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Navidea Biopharmaceuticals Announces Launch of Phase 3 Clinical Trial in Rheumatoid Arthritis

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 launch of the NAV3-33 Phase 3 clinical trial titled “Evaluation of Tc99m Tilmanocept Imaging for the Early Prediction of Anti-TNFα Therapy Response in Patients with Moderate to Severe Active Rheumatoid Arthritis (RA).”

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-TNFα therapy. Trial details will be posted to clinicaltrials.gov.

Rheumatoid Arthritis 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.

The data from the Company’s completed NAV3-31 Phase 2b trial demonstrated that Tc99m tilmanocept can provide robust, quantitative imaging in both healthy controls and in patients with active RA, and that this imaging is reproducible and can define joints with and without RA-involved inflammation. The Phase 2b also provided evidence in support of the hypothesis that Tc99m tilmanocept can provide an early prediction of treatment efficacy in patients switching to an anti-TNFα therapy.

The design of the Phase 3 trial is built upon insights and data from this completed Phase 2b study, as well as input from the recent End of Phase 2 Type B meeting with the FDA. The NAV3-33 Phase 3 trial will involve Tc99m tilmanocept imaging in patients with RA who are about to begin an anti-TNFα therapy. Planar (two-dimensional) images of the hands and wrists taken at baseline prior to initiation of therapy and at week 5 following start of therapy will be quantitatively evaluated to assess changes in Tc99m tilmanocept signal localization, if any, in order to predict treatment response or non-response as determined by standard

clinical assessments at three and six months post therapy start.

Dr. Michael Rosol, the Company's Chief Medical Officer, said, "This is a critical milestone in our RA program and for the Company as a whole. Throughout this program's development, we have worked closely with expert rheumatologists and nuclear medicine specialists, and we believe we are on the right path to bringing a valuable tool to bear to meet a large unmet medical need in patients with RA." Dr. Rosol continued, "Success would mean that we can provide rheumatologists and those suffering with RA a noninvasive, quantifiable, early indicator of whether or not an anti-TNFα treatment is working. This could bring enormous benefit to these patients by assisting physicians in putting them on the right course of treatment earlier than is possible today."

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 fact that the valuation by LifeSci Partners of our Tc99m tilmanocept pipeline product is subject to and based on numerous assumptions about the commercial success of the product, expected associated costs, and the outcome of various risks, including the outcome of clinical trials, that could affect the timetable for revenues, among other assumptions, that actual outcomes are likely to vary from such assumptions, resulting in variations from the possible results set forth in the valuation report; 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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