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Navidea Biopharmaceuticals Announces Additional Results from Lymphoseek® Phase 3 Clinical Trial in Head and Neck Cancer at American College of Surgeons 2013 Annual Clinical Congress

– Lymphoseek Successful in Sentinel Lymph Node Identification for Primary and Secondary Endpoints Compared with Pathology Gold Standard –

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB), a biopharmaceutical company focused on precision diagnostic radiopharmaceuticals, today announced the presentation of additional results from its pivotal Phase 3 clinical trial (NEO3-06) for Lymphoseek® (technetium Tc 99m tilmanocept) Injection in patients with head and neck squamous cell carcinoma. Navidea previously announced that the NEO3-06 study met the primary false negative rate efficacy endpoint of accurately identifying sentinel lymph nodes (SLNs) in subjects with squamous cell carcinoma of the head or in the mouth, as compared to the removal of all lymph nodes during multiple level nodal dissection surgery of the head and neck. This surgery is considered the “gold standard” to determine the presence and extent of cancer spread in lymph nodes of patients with head and neck squamous cell carcinoma. The now completed full study report indicates that Lymphoseek also met all other pre-specified study endpoints, including sensitivity, negative predictive value and overall accuracy relative to the pathology status of non-SLNs. No differences were observed in the ability of Lymphoseek to detect SLNs between same-day or subsequent-day surgery following Lymphoseek injection. Lymphoseek is a novel, receptor-targeted, small-molecule radiopharmaceutical approved by the U.S. Food and Drug Administration for use in lymphatic mapping to assist in the localization of lymph nodes draining primary tumor in patients with breast cancer or melanoma. The results were presented at the American College of Surgeons 2013 Annual Clinical Congress by Amit Agrawal, MD, Associate Professor, The Ohio State University College of Medicine, Department of Otolaryngology – Head and Neck Surgery, a lead investigator on the NEO3-06 Phase 3 clinical trial.

“Thousands of patients with head and neck cancer stand to benefit from accurate diagnostic evaluation of their condition, and we are pleased that the final results for Lymphoseek from our NEO3-06 Phase 3 clinical trial are being presented to surgeons attending the prestigious American College of Surgeons Clinical Congress,” said Mark Pykett, VMD, PhD, Chief Executive Officer of Navidea. “The NEO3-06 trial is representative of Navidea’s global strategy to expand Lymphoseek utilization into multiple cancer types with the aim of assisting physicians in improving accuracy and evaluating the extent of disease. As previously announced, we closed the NEO3-06 trial at the recommendation of the Data Safety Monitoring Committee. Based on study results and data analysis and dialogue with

the U.S. Food and Drug Administration (FDA), we are working to file an sNDA for Lymphoseek with the FDA by the end of this year and anticipate EMA action related to the EU MAA for Lymphoseek also by year end."

"Surgeons who perform lymphatic mapping procedures in patients with head and neck cancer face unique challenges," commented Dr. Stephen Y. Lai, MD, PhD, FACS, Associate Professor, Department of Head and Neck Surgery, The University of Texas MD Anderson Cancer Center and a lead investigator on the NEO3-06 Phase 3 clinical trial. "Anatomically, we confront a density of lymph nodes and vessels that are compacted into small, tight spaces, which can impede the vascular flow of certain radiolabeled lymphatic mapping agents and hinder our ability to reliably locate appropriate lymph nodes. We also factor in considerations that the face and neck are highly sensitive areas and the impact that excess surgery can have on the patient. The NEO3-06 clinical study is distinct in comparing the performance of Lymphoseek to the pathological 'gold standard' of multiple level neck dissection, an extensive procedure in which a large portion of the head and neck lymph node tissue may be removed."

"Many surgeons favor removing entire regional lymph node basins because lymphatic metastases may develop in more than 20% of oral cancer patients," continued Dr. Lai. "However, excision at this scale may produce unnecessary morbidity and side effects, leading to over-treatment for approximately 80% of the patients with pathology-negative lymph nodes. Receptor-targeted lymphatic mapping agents like Lymphoseek may facilitate the diagnostic evaluation of these patients, and help spare them possible morbidity from full regional lymph node dissections."

"Lymphoseek demonstrated statistically significant results in this trial, achieving a false negative rate of only 2.56% and nearly 99% overall accuracy. We believe these results speak to the ability of the product to identify appropriate tumor-draining lymph nodes," said Frederick O. Cope, PhD, FACN, Senior Vice President and Chief Scientific Officer at Navidea. "This next-generation lymphatic mapping agent also demonstrated key performance metrics in determining sensitivity and negative predictive value. Importantly, the results also revealed that there was no difference in Lymphoseek clinical performance between same-day or subsequent-day surgery following injection of the product, which may be an important consideration for busy surgeons who often require flexibility in scheduling lymphatic mapping procedures."

