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Navidea Biopharmaceuticals Announces the Notice of Allowance for U.S. Patent Application for Key Component of the Company's Cancer Immunotherapy Pipeline

Targeted therapeutics designed to alter the behavior of macrophages to rally the body's immune response against tumors

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 it has received a Notice of Allowance from the U.S. Patent and Trademark Office for its patent application titled, "Compositions And Methods For Altering Macrophage Phenotype (US Application #16/832,620)." Broadly, this patent covers the ability of Navidea's constructs to stimulate the body's immune response against tumors through targeted delivery of payloads (e.g., doxorubicin, paclitaxel, and bisphosphonates) that change the nature of macrophages to make them more proinflammatory. These constructs have demonstrated the ability to rally an immune response against tumors and make other therapies work more effectively against those tumors in preclinical studies. If confirmed in clinical trials, the ability to increase the efficacy of cancer therapeutics by harnessing the body's immune system could bring significant benefits to patients.

The Notice of Allowance concludes the substantive examination of the patent application and is expected to result in the issuance of a U.S. patent after administrative processes are completed. When issued, this patent will protect key elements of Navidea's cancer immunotherapy product pipeline. Navidea's cancer immunotherapy product pipeline consists of a series of mannosylated-amine dextrans ("MADs") that carry small molecule drug payloads that are attached to MADs by degradable linkers. The MADs bind to CD206 receptors on tumor associated macrophages ("TAMs") and related cells such as dendritic cells and myeloid derived suppressor cells. The degradable linkers are designed to release their small molecule payloads inside the CD206 expressing cells. The small molecule payloads are designed to induce proinflammatory behaviors in these cells.

In tumors, TAMs and their cellular relatives create an immunosuppressive tumor environment that prevents other types of immune cells from attacking cancer cells, thus permitting cancer cells to survive and grow. In addition, this immunosuppressive tumor environment decreases the effectiveness of a wide variety of other cancer therapies, including other cancer immunotherapies. Navidea's MAD-based cancer immunotherapies alter the behavior of macrophages to make them less immunosuppressive and more

proinflammatory, or antitumor. Studies in mouse models of cancer have shown that Navidea's MAD-based immunotherapies can enhance the effectiveness of other cancer immunotherapies and significantly reduce tumor growth. The results of these studies have been presented at the New York Academy of Sciences (2021), the Tumor Myeloid-Directed Therapies meeting (2022), and at the 2022 annual meeting of the Society for Immunotherapy of Cancer.

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, "We are excited about this development that significantly improves our valuable therapeutics intellectual property and strategic partnership potential. This important patent application covers key intellectual property critical to the continued development of our therapeutics pipeline. Our targeted cancer immunotherapeutics have the potential to address the large unmet medical need in oncology, improve the lives of a great number of individuals, and bring significant value to Navidea's shareholders."

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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