July 2, 2015

Navidea Reports Clinical Data Demonstrating Manocept™ Agent Localizes in Multiple KS Lesions

- Reinforces Therapeutic Potential of Targeting Activated Macrophages via the CD206 Receptor-

- Data also suggest a new origin of KS as a macrophage fusion tumor -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB) and its subsidiary, Macrophage Therapeutics, Inc., today announced that imaging results from the Manocept™ clinical trial in Kaposi's Sarcoma (KS) and other preclinical studies were presented at the 18th International Workshop on Kaposi's Sarcoma Herpesvirus (KSHV) and Related Agents in Hollywood, Florida. The clinical imaging study, using Tc 99m tilmanocept, a Manocept platform product, in both HIV+ and HIV- patients suggests that KS tumor lesions, both cutaneous and suspected extra-cutaneous sites, can be easily visualized and mapped, demonstrating that this technique may potentially provide a means for routine patient assessment. The results also show that use of Manocept represents a potential therapeutic pathway for targeting tumor associated macrophages (TAMs). Manocept agents are designed to target CD206, which is highly expressed on TAMs and the KS tumor itself. As a potential therapeutic, Manocept could be used as a precision vehicle to deliver payloads to tumor sites throughout the body.

"These pre-clinical and clinical studies support using Kaposi's sarcoma as a model tumor system for evaluating therapeutic approaches for the Manocept platform in other forms of solid tumors," commented Michael Tomblyn, M.D., Navidea's Chief Medical Officer. "They provide evidence that Manocept agents can target CD206 and are internalized into tumor associated macrophages and tumor cells. This along with clinical observations that demonstrate tilmanocept can be used to image KS tumors both externally and internally indicates excellent potential for immunotherapeutic utility."

"Using a targeted imaging agent like tilmanocept in this group of HHV8+patients represents an elegant approach to potentially detect internal KS lesions that would previously be difficult or impossible to non-invasively locate," commented Toby Maurer, M.D., FAAD, Professor of Dermatology at the University of California, San Francisco (UCSF), and Chief of Dermatology at San Francisco General Hospital and Trauma Center, who co-led the clinical study at UCSF with Michael S. McGrath, M.D., PhD. "Further, the specificity and the ability to quantify tumor burden could enable regular patient evaluations and monitoring of therapeutic effectiveness addressing important unmet patient needs."

Five Human Herpes Virus8 positive (HHV8+) patients (4 HIV+, 1HIV-) were enrolled in the NAV03-12 study. Patients received a single subcutaneous injection of Technetium Tc 99m

tilmanocept in the region of a cutaneous KS lesion and imaging was performed at 1, 4 and 24-hours post-injection to visualize localization of tilmanocept. Results represented by whole body Single-Photon Emission Computed Tomography (SPECT/CT) imaging scans from study patients were presented. Collectively, the scans show localization of tilmanocept and detected multiple cutaneous lesions in the extremities, face and genitalia, as well as extra-cutaneous localization found in the nasopharynx, lymph nodes and brain. Results also indicate that KS lesions are anatomically linked in chains by and within the lymph ducts. The study concludes that both HIV+ and HIV- patients have pan-tumor expression of CD206, strongly suggests tilmanocept crosses the blood brain barrier and that a Manocept-drug conjugate may have the potential as a therapeutic with high target effect and low off-target concerns.

The data from these studies also suggest a novel theory on the genesis of KS in which KS arises from an HHV8 infected macrophage type cell and its interaction with the lymphatic system. This interaction provides the means for access of the KS through CD206 receptor for diagnosis, evaluation, and potential therapy using the Manocept platform.

Navidea and Macrophage Therapeutics plan a webcast to provide investors with a complete look at the data being presented at the International Workshop on Kaposi's Sarcoma Herpesvirus (KSHV) and Related Agents conference on July 7, 2015 at 1:00 pm EDT. Webcast details will be available on the Navidea website.

About the Manocept™ CD206-targeting platform

The 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. This flexible and versatile platform acts as an engine for purpose-built molecules that may enhance diagnostic accuracy, clinical decision-making, targeted treatments and ultimately patient care. As a diagnostic tool, the Manocept technology has the potential to utilize a breadth of imaging modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection. By adding a therapeutic agent on the Manocept molecular backbone, there is the potential to develop novel, targeted immunotherapies specifically designed to selectively deliver an agent that can kill or alter disease-associated macrophages. Navidea’s FDA-approved precision diagnostic imaging agent, Lymphoseek® (technetium 99m tilmanocept) injection, is representative of the platform’s ability to successfully exploit this mechanism and offer the potential for development of new CD206-targeted diagnostic agents and therapeutics.

About Kaposi’s Sarcoma

Kaposi sarcoma (KS) is a cancer that develops from the cells that line lymph nodes or blood vessels. It usually appears as tumors on the skin or on mucosal surfaces such as inside the mouth, but tumors can also develop in other parts of the body, such as in the lymph nodes (bean-sized collections of immune cells throughout the body), the lungs, or digestive tract. The abnormal cells of KS form purple, red, or brown blotches or tumors on the skin. These affected areas are called lesions. The skin lesions of KS most often appear on the extremities, trunk and face. AIDS-related KS is the most common type of KS in the United States which develops in people who are infected with HIV, the virus that causes AIDS. KS can also develop in people whose immune systems have been suppressed after an organ transplant and is called transplant-related KS.[1]

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.

About Macrophage Therapeutics

Macrophage Therapeutics, a newly created subsidiary of Navidea Biopharmaceuticals, Inc. (NAVB), is developing therapeutics using the patented Manocept immunotherapy platform licensed from Navidea to target over-active macrophages implicated in cancer, cardiovascular, central nervous system, autoimmune, antiviral, and skin diseases. Manocept specifically targets CD206, or the mannose receptor prevalent on over-active macrophages. The technology enables highly specific targeted delivery of active (either existing or yet to be developed) agents that can modulate the activity of over-active macrophages that have been implicated in many diseases. Targeted delivery should significantly enhance a given compound's efficacy and safety.

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.

[1] American Cancer Society web accessed 22May2015. http://www.cancer.org/cancer/kaposisarcoma/detailedguide/kaposi-sarcoma-what-is-kaposi-sarcoma

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