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Navidea Data for Manocept™ CD206 Targeting Platform Demonstrate Potential to Impact Tumor-Associated Macrophages and Kaposi's Sarcoma Tumor Cells

- Preclinical and Clinical Results Reported at American Association of Cancer Research (AACR) -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB), today reported data at the American Association of Cancer Research (AACR) Annual Meeting 2015 demonstrating that the Manocept™ molecule selectively binds to, and is continuously internalized by, tumor-associated macrophages (TAMs) and Kaposi's sarcoma (KS) tumor cells in a preclinical model. Preliminary results from a clinical study also demonstrated that a single, subcutaneous injection of Technetium Tc 99m tilmanocept (Lymphoseek®), an FDA-approved Manocept-based imaging agent, detects and localizes in KS tumors and the lymph nodes involved in draining the KS tumor fields.

Collectively, the data demonstrate the potential for Manocept-based molecules to be used therapeutically to treat Kaposi's sarcoma. Manocept is designed to target CD206, which is expressed on TAMs and KS tissue. Modulation, including killing or modification of macrophage and KS expression profiles, represents a potential for a paradigm-shifting immunotherapeutic strategy.

Rick Gonzalez, Navidea President and Chief Executive Officer stated "These new results for Navidea's Manocept program represent an important scientific advance and are a direct result of our oncology expertise and understanding of macrophage targeting in immunology. As the immuno-oncology field continues to show great promise, we believe our CD206 macrophage targeting platform could yield an important new development pathway for future immuno-oncology therapeutics which we expect to be primarily funded through non-dilutive grants. We look forward to presenting additional data supporting and extending the use of Manocept in cancer very soon."

The poster presentation, titled *Tumor associated targeting with Manocept: HIV associated Kaposi's sarcoma as a model system in humans* (#5026; Section 11, Therapeutics and Therapeutics Models; 8:00 AM – 12:00 PM), is based on data from studies led by Michael S. McGrath, M.D., Ph.D. and Toby Maurer, M.D., at the University of California San Francisco.

"The Manocept platform's ability to precisely target the CD206 mannose receptor in both macrophages and tumor cells as seen in this KS model system has the potential for a potent targeting tool to not only identify disease but to deliver therapeutic agents to the tumor cells addressing a broad unmet need for patients with Kaposi's sarcoma," said Dr. McGrath,

Professor, Departments of Laboratory Medicine, Pathology, and Medicine, UCSF.

“The data generated with human cancer cells confirm that our delivery system can target tumor-associated macrophages, which are critical to the growth and survival of many different forms of cancer,” commented Frederick Cope, Ph.D., M.S., FACN, Navidea Senior Vice President and Chief Scientific Officer and Chief Scientific Officer of Macrophage Therapeutics. “Further, the evidence that the receptor we target, CD206, internalizes our delivery agent provides strong evidence for our therapeutic strategy in KS as well as other forms of solid tumors. Ongoing studies with different therapeutic moieties attached to our delivery platform are underway. We look forward to reporting the complete results of the NAV03-12 study and other results in the near term.”

Ex vivo and in vivo results

Using a fluorescent-tagged imaging agent Cy3-Manocept, the presence of CD206, the mannose receptor, on tumor-associated macrophages (TAMs) as well as a majority of KS tumor cells was confirmed from fresh KS tissue. In addition, results determined CD206 was the most prevalent antigen for both KS tumor spindle cells and TAMs and Cy3-Manocept avidly bound to CD206 expressing macrophages. Continuous and ongoing uptake of Cy3-Manocept into CD206 positive macrophages was seen in a time study with doses of increasing Cy3-Manocept concentrations.

To examine these results further, Navidea began a clinical study [NAV03-12](#) using Technetium Tc 99m tilmanocept to detect tumors and involved lymph nodes in KS patients. Preliminary results represented by a whole body SPECT/CT imaging scan from a NAV03-12 study patient were presented. The patient received a single subcutaneous injection of Technetium Tc 99m tilmanocept in the region of the patient’s cutaneous KS lesions and imaging was performed 4-hours post-injection to visualize localization of KS in the patients. The scan detected visceral KS tumors, showing localization and involved lymph nodes. Complete results of this clinical study are expected to be reported in the coming months.

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 Biopharmaceuticals, Inc.

Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB) is a commercial stage precision medicine 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™, NAV4694, and NAV5001, 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 by the EMA 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. (NAV), 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 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.

Photos/Multimedia Gallery Available:

<http://www.businesswire.com/multimedia/home/20150422005533/en/>

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