Medicine and Biology

– Potential of Navidea's Manocept Platform to Therapeutically Target Disease Validated by Lymphoseek® –

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB), announced a publication in Nuclear Medicine and Biology, the official journal of the Society of Radiopharmaceutical Sciences, which describes the clinical linkage between immunodiagnostic and immunotherapeutic agents. This process is exemplified by the self-transforming nature of Navidea's Manocept™ immunotargeting platform which provides high specificity against receptor-bearing targets and is a promising approach to immunotherapy.

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The first product of the Manocept platform, Lymphoseek® (technetium Tc 99m tilmanocept) injection was launched as a novel immunodiagnostic agent approved by the FDA and used in breast, melanoma and oral cavity cancer sentinel lymph node biopsy (SLNB) procedures. Lymphoseek has demonstrated its effectiveness through many evidence-based studies in SLNB, due to its unique structure and targeting of CD206 found on macrophages in tumor-draining lymph nodes. Its Manocept backbone, enabled by the ability to interchange radionuclides for biological modifier molecules, has the potential to target macrophage-mediated diseases and deliver an effective, specifically targeted drug for purposes of disease treatment and reducing or eliminating side effects.

"Past therapeutic strategies attempting to harness the power of the immune system to manage, treat or kill macrophages in disease states like cancer and inflammatory conditions have had limited to no success," said Michael S. McGrath, M.D., Ph.D., Professor, Departments of Laboratory Medicine, Pathology, and Medicine at the University of California, San Francisco (UCSF). "The Manocept platform possesses a unique potential to not only target aberrant macrophages for detection or treatment but also shields non-affected cells, which could profoundly address broad unmet needs for patients both diagnostically and therapeutically."

"These newly published results highlight the remarkable specificity and sensitivity of the Manocept platform, and its plasticity which allow it to exploit the natural history of macrophage-mediated diseases," said Frederick O. Cope, Ph.D., M.S., FACN, Navidea's Chief Scientific Officer. "It is rare to find a platform that selectively targets activated macrophages, which are central to the immune system. These results provide further validation of the Manocept platform, as we continue to build a pipeline of additional

immunodiagnostic and immunotherapeutic products across oncology, inflammatory and infectious diseases."

Summary of Results

A series of studies supported by patient exposure to immunodiagnostic imaging drug, targeting studies, patient explant studies, and *in vivo* and *ex vivo* animal data examined Manocept agents including 99mTc-tilmanocept, Cy3-tilmanocept, and Manocept-doxorubicin. These studies validated the self-transforming nature of the Manocept platform from immunodiagnostic imaging to effective Manocept therapeutic targeting. Data from studies in several macrophage-mediated diseases including Kaposi's sarcoma, rheumatoid arthritis, and cardiovascular disease show that Manocept platform compounds bind almost exclusively to human macrophages and that the mannose receptor (CD206) is the major receptor for its recognition. For complete details of the studies, findings and results, **"The Inextricable Axis of Targeted Diagnostic Imaging And Therapy: An Immunological Natural History Approach"** appears in the March 2016 print journal Nuclear Medicine and Biology. *2016 Nuclear Medicine and Biology.* Volume 43, Issue 3, Pages 215–225.*[doi: 10.1016/j.nucmedbio.2015.11.007].*

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%).

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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. The development activities of the Manocept immunotherapeutic platform will be conducted by Navidea in conjunction with its subsidiary, Macrophage Therapeutics. 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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