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Navidea Receives IRB Approval for its Lymphoseek® Rheumatoid Arthritis Clinical Trial Protocol

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB) announced that it has received Institutional Review Board (IRB) approval from the University of California, San Francisco School of Medicine for a clinical study examining the ability of Lymphoseek®(technetium Tc 99m tilmanocept) injection, a Manocept™ platform product, to specifically identify active rheumatoid arthritis (RA) in pre-identified RA-affected joints. The study will begin enrolling patients shortly. Additionally, Navidea has received WIRB IRB approval to expand this study to other study sites at Navidea's discretion.

"This IRB approval is an important and significant advancement in the expansion of the Manocept platform as we can now start enrollment in this seminal RA immunodiagnostic study." said Frederick O. Cope, Ph.D., Chief Scientific Officer of Navidea. "We believe in the medical value of Manocept platform to enhance the specific diagnosis of inflammatory and infectious diseases to benefit patient care and guide treatment."

About the RA Clinical Study

This study has been designed as an open-label, Phase 1 clinical study of up to 18 individuals to investigate the ability of a subcutaneous injection of Tc 99m-*tilmanocept* to identify RA inflamed joints in active RA subjects by SPECT and SPECT/CT imaging. The study will enroll four cohorts of subjects: participants with active RA and arthritis-free individuals evaluating two different *tilmanocept* doses in each group. Results of this study will be used to determine *tilmanocept's* ability to localize in subjects with RA and show concordance with clinical symptoms, compare the intensity between the two dose groups, and compare localization between active RA and arthritis-free subjects. Study results will help to inform the trial design for follow-on studies. This study is supported by NIH/NIADDK grant number:1R44AR067583-01A1.

Study details can be found at: https://clinicaltrials.gov/ct2/show/NCT02683421?term=lymphoseek&rank=11.

About Rheumatoid Arthritis

RA is a chronic disease affecting 1.6 million in the US. The immune system plays an important role in RA. Cells of the immune system invade tissues that line the joints (the synovium), causing inflammation and over time damage the cartilage and bone. It can lead to long-term joint damage, resulting in chronic pain, loss of function and severe disability. RA can be hard to detect because it may begin with subtle symptoms, such as achy joints or a little stiffness in the morning. Also, many diseases behave like RA early on. There is no

single test that confirms an RA diagnosis. Currently there is no approach to reliably detect, evaluate or therapeutically target the macrophage inflammatory component which is a key driver of progression. Misdiagnosis results in billions of dollars being spent each year unnecessarily on therapies, which may also result in significant side effects.

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. 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.

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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, our ability to repay our debt, the outcome of the CRG litigation, 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 The Company undertakes no obligation to publicly update or revise any forward-looking statements.

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