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Navidea Biopharmaceuticals Manocept™ Platform Featured in Nature Outlook: Medical Imaging

Data regarding receptor-targeted precision diagnostic imaging for multiple disorders appears in October 31st issue of Nature

Manocept Advisory Board formed to contribute to platform advancement

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSEMKT:NAVB), a biopharmaceutical company focused on precision diagnostic radiopharmaceuticals, today announced the online publication of a special supplement *Nature Outlook: Medical Imaging* which will appear in the 31 October issue of *Nature*, and in which new collaborative data from proof-of-principle studies of the Company's Manocept™ platform will be featured. The supplement produced with the support of Navidea includes a White Paper entitled *"Innovations in receptor-targeted precision imaging at Navidea: Diagnosis up close and personal"* which provides new insights into the use of*Cy3-tilmanocept*, a fluorescent-labeled agent derived from the same platform underlying the Company's Lymphoseek® (technetium 99m tilmanocept) Injection product. The online edition also includes several peer-reviewed articles published previously by Nature Publishing Group that reinforce the principle of CD206 mannose receptor targeting using Manocept compounds to identify macrophages. This principle supports the potential broad application of novel Manocept agents for diagnosis and staging across a range of disease states, including Kaposi's sarcoma, rheumatoid arthritis, tuberculosis, metastatic disease, systemic lupus erythrematosus, and vascular inflammation, among others.

"We are extraordinarily pleased to highlight the capability of our Manocept platform in N*ature* magazine," commented Dr. Mark Pykett, Navidea CEO. "We believe this platform may unfold important new opportunities for the Company across a range of clinical indications where significant unmet medical need exists. Having already made substantial investment in the underlying approach for our approved product Lymphoseek, we believe the applications enabled by the Manocept platform have the potential to significantly expand the commercial potential of our technology and franchise. We believe now is the appropriate time to leverage the platform and accelerate realization of its additional potential. With a recently completed financing to augment our balance sheet as product revenue advances, we believe the Manocept platform is well-positioned for near-term progress and look forward to unfolding new opportunities in the near future."

"The collaborative studies presented in this Nature publication focused on establishing the ability of a fluorescent-labeled tilmanocept to target macrophages in three disease states which are representative of broader macrophage-associated disorders: Rheumatoid Arthritis (RA), Kaposi's Sarcoma (KS) and Tuberculosis (TB)," said Frederick Cope, PhD, FACN,

Senior Vice President and Chief Science Officer at Navidea. “The data indicate that CD206-targeting using Manocept-derived molecules may prove to be a potent tool for addressing unmet clinical needs such as localizing, staging and assessing disease activity in multiple therapeutic areas.”

Experimental Results

The proof-of-principle studies highlighted in the Navidea article directly examined the ability of a Manocept agent to target macrophages in several autoimmune and infectious diseases represented by RA, KS and TB, which may extend to other recognized macrophage-mediated disorders including those in oncology, cardiology, and inflammation.

The RA studies demonstrated the feasibility of using *Cy3-tilmanocept* injected intravenously as a predictive biomarker in the prodromal phase of RA in an animal model with induced arthritis in the external joints. Imaging results showed preferential localization of macrophages in affected joints, with little to no localization in unaffected joints. The researchers concluded that use of such an approach may lead to earlier identification of patients with RA, potentially resulting in earlier diagnosis and improved patient management.

The TB evaluation targeted CD206 using *Cy3-tilmanocept* to image human monocyte-derived macrophages infected with *M. tuberculosis.* Confocal microscopy showed that Cy3-*tilmanocept* specifically co-localized in the macrophages infected with TB, enabling the identification of only macrophage-involved tissue. These data suggest that the ability to target CD206 and identify disease-associated macrophages may potentially be broadly applicable in the development of new TB diagnostics.

The Kaposi’s Sarcoma studies demonstrated the ability of *Cy3-tilmanocept* to identify and localize specifically to macrophage CD206 in human primary KS lesions. In tumor tissue from over 60 KS patients, greater than 91% of KS tumor cells and tumor-associated macrophages expressed CD206 and bound and internalized *Cy3-tilmanocept*, affording a precise means of identifying these cells in KS lesions. With few current tumor-specific diagnostic options to determine if and where the tumor has spread from the skin, an imaging approach using the Manocept platform has the potential to improve patient staging and treatment regimens.

“The work cited in this article and conducted by several members of Navidea’s Manocept Advisory Board is extremely encouraging science, and affords a broad opportunity in multiple disease states for innovative diagnostic imaging. Macrophages participate in a large number of biologic processes, ranging from cancer to atherosclerosis. By targeting the mannose receptor it is possible to localize the sites and determine the extent of macrophage-associated inflammation,” commented H. William Strauss, MD, Attending Physician Emeritus, Molecular Imaging and Therapy Service at Memorial Sloan-Kettering Cancer Center. “The mannose receptor is a key portal for imaging pathological states, and the Manocept platform may provide the potential for new and more focused clinical decision making and therapeutic choices for patients.”