Lymphoseek Data Presented at the American College of Surgeons 2013 Annual Clinical Congress

"Results from a prospective Phase 3 multi-institutional trial of 99m-Tc-tilmanocept, a CD206-targeted molecular sentinel node mapping agent, in head/neck squamous cell carcinoma" (NEO3-06 Phase 3 Clinical Trial). The primary endpoint for the NEO3-06 trial was based on the number of subjects with pathology-positive lymph nodes (lymph nodes found to harbor cancer) following a multiple level lymph node dissection and required a minimum of 38 subjects whose lymph nodes contained pathology-confirmed disease. Of the more than 80 subjects enrolled in the NEO3-06 trial, 39 subjects were determined to have pathology-positive lymph nodes. Results demonstrated that Lymphoseek correctly identified 38 of these 39 patients, for an overall False Negative Rate (FNR) of 2.56%. This was statistically significant ($p=0.0205$) against the statistical threshold for success. These findings indicate that Lymphoseek accurately identified SLNs in these trial subjects, and is likely to be

predictive of overall node pathology status. FNR is the rate of occurrence of negative test results in subjects known to have the disease for which the individual is being tested. Moreover, multiple level nodal dissection of patients in the trial with cancer-positive lymph nodes led to an average removal of 38 lymph nodes per patient, whereas Lymphoseek on average led to the removal of approximately 4 lymph nodes, representing a substantial reduction in potential morbidity for patients with head and neck cancer undergoing single lymph node biopsy.

Secondary endpoints for the NEO3-06 trial were the determination of sensitivity, negative predictive value (NPV) and overall accuracy of Lymphoseek relative to the pathology status of non-SLNs; and determination of the detection rate of SLNs by Lymphoseek and rate of tumor detection in non-SLNs. Lymphoseek demonstrated a sensitivity rate of 97.6%, an NPV of 97.8% and overall accuracy of 98.8%. No differences were observed in the ability of Lymphoseek to detect SLNs between same-day or subsequent-day injection and surgery. The trial also evaluated safety through observation of adverse events, clinical laboratory tests, vital signs, electrocardiograms and physical examinations. There were no deaths associated with the trial. Of 13 serious adverse events, none were determined to be related to Lymphoseek and no adverse events led to discontinuation from the trial.

"Comparison of false negative rates and overall accuracy of sentinel lymph node biopsy in Phase 3 99m-Tc-tilomanocept vs. ACOSOG-Z0360 99m-Tc-sulfur colloid in head/neck squamous cell carcinoma."

Francisco J. Civantos, MD, FACS, University of Miami School of Medicine, Miami, Fla., was lead author on a second presentation that compared Lymphoseek performance data from the Phase 3 NEO3-06 clinical trial with published data from the ACOSOG Z-0360 trial, which was conducted using radiolabeled sulfur colloid. Lymphoseek identified sentinel lymph nodes (SLNs) in subjects with squamous cell carcinoma of the head or neck (SCC) with a False Negative Rate (FNR) of 2.56% and sulfur colloid demonstrated an FNR of 9.8%. Lymphoseek identified SLNs with an overall accuracy of 99%, whereas the overall accuracy of sulfur colloid was 97%. There was no difference between SLN procedures performed with Lymphoseek on the same day as injection versus procedures that were conducted the following day, more than 15 hours after injection.

About the Lymphoseek Phase 3 Clinical Trial (NEO3-06) in Head and Neck Cancer

Navidea's Phase 3 clinical trial (NEO3-06) of Lymphoseek was a prospective, open-label, multicenter, within-patient study of Lymphoseek® (technetium Tc 99m tilmanocept) Injection. It was designed to identify sentinel lymph nodes (SLNs) and determine the false negative rate (FNR) associated with Lymphoseek-identified SLNs relative to the pathological status of non-SLNs in head and neck and intraoral squamous cell carcinoma. The NEO3-06 study was a supplement to previously conducted Phase 3 trials of Lymphoseek in breast cancer and melanoma that were designed to establish Lymphoseek as an effective radiopharmaceutical agent for use in lymphatic mapping procedures to identify the lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. Those studies formed the basis of the NDA registration package upon which the U.S. Food and Drug Administration based its approval of Lymphoseek in March, 2013. Navidea conducted the NEO3-06 clinical study to provide evidence of Lymphoseek performance in a third cancer type and to potentially enhance and expand its product label.

Navidea previously announced top-line, interim results from the NEO3-06 trial in April, 2013.

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. (NYSE MKT:NAVB) is a biopharmaceutical company focused on the development and commercialization of precision diagnostics and radiopharmaceutical agents. Navidea is actively developing four radiopharmaceutical agent platforms – Lymphoseek®, NAV4694, NAV5001 and RIGScan™ – to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making and, ultimately, patient care. Navidea's first commercial agent, Lymphoseek, was approved the U.S. 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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