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Navidea Joins Essex Woodland's Rheumco to Develop Radiopharmaceuticals for Detection and Treatment of Arthritic Diseases

- Combining Manocept™ with Rheumco's Tin-117m radioisotope to enable earlier disease detection and localized therapy -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAV) today announced that it has formed a joint enterprise with Essex Woodlands-backed Rheumco, LLC, to develop and commercialize radiolabeled diagnostics and therapeutics for rheumatologic and arthritic diseases. The joint enterprise, called R-NAV, LLC, will combine Navidea's proprietary Manocept CD206 macrophage targeting platform and Rheumco's proprietary Tin-117m radioisotope technology to focus on leveraging the platforms across several indications with high unmet medical need:

- 1) Detection of rheumatoid arthritis (RA) initially using Tc-99m tilmanocept, commercially known as Lymphoseek® (technetium Tc-99m tilmanocept) Injection,
- 2) Combination of the Manocept platform with Tin-117m for detection and treatment of RA,
- 3) Detection and treatment of human and veterinary osteoarthritis (OA) using the Tin-117m technology, and
- 4) Treatment of pediatric hemophilic arthropathy (PHA); a rare rheumatologic condition.

"We chose to combine our proprietary Tin-117m technology with Navidea's Manocept CD206 receptor- targeting technology due to its unique ability to seek out and attach itself to immune cells responsible for detrimental inflammation in arthritic conditions," said Gilbert Gonzales, M.D., Founder, Rheumco, and R-NAV Director.

Immanuel Thangaraj, Managing Director and Partner at Essex Woodlands and R-NAV Director, added, "A broad-based approach using radiopharmaceuticals would enable earlier detection and therapeutic intervention before irreversible damage occurs in joints, distinguish between autoimmune and degenerative diseases, and potentially improve patient outcomes and quality of care."

"Through this partnership, we will for the first time explore the development of our Manocept technology for therapeutic uses, expanding the commercial potential of the platform beyond the important role it currently plays in cancer detection," said Michael Goldberg, M.D., Navidea Interim Chief Executive Officer. "We believe R-NAV may help accelerate development of both diagnostic and therapeutic applications of our Manocept platform in a cost-effective manner, capitalizing on the proven pathway established by the FDA approval of Lymphoseek, the first US FDA-approved product from the Manocept platform. The R-NAV joint enterprise allows us to leverage our broad Manocept technology platform for

therapeutic and diagnostic applications, including global license rights to tilmanocept, to multiply the available funding, create optionality, and efficiently expand our product pipeline outside of Navidea as we focus our internal resources on Lymphoseek commercialization and market growth.”

R-NAV will focus on deploying the two technology platforms as an ideal combination for the development of novel diagnostic and therapeutic agents for rheumatologic and arthritic conditions. For a number of years, Essex Woodlands and Rheumco have invested in the development of their patented, high-specific-activity Tin-117m technology to optimize its therapeutic potential and safety profile. Tin-117m possesses unique imaging and therapeutic properties not found in alternative medical isotopes, including its ability to locally target disease-causing cells without damaging adjacent healthy tissue. Navidea’s Manocept technology is able to quickly seek out and attach to certain immune cells expressing CD206, called macrophages. Macrophages are an emerging participant in disease-associated inflammation, which has been found to play a role in conditions such as RA, cancer, and heart disease.

“We decided to form the joint enterprise with Rheumco and Essex Woodlands and their financial partners given their successful track record of investing and building innovative medical technologies and the resources they will be able to contribute to this venture,” said Mark Pykett, V.M.D., Ph.D., Head of Navidea’s Manocept development program and R-NAV Director. “Together, with this proof statement for our technology platforms, we have the opportunity to help the millions of patients diagnosed each year with arthritic conditions as well as the very serious rare disease, pediatric hemophilic arthropathy, for which there are no effective treatment options available today.”

