May 26, 2016

$1.8 Million Fast-Track NIH SBIR Grant for Manocept™ Immunotherapeutics Evaluation in Kaposi's Sarcoma Awarded to Navidea

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB) announces the receipt of an initial notice of award for a Fast- track Small Business Innovation Research (SBIR) grant providing for up to $1.8 million from the National Institutes of Health's (NIH) National Cancer Institute (NCI) to fund evaluation of an investigational Manocept™-based immunotargeted treatment for Kaposi's Sarcoma (KS). The novel Manocept construct is designed to specifically deliver doxorubicin, a chemotoxin, which can kill KS tumor cells and their tumor-associated macrophages (TAMs) potentially altering the course of cancer. KS is a serious and potentially life threatening illness in persons infected with the human immunodeficiency virus (HIV) and the third leading cause of death in this population worldwide. The prognosis for patients with KS is poor with high probabilities for mortality and greatly diminished quality of life. The development activities of the Manocept immunotherapeutic platform will be conducted by Navidea and its subsidiary, Macrophage Therapeutics.

The funds for this Fast-track grant (National Cancer Institute of the National Institutes of Health under Award Number R44CA206788) will be released in three parts, which together have the potential to provide up to $1.8 million in resources over 2.5 years with the goal of completing an investigational new drug (IND) submission for a Manocept construct (MT1000 class of compounds) consisting of tilmanocept linked to doxorubicin for the treatment of KS. The first part of the grant will provide $232,000 to support analyses including *in vitro* and cell culture studies and will be followed by Part 2 and 3 animal testing studies. If successful, the information from these studies will be combined with other information in an IND application that will be submitted to the U.S. Food and Drug Administration (FDA) requesting permission to begin testing the compound selected in human KS patients.

"We believe that given the data to date from the Manocept platform, these studies along with a host of other human tumor model studies ongoing and planned for animal testing will provide a powerful gateway to a new class of anti-TAM immunotherapies directed at solid tumors. A drug that selectively kills cells that are highly expressing CD206 is expected to have an overwhelming, immediate, conspicuous and easily measured effect on KS tumors," said Frederick Cope, Ph.D., M.S., F.A.C.N., C.N.S., Senior Vice President and Chief Scientific Officer of Navidea. "This grant will bring us to submission of an IND and the first time human evaluation for a Manocept immunotherapeutic. We anticipate if trials are successful, we can bring an effective and life-sparing new therapy to KS patients who are in desperate need for such a new treatment."

“The Manocept platform may offer a unique approach to the treatment of Kaposi's sarcoma (KS) and is, we believe, a translational portal to the therapy of a number of other solid tumors in which macrophages and tumor-associated macrophages play a key role in tumorigenesis and metastasis,” said Michael Goldberg, M.D. Chairman of the Board of Navidea, “We believe that KS serves as model for a development strategy that can be expanded to other macrophage-dependent solid tumors as well as a model for therapeutics targeting viruses that incubate in macrophages. We are encouraged that our therapeutic program has been recognized by the NIH so soon after we began our therapeutic development effort. We plan on submitting additional grant requests as soon as we obtain results from the multiple ongoing studies in various cancer models, which should read out shortly.”

About the MT1001 Study Efforts in KS

These IND-enabling studies will be conducted in three parts. Part 1 studies require *in vitro and* cell culture experiments related to safety and efficacy of an intravenous injection of MT100. In Part 2 and 3, nine preclinical animal studies will build on the Part 1 results and will further refine safety and efficacy variables including dosing and drug administration regimens and evaluating the feasibility of the MT 1000-class of molecules, as a novel treatment for KS. Following these studies, Navidea expects to submit an IND application to the FDA seeking permission to begin Phase 1/2 clinical evaluation of MT1001 in KS patients.

About KS

Kaposi sarcoma (KS) is a serious and potentially life threatening illness in persons infected with the HIV, the causative agent of acquired immunodeficiency syndrome (AIDS). Tumor associated macrophages (TAMs) constitute an important tumor component for most types of cancer (including KS) that contributes to tumor growth and protection from immune responses. Navidea, through its subsidiary Macrophage Therapeutics, is developing a receptor targeted drug construct that may be able to effectively treat KS and could contribute to effective immunotherapy for a wide variety of cancers.

About the Manocept™ CD206-targeting platform

Navidea Biopharmaceuticals is developing Manocept, a new pharmaceutical platform technology, targeting cells that express the macrophage mannose receptor (CD206). A wide variety of immune-targeting applications for this platform technology are envisioned. 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 an immunodiagnostic tool, the Manocept technology can utilize a breadth of imaging modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection. By linking 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. MT1000 class of compounds , consisting of a Manocept construct linked to doxorubicin, is the first in a series of drug delivery constructs that will utilize Navidea’s Manocept CD206 targeted drug delivery platform. Navidea’s FDA-approved immunodiagnostic 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 immunodiagnostic agents and immunotherapeutics. The development activities of the Manocept immunotherapeutic platform will be conducted by Navidea‘s subsidiary, Macrophage Therapeutics.

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.

About Macrophage Therapeutics

Macrophage Therapeutics, Inc., a 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, 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 statements.

View source version on businesswire.com:
http://www.businesswire.com/news/home/20160526006136/en/

Navidea Biopharmaceuticals
Investors & Media
Sharon Correia, 978-655-2686
Senior Director, Corporate Communications

Source: Navidea Biopharmaceuticals, Inc.