You can view the entire Outlook supplement at: http://www.nature.com/nature/outlook/medical-imaging/index.html and see the Navidea article at www.nature.com/nature/outlook/medical-imaging/pdf/navidea-white-paper.pdf.

Manocept™ Advisory Board

In connection with publication of this positive initial data, Navidea also announces the formation of its Manocept Advisory Board. “The Manocept Advisory Board was formed to bring together some of the best scientific and medical advisors in the field of macrophage science and macrophage-mediated diseases to share insight and direction as Navidea seeks to prioritize and advance these encouraging early stage results,” added Mark Pykett. “We are very pleased to bring this highly regarded team of experts in their fields together as we seek to move this potentially valuable platform forward.”

Members of the board include: Steven Grinspoon, MD, Professor of Medicine, Harvard Medical School and Director, Program in Nutritional Metabolism, Massachusetts General Hospital; Wael Jarjour, MD, Associate Professor, Director, Division of Rheumatology & Immunology, The Ohio State University; Michael S. McGrath, MD, PhD, Professor, Departments of Laboratory Medicine, Pathology, and Medicine, **University of California, San Francisco;** Jagat Narula, MD, PhD, MACC, Associate Dean for Global Affairs, Professor of Medicine, Cardiology, Mount Sinai Hospital; Thomas Rosol DVM, PhD, Professor, College of Veterinary Medicine, The Ohio State University; Larry Schlesinger, MD, Professor of Medicine, Chair of the Department of Microbial Infection and Immunity, Director of the Center for Microbial Interface Biology, The Ohio State University; H. William Strauss, MD, Attending Physician Emeritus, Molecular Imaging and Therapy Service, Memorial Sloan-Kettering Cancer Center; David Vera, PhD, Professor of Radiology, **University of California, San Diego Moores Cancer Center,** and Kenneth Williams, PhD, Professor of Biology, Boston College.

About The Manocept™ Platform

Navidea’s 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 where diagnostic uncertainty exists. This flexible and versatile platform acts as an engine for purpose-built molecules that may enhance diagnostic accuracy, clinical decision-making and ultimately patient care, while offering the potential to utilize a breadth of diagnostic modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection. The Company’s FDA-approved precision diagnostic lymphatic mapping agent, Lymphoseek (technetium 99m tilmanocept) Injection, is representative of the ability to successfully exploit this mechanism to develop powerful, new diagnostic agents.

About Lymphoseek®

Lymphoseek® (technetium Tc 99m tilmanocept) Injection is a novel, receptor-targeted, small-molecule radiopharmaceutical used in lymphatic mapping procedures that are performed to help in the diagnostic evaluation of potential cancer spread for patients with breast cancer and melanoma. Lymphoseek is designed to identify the lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. Lymphoseek was approved by the U.S. Food and Drug Administration in March, 2013 for use in lymphatic mapping to assist in the localization of lymph nodes draining a primary tumor in patients with breast cancer or melanoma. The Company anticipates continuing development of Lymphoseek into other solid tumor areas that may include head and neck cancers, prostate cancer, thyroid cancer, lung/bronchus cancers, colorectal cancer and

others.

Accurate diagnostic evaluation of cancer is critical, as it guides therapy decisions and determines patient prognosis and risk of recurrence. According to the American Cancer Society, approximately 232,000 new cases of breast cancer, 77,000 new cases of melanoma and 67,000 new cases of head and neck/oral cancer are expected to be diagnosed in the United States in 2013.

U.S. Indication and Important Safety Information About Lymphoseek

Indication

Lymphoseek (technetium Tc 99m tilmanocept) Injection is a lymphatic mapping agent indicated for use with a hand-held gamma counter to assist in the localization of lymph nodes draining a primary tumor site in patients with 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.

The most common adverse reactions are 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. (NYSEMKT:NAVB) is a biopharmaceutical company focused on the development and commercialization of precision diagnostics and radiopharmaceutical agents. Navidea is developing multiple precision diagnostic products and platforms including NAV4694, NAV5001, Manocept™ and RIGScan™, to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making and, ultimately, patient care. Lymphoseek® (technetium 99m tilmanocept) Injection, Navidea's first commercial product from the Manocept platform, was approved by the FDA in March 2013. Navidea's strategy is to deliver superior growth and shareholder return by bringing to market novel radiopharmaceutical agents and advancing the Company's pipeline through selective acquisitions, 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.

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