R-NAV will be initially funded primarily through a \$4 million investment from Infinity Capital III, of Houston-based McRay Money Management, and other third-party private investors working closely with Essex Woodlands, and underpinning the technology contributions from Rheumco and Navidea. Navidea has committed an additional \$1 million to support R-NAV’s development efforts to be paid in equal installments over three years. In exchange for its cash, in-kind and technology contributions, Navidea has received both common units and Preferred Series A units of R-NAV and will initially own approximately 30% of the combined entity. Joint oversight of R-NAV is shared between Navidea, Rheumco, Infinity Capital III of Houston-based McRay Money Management, and the other investors. Navidea also has an option to acquire, at its sole discretion prior to Phase 3 clinical study, imaging products derived from the Manocept platform, and therapeutic products combining Manocept agents from Navidea with the Tin-117m technology for commercialization.

Detection of RA, a chronic, progressive, systemic autoimmune disorder, is the nearest-term opportunity being pursued by R-NAV. Clinicians are often faced with diagnostic confusion early in disease progression resulting in inaccurate diagnosis when existing therapies could be most effective. There is currently no approach to reliably detect, evaluate or therapeutically target the macrophage inflammatory component of RA, which is a key driver of RA pathogenesis. Misdiagnosis results in billions of dollars being spent each year unnecessarily on therapies, which may result in significant side effects. According to the Centers for Disease Control (CDC), the overall cost of arthritis and other rheumatic conditions in the U.S. was approximately \$128 billion in 2003. Of this, \$80.8 billion was due to direct costs and \$47 billion was due to indirect costs (lost wages only). The CDC also

notes that in 2004 arthritis resulted in 78 million physician visits and 5 million hospitalizations having a principal or secondary diagnosis of arthritis. Further, current intervention using methotrexate or biologics is costly, associated with side effects, and in many cases does not adequately treat the disease or the underlying inflammatory pathology. A targeted imaging agent such as Manocept could assist physicians and healthcare providers to better diagnose patients and allow for earlier and more effective intervention, and use of a Tin-117m therapeutic could improve and localize therapeutic intervention for the same patients.

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, therapeutic delivery and ultimately patient care, while offering the potential to utilize a breadth of radioisotopes and diagnostic imaging modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection. The Company's FDA-approved precision diagnostic lymphatic mapping agent, Lymphoseek® (technetium Tc-99m tilmanocept) Injection, is representative of the ability to successfully exploit this mechanism to develop powerful, new diagnostic agents.

About Tin-117m Technology

Tin-117m is a unique radioisotope that has the potential to both identify and treat multiple disease areas that include rheumatoid arthritis, vulnerable plaque, cancers, and other medical problems. Tin-117m has two significant energy emissions, a SPECT gamma photon similar to Tc-99m enabling imaging, and conversion electrons ideally suited for therapeutic applications. When linked to a targeting molecule, the radiopharmaceutical complex selectively binds to its specific target. This enables both imaging and therapy to a localized disease area limiting its therapeutic effect to the desired tissue without damage to adjacent healthy tissue and using remarkably low doses of radiopharmaceutical.

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 with breast cancer, melanoma and head and neck cancer patients with oral cavity carcinoma. 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 lymphatic mapping to assist in the localization of lymph nodes draining a primary tumor in patients with breast cancer or melanoma and for use in guiding sentinel lymph node biopsy in head and neck cancer patients with squamous cell carcinoma of the oral cavity. The Company anticipates continuing development of Lymphoseek into other solid tumor areas.

Accurate diagnostic evaluation of cancer is critical, as it guides therapy decisions and determines patient prognosis and risk of recurrence. According to publicly available

information, 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 are expected to be diagnosed in the United States in 2014, 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 (technetium Tc 99m tilmanocept) Injection is indicated, using a hand-held gamma counter, for:

- Lymphatic mapping to assist in the localization of lymph nodes draining a primary tumor site in patients with breast cancer or melanoma;
- Guiding sentinel lymph node biopsy, in patients with clinically node negative squamous cell carcinoma (SCC) of the oral cavity.

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 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 NAV1800 (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 Tc-99m tilmanocept) Injection, Navidea's first commercial product from the Manocept platform, was approved by the FDA in March 2013. For more information, please visit www.navidea.com.

About Rheumco, LLC.

Rheumco, LLC is a privately held early-stage pharmaceutical development company focused on rheumatological applications using Tin-117m. Tin-117m is a theranostic isotope that can be used for medical imaging and therapeutic applications.

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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