July 28, 2015

Navidea and Massachusetts General Hospital to Evaluate Manocept™ for Detection of Cardiovascular Disease with NIH Grant

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB), is announcing the receipt of a notice of award for a Phase 1 Small Business Innovation Research (SBIR) grant providing $321K from the National Heart Lung and Blood Institute (NHLBI), National Institutes of Health (NIH). The study, to be done in collaboration with Massachusetts General Hospital (MGH) and Harvard Medical School, will examine the ability of Tc 99m-tilmanocept, a Manocept™ platform product, to localize in high-risk atherosclerotic plaques. These specific plaques are rich in CD206 expressing macrophages and are at high-risk for near term rupture resulting in myocardial infarctions, sudden cardiac death and strokes, accumulatively the leading cause of death in the US.

The consequences of atherosclerosis and the cardiovascular disease (CVD) that atherosclerosis causes, while severe in all populations of people, are particularly concentrated in HIV+ patients. “This Phase 1 pilot study may provide evidence that Tc99m-tilmanocept localizes in atherosclerotic plaques which would enable potential development of a diagnostic imaging agent that could benefit not only HIV+ patients but millions of people,” said Michael Tomblyn, M.D., Navidea’s Chief Medical Officer. “Positive outcomes would also support our Manocept development vision of a larger program that seeks to evaluate tilmanocept as a targeting vehicle to deliver therapies intended to limit or reverse atherosclerosis directly to plaques that could reduce cardiovascular disease (CVD) risk and improve outcomes for this patient population.”

“HIV infected patients suffer disproportionally from atherosclerosis and CVD,” commented Steven Grinspoon, M.D., Professor of Medicine at Harvard Medical School, Director MGH Program in Nutritional Metabolism, Co-Director of the Nutrition Obesity Research Center at Harvard and the study’s lead investigator. “There exists a profound and highly significant unmet need for means to better diagnose and treat atherosclerosis in all patients but particularly so in HIV patients. Manocept’s proven specificity for CD206 presents a clinically exploitable target with potential to achieve significant diagnostic and therapeutic results where few other approaches have progressed.”

About the Phase 1 SBIR Clinical Study
Recently, it has been observed that CD206 expressing macrophages densely populate vulnerable plaques or thin cap fibroatheromas (TCFA) but not other kinds (i.e., stable) of atherosclerotic plaques. A primary goal for this grant involves an approved clinical investigation of up to 18 individuals with and without aortic and high risk coronary atherosclerotic plaques and with and without HIV infection to determine the feasibility of

99mTc-tilmanocept to image high risk plaque by SPECT/CT. Results have the potential to provide evidence of the potential of 99mTc-tilmanocept to accumulate in high risk morphology plaques, the ability to make preliminary comparisons of aortic 99mTc-tilmanocept uptake by SPECT/CT in each group, and to evaluate the ability of 99mTc-tilmanocept to identify the same aortic atherosclerotic plaques that are identified by contrast enhanced coronary computed tomography angiography (CCTA) and/or PET/CT.

About Atherosclerosis

Atherosclerosis is a chronic, progressive inflammatory condition resulting, over the course of years or decades, in the formation of atherosclerotic plaques in the walls of arteries. Atherosclerosis is the underlying pathology in the majority of cases of cardiovascular disease (CVD)[1] and a significant proportion of cases of stroke[2]. CVD and stroke are the first and fourth leading causes of mortality in the US[3], respectively. Persons with advanced atherosclerosis are frequently asymptomatic until one of their atherosclerotic plaques ruptures, leading to blood clot formation, which restricts blood flow to tissues. By this mechanism, rupture of atherosclerotic plaques causes myocardial infarctions, sudden cardiac deaths and strokes.

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.

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.

Resources:

1. Burke AP, Virmani R. Pathophysiology of acute myocardial infarction. Med Clin North Am. 2007 Jul;91(4):553-72; ix. PMID: 17640536
2. Pelisek J, Eckstein HH, Zernecke A. Pathophysiological mechanisms of carotid plaque vulnerability: impact on ischemic stroke. Arch Immunol Ther Exp (Warsz). 2012 Dec;60(6):431-42. PMID: 22945688
3. Murphy SL, Xu JQ, Kochanek KD. Deaths: Final data for 2010. National vital statistics reports; vol 61 no 4. Hyattsville, MD: National Center for Health Statistics. 2013. http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_04.pdf

View source version on businesswire.com:
http://www.businesswire.com/news/home/20150728005557/en/

Navidea Biopharmaceuticals
Investors
Tom Baker, 617-532-0624
tbaker@navidea.com
Media
Sharon Correia, 978-655-2686
Associate Director, Corporate Communications

Source: Navidea Biopharmaceuticals, Inc.