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Navidea Biopharmaceuticals Announces Opening of Nine New Sites in its Pivotal Phase 3 Trial in Rheumatoid Arthritis and Termination of Binding Memorandum of Understanding with Jubilant Radiopharma

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 opening of nine additional sites for recruitment into its pivotal NAV3-33 Phase 3 clinical trial titled "Evaluation of Tc 99m Tilmanocept Imaging for the Early Prediction of Anti-TNF α Therapy Response in Patients with Moderate to Severe Active Rheumatoid Arthritis (RA)." A total of 12 sites open for the NAV3-33 study will enable faster patient enrollment and data gathering.

This Phase 3 trial will establish the ability of Tc99m tilmanocept imaging to serve as an early predictor of treatment response in rheumatoid arthritis ("RA") patients switching to an anti-TNF α therapy. Trial details are posted on clinicaltrials.gov.

RA is a serious and potentially debilitating disease. The standard practice of treating RA is to monitor patients initiating new RA therapies over a course of three to six months and, in those patients for which the new therapies prove to be ineffective, to change their treatments to an alternative therapy with a different mechanism of action. This trial-and-error process of appropriate treatment selection may take several months to more than a year to arrive at an adequate treatment for any RA patient. Imaging with Tc99m tilmanocept, a synthetic molecule with high affinity to CD206 receptors expressed on activated macrophages, offers the potential to provide an early predictor of clinical response by providing an objective, quantifiable readout of changes in macrophage density in the joints of patients undergoing initiation or change of therapy. These macrophage density changes may be observable weeks before disease modification can be detected with standard clinical assessments and are predictive of treatment response.

Tilmanocept imaging could provide rheumatologists and those suffering with RA a noninvasive, quantifiable, early indicator of whether or not an anti-TNF α treatment is working, and this could bring enormous benefit to these patients by assisting physicians in putting them on the right course of treatment earlier than is currently possible.

The Company also announced the termination of the Memorandum of Understanding ("MOU") with Jubilant Radiopharma, originally signed on August 9, 2020. The MOU with Jubilant Radiopharma outlined the terms and framework for an Exclusive License and Distribution Agreement for Navidea's diagnostic imaging agent Tc99m tilmanocept

(technetium Tc99m tilmanocept injection) in the United States, Canada, Mexico, and Latin America. In connection with the MOU, Jubilant Radiopharma also made a \$1 million equity investment in exchange for a limited exclusivity period. Since the original signing of the MOU, Navidea has advanced Tc99m tilmanocept for indications in RA through its Phase 2B proof of concept trial and into the currently enrolling Phase 3 trial as well as the Phase 2B tilmanocept joint localization to joint biopsy study.

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, “We have generated significant data in support of our hypotheses that Tc99m tilmanocept can provide early prediction of treatment response to anti-TNF α therapy in RA, and we look forward to completion of the RA trials. The additional new sites we have opened will help significantly in this process.” Dr. Rosol continued, “Moving forward unencumbered by the exclusivity agreement, we now have the opportunity to discuss partnerships with other companies whose long-term interests align with our global business development strategy as we continue to advance towards U.S. Food and Drug Administration New Drug Application submission and beyond.”

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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