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Navidea Biopharmaceuticals Announces NIH Grant Award to UC San Diego for Clinical Study Evaluating Tc99m Tilmanocept as a Kidney Imaging Agent

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE American: NAVB) (“Navidea” or the “Company”), a company focused on the development of precision immunodiagnostic agents and immunotherapeutics, today announced the granting of a National Institutes of Health (“NIH”) award to the University of California San Diego School of Medicine for the proposal entitled, “Renal Molecular Imaging of Mesangial Cell Function with Tc-99m-Tilmanocept.” The award (Project Number: 1R01DK127201-01), from the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH, was granted to Co-Principal Investigators UC San Diego faculty Carl Hoh, MD and David Vera, PhD, of the Department of Radiology, and Charles Ginsberg, MD, MAS, of the Department of Medicine, Division of Nephrology.

The worldwide prevalence of diabetes is expected to increase to 642 million within two decades. Approximately 40% of people with diabetes will go on to develop diabetic nephropathy (“DN”) – a form of chronic kidney disease (“CKD”). Typically, diabetic nephropathy develops relatively slowly over the course of decades, as indicated by slow increases in certain serum and urine markers over time. The current standard-of-care for monitoring the development of CKD is periodic assessment of these aforementioned markers. However, twenty percent of diabetic patients who develop CKD experience a more rapid development of DN. Consequently, there is an unmet medical need for routine surveillance during the first decade of CKD.

In this Phase 1 clinical study being conducted at UC San Diego Health, Tc99m tilmanocept will be used as an imaging agent to evaluate a key component of the kidneys, the mesangial cells, as a biomarker for diabetic nephropathy. The molecular target for Tc99m tilmanocept, CD206, is expressed on these mesangial cells of the kidney. The expansion of mesangial cells is an early hallmark of diabetic nephropathy, and the ability to reliably image them noninvasively could provide an important tool for physicians to evaluate diabetic patients for early signs of the disease.

This trial will be an open-label study investigating the biodistribution at two dose levels (2.0 and 20 nmol) of Tc99m tilmanocept. Four groups of patients at each dose (10 subjects each), will be studied: 1) No CKD, 2) early CKD, 3) moderate CKD, and 4) advanced CKD. Within each group, 50% of participants will have diabetes. Expected results include kidney image sets and biodistribution of Tc99m tilmanocept that reflects pathology. This study is a necessary step toward FDA approval of Tc99m tilmanocept as a kidney imaging agent.

From the proposal's Public Health Relevance Statement: "This proposal will use kidney SPECT/CT of Tc-99m-tilmanocept to evaluate the mesangial changes seen in diabetics across the spectrum of kidney disease as well as persons with hypertensive kidney disease, the next most common cause of kidney disease in patients with diabetes. We aim to demonstrate that these different disease types and stages can be differentiated with Tc-99m-tilmanocept SPECT/CT and can thus be used for future trials evaluating early diagnosis and treatment of diabetic nephropathy."

Dr. David Vera, Co-Principal Investigator, said, "Our goal is a simple 'first-line' diagnostic tool for nephrologists to determine which of their patients with diabetes are at risk of chronic kidney disease." Dr. Hoh added, "an additional potential benefit to a Tc-99m-tilmanocept kidney imaging study may be an additional modality for screening of renal cancer." Dr. Ginsberg stated, "considering the increasing armament of drugs to combat diabetic nephropathy, an imaging study that can diagnose this disease early in its course has tremendous therapeutic implications."

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, "We are pleased that the NIH has funded this important Phase 1 study at UC San Diego, run in part by the inventor of tilmanocept, Dr. David Vera." Dr. Rosol continued, "Navidea has had a long and productive relationship with Dr. Vera and his collaborators at UC San Diego, and we will be keenly watching for the results of this study addressing this area of large unmet clinical need. Today's announcement exemplifies the broad reach of our tilmanocept platform. The development pipeline remains robust and we are excited to continue developing new and valuable applications for our core technology."

Dr. Vera, together with Drs Anne Wallace and Carl Hoh, developed Tc99m tilmanocept at UC San Diego Moores Cancer Center as an agent to help detect and map cancers that have reached the lymph nodes. Cancer clinical trials showed that it better detected cancer and provided more accurate staging.

About Navidea

Navidea Biopharmaceuticals, Inc. (NYSE American: NAVB) is a biopharmaceutical company focused on the development of precision immunodiagnostic agents and immunotherapeutics. Navidea is developing multiple precision-targeted products based on its Manocept™ platform to enhance patient care by identifying the sites and pathways of disease and enable better diagnostic accuracy, clinical decision-making, and targeted treatment. Navidea's Manocept platform is predicated on the ability to specifically target the CD206 mannose receptor expressed on activated macrophages. The Manocept platform serves as the molecular backbone of Tc99m tilmanocept, the first product developed and commercialized by Navidea based on the platform. 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.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We have based these forward-looking statements largely on our

current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements include our expectations regarding pending litigation and other matters. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: our history of operating losses and uncertainty of future profitability; the final outcome of any pending litigation; our ability to successfully complete research and further development of our drug candidates; the timing, cost and uncertainty of obtaining regulatory approvals of our drug candidates; our ability to successfully commercialize our drug candidates; dependence on royalties and grant revenue; our ability to implement our growth strategy; anticipated trends in our business; our limited product line and distribution channels; advances in technologies and development of new competitive products; our ability to comply with the NYSE American continued listing standards; our ability to maintain effective internal control over financial reporting; the impact of the current coronavirus pandemic; and other risk factors detailed in our most recent Annual Report on Form 10-K and other SEC filings. You are urged to carefully review and consider the disclosures found in our SEC filings, which are available at http://www.sec.gov or at http://ir.navidea.com.

Investors are urged to consider statements that include the words “will,” “may,” “could,” “should,” “plan,” “continue,” “designed,” “goal,” “forecast,” “future,” “believe,” “intend,” “expect,” “anticipate,” “estimate,” “project,” and similar expressions, as well as the negatives of those words or other comparable words, to be uncertain forward-looking statements.

You are cautioned not to place undue reliance on any forward-looking statements, any of which could turn out to be incorrect. We undertake no obligation to update publicly or revise any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this report. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements.

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