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Navidea Biopharmaceuticals Announces Acceptance of Therapeutics Focused Abstract for Presentation at the Frontiers in Cancer Immunotherapy Symposium

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 that the results from the Company's preclinical studies of its targeted cancer immunotherapeutic agent will be presented as a poster at the New York Academy of Science's (NYAS) Frontiers in Cancer Immunotherapy Symposium 2021. The poster is titled, "Targeted Delivery of Doxorubicin (DOX) to Tumor Associated Macrophages (TAMs) Beneficially Alters the Tumor Immune Microenvironment and Synergizes the Activity of Anti-CTLA4."

In these studies, Navidea's CD206-targeted therapeutic construct containing doxorubicin linked to its mannosylated dextran backbone (Man-Dox) demonstrated the ability to drive phenotypic change in immune cells towards an activated pro-inflammatory and cell-killing state *in vitro* and, in conjunction with an approved immunotherapeutic, demonstrated a synergistic effect on tumor growth inhibition in a relevant animal model. The cellular target of Navidea's Man-Dox agent is the macrophage mannose receptor, CD206. CD206 is expressed on TAMs that play a critical role in regulating the tumor microenvironment and which provide a target for immunotherapies to rally the body's own immune system in the fight against cancer.

In *in vitro* studies, treatment of human macrophages with Man-Dox drove macrophages from an immunosuppressive phenotype to an immune stimulatory, pro-inflammatory state. In mouse experiments using the syngeneic CT26 tumor model, Man-Dox, in combination with anti-CTLA4 therapy, showed a significant reduction in tumor growth compared to treatments with either agent alone or with free doxorubicin. Anti-CTLA4 improves anti-tumor immune responses by blocking a check point inhibitor that prevents stimulation of adaptive immune cells by pro-inflammatory macrophages. These new findings support Navidea's hypothesis that driving the TAM phenotype towards a pro-inflammatory state with Man-Dox in concert with an approved immunotherapy provides a synergistic effect on tumor cell killing. These results demonstrate that Navidea's targeted Man-Dox construct can improve the efficacy of an existing immunotherapy and support further studies to help define optimal dosing strategies to maximize this synergistic effect.

This year's conference will be virtual and will take place from May 12th through May 14th. Navidea's presentation will provide a more detailed look at analysis of these data.

Information regarding registration for the symposium can be found on the NYAS website

([link here](#)).

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, “We are delighted by the recognition of the importance of our preclinical results by the symposium committee and the opportunity to present our results at this internationally recognized meeting.” Dr. Rosol continued, “This important work demonstrates both a mechanism of action as well as efficacy in relevant *in vitro* and *in vivo* model systems. These positive results help lay the foundation for moving forward into an FDA IND application followed by first in human studies.”

Jed Latkin, Navidea’s Chief Executive Officer, said, “This is truly a tribute to the many hours of hard work spent by our dedicated team to hone in on a compound that shows remarkable design, enabling this and future pre-clinical clinical work.”

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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