September 15, 2022

Navidea Biopharmaceuticals Announces Presentation of Results from its Two Phase 2B Clinical Trials in Rheumatoid Arthritis at Upcoming American College of Rheumatology Annual Meeting

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 completed NAV3-31 Phase 2B clinical study as well as the preliminary results of its ongoing NAV3-32 Phase 2B study have been accepted for presentation as posters at the Annual Meeting of the American College of Rheumatology (“ACR”), to be held November 10-14, 2022 in Philadelphia, PA (virtual and in person) (“ACR Convergence 2022”).

In the completed NAV3-31 Phase 2B study (NCT03938636) titled “Evaluation of the Precision and Sensitivity of Tilmanocept Uptake Value (TUV) on Tc99m Tilmanocept Planar Imaging” (Abstract #1977), 30 rheumatoid arthritis (“RA”) patients with active RA set to start anti-tumor necrosis factor alpha (“TNFα”) therapy were enrolled and followed for 24 weeks. Tc99m tilmanocept (“TIL”) imaging performed at baseline and week 5 following therapy initiation had high overall accuracy at predicting American College of Rheumatology 50 (“ACR50”) clinical response at 12 and 24 weeks (27/30 and 24/28 subjects, respectively) after therapy start. TIL imaging demonstrated high specificity (0.96 at weeks 12 and 24), positive predictive value (0.75 and 0.67, respectively), and negative predictive value (0.92 and 0.88, respectively), and the combination of TIL imaging data with serological and clinical markers in a multivariate model gave an area under the curve of 0.95 for prediction of response at week 24. These results indicate that marked changes in TIL uptake by week 5 presage clinical efficacy evaluations at week 12 and week 24 of treatment and demonstrate that TIL imaging can provide quantifiable imaging assessment of RA-involved joints that enables an objective, early prediction of clinical response.

In the ongoing NAV3-32 Phase 2B study (NCT04078191) titled, “A Comparison of Tc99m Tilmanocept Quantitative Imaging With Immunohistochemical (IHC) Analysis of CD206 Expression in Synovial Tissue From Subjects Clinically Diagnosed With Rheumatoid Arthritis (RA)” (Abstract #1979), the primary objective is to assess the relationship between joint-specific TIL uptake and the pathobiology of RA-involved joint tissue. Preliminary results on the first eleven patients indicates that quantitative TIL uptake in the hands and wrists of patients is proportional to the amount of macrophage involvement in an individual RA patient’s joint inflammation. The cellular composition of RA-inflamed joints is known to vary between patients and is frequently separated into one of three pathotypes: fibroid, diffuse

myeloid, and lympho-myeloid. Knowledge of an individual RA patient's pathotype may be clinically important because it may predict to which RA therapy a patient is likely to respond. Imaging with TIL, a high affinity ligand to CD206 expressed on activated macrophages, offers the potential to distinguish between pathotypes without need of invasive biopsy. In these preliminary results, TIL uptake in RA-inflamed joints was able to discretely differentiate patients with the fibroid pathotype (i.e., low macrophage involvement) from those having either the diffuse myeloid or lympho-myeloid pathotypes of RA (i.e., higher macrophage involvement). This could have significant implications for decision making onto which therapy a patient is placed.

Overall, data from these two studies supports the hypothesis that TIL imaging has the potential to provide rheumatologists and those suffering with RA a noninvasive, quantifiable, early indicator of whether or not an anti-TNFα treatment is working or likely to work. This could bring significant benefit to these patients by assisting physicians in putting them on the right course of treatment earlier than is currently possible.

Abstracts and presentation session information can be found on the ACR Annual Meeting website at:

https://acrabstracts.org/abstract/tc99m-tilmanocept-imaging-predicts-clinical-response-in-rheumatoid-arthritis-patients-beginning-new-anti-tnf%ce%b1-therapy/

and

https://acrabstracts.org/abstract/tc99m-tilmanocept-imaging-can-differentiate-the-fibroid-pathotype-of-rheumatoid-arthritis-from-non-fibroid-pathotypes-in-patients/

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, "We are delighted by the opportunity to present these results with our collaborators at this internationally recognized meeting." Dr. Rosol continued, "As we continue to enroll both in the NAV3-32 TIL imaging-to-biopsy study as well as the NAV3-33 Phase 3 study in RA, this is the type of external validation of our work that reflects the recognized medical need for a robust, objective, noninvasive means of predicting clinical response to anti-TNFα therapies."

RA is a chronic disease affecting over 1.3 million Americans and as much as 1% of the worldwide population[1]. If the product is successfully developed, Navidea would expect to play a major role in the management of RA patients worldwide.

Reference

1. https://www.rheumatoidarthritis.org/ra/facts-and-statistics/

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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