

February 7, 2022



Navidea Biopharmaceuticals Announces Research Agreement with the University of Pennsylvania Evaluating Tc99m Tilmanocept as a Prognostic Marker for Glioblastoma

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 signing of a Sponsored Research Agreement with the University of Pennsylvania ("Penn") for a project to evaluate the use of Tc99m tilmanocept imaging in glioblastoma as a prognostic agent for tumor growth rate and overall survival. The research is led by Principal Investigator Ali Nabavizadeh, MD, of the Department of Radiology in the Perelman School of Medicine at Penn.

Glioblastoma ("GBM") is the most aggressive and most common primary central nervous system tumor in adults and there is an urgent need for new therapies. Macrophages play an important role in tumor biology. They are a major population of non-cancer cells in GBM, representing as many as half of all cells in some cases. These Tumor Associated Macrophages ("TAMs") may then be a viable target for tumor therapies or serve as a biomarker for monitoring tumor status.

Broadly, active macrophages can be of a tumor suppressing type (M1 macrophages) or of a tumor promoting type (M2 macrophages). The TAMs are typically M2-like and are known to express high levels of CD206, the macrophage mannose receptor that Tc99m tilmanocept targets. This research has as its hypothesis that the M2 TAMs in GBM can be imaged with Tc99m tilmanocept, and that this imaging can serve as a predictive tool for outcome with and without use of an immunotherapy that works in part to change the M2-like macrophage population to a more M1-like state, promoting tumor killing.

In these preclinical studies, Tc99m tilmanocept imaging will be evaluated in correlation with tumor growth rate, and in separate studies Tc99m tilmanocept imaging will be performed before and after anti-interleukin-6 therapy, which has been shown to promote TAM switching from the M2 to M1 state. Study endpoints will include quantitative imaging compared to pathology and overall survival.

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, "We are pleased to sponsor this important work with Dr. Nabavizadeh at Penn. This is another in a line of research collaborations we have had with the highest level of researchers at top tier institutions." Dr. Rosol continued, "Today's announcement exemplifies the broad reach of our tilmanocept

platform. The development of applications of Tc99m tilmanocept as a prognostic biomarker in cancers could have far-reaching implications for monitoring patient treatment and making decisions about therapeutic benefit. We are excited to continue to develop new and valuable applications for our core technology.”

“TAMs are a very important component of immune microenvironment in GBM, and it is crucial to have reliable imaging biomarkers to quantify and monitor TAMs during the course of treatment,” Dr. Nabavizadeh said. “The advantage of Tc99m tilmanocept is that it is already being used in patients for another research indication which means that we can move forward to human GBM patients under an Investigational New Drug Application (IND) if our preclinical studies show promising results.”

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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Source: Navidea Biopharmaceuticals, Inc.