

April 20, 2022



# Navidea Biopharmaceuticals Announces Positive Preliminary Results of Its Ongoing Phase 2B Study Comparing Tc99m Tilmanocept Imaging with Histopathology of Joints from Patients with Rheumatoid Arthritis

*Data support hypothesis that Tc99m tilmanocept imaging can differentiate fibroid pathotype of rheumatoid arthritis from non-fibroid pathotypes*

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 preliminary results from the ongoing NAV3-32 Phase 2B study 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)." Preliminary results on the first eleven patients indicates that quantitative Tc99m tilmanocept uptake in the hands and wrists of patients is proportional to the amount of macrophage involvement in an individual rheumatoid arthritis ("RA") patient's joint inflammation. Additionally, Tc99m tilmanocept 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).

The primary objective of this study is to assess the relationship between joint-specific tilmanocept uptake values and the pathobiology of RA-involved joint tissue. This is being accomplished by taking biopsy samples from joints of patients with RA following imaging with Tc99m tilmanocept. The images are being evaluated using Navidea's proprietary imaging analysis method to determine the amount of Tc99m tilmanocept uptake in the joint to be biopsied. The biopsy tissues are being evaluated by a pathologist using immunohistochemical ("IHC") staining to determine the cellular composition, including macrophage content, in the inflammatory tissue of the RA-involved joint. The cellular composition of RA-inflamed joints is known to vary between patients and is frequently separated into one of three pathotypes termed 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. It is Navidea's hypothesis that the imaging signal will correlate with the number and density of activated macrophages in the joints of RA patients, and that this imaging signal can provide important information about not only the disease status of the patient, but also indicate which pathotype of RA that

the patient has. Enrollment is to continue until a minimum of four patients of each of the three pathotypes- fibroid, diffuse myeloid, and lympho-myeloid- have been enrolled and had both assessable imaging and biopsy performed.

At the current time, a total of eleven patients have had Tc99m tilmanocept imaging followed by synovial tissue biopsy in an inflamed joint of their hands or wrists. Quantitative image analysis was performed prior to biopsy. Image analyses conducted before the biopsies has been able to separate the subjects into at least 2 distinct and nonoverlapping classes of subjects. Seven of the subjects had relatively lower levels of Tc99m tilmanocept uptake. All seven of these subjects were found to have the fibroid pathotype. Of the remaining 4 subjects, 3 had the diffuse myeloid pathotype and 1 had the lympho-myeloid pathotype. Furthermore, those subjects with either the diffuse myeloid or lympho-myeloid pathotypes had, on average, more than 3 times more Tc99m tilmanocept uptake as the average subject with the fibroid pathotype. The pathologist who evaluated these biopsies was blinded to the imaging results prior to completing their report. These early results support the hypothesis that those patients with low levels of Tc99m tilmanocept localization in their hand and wrist joints have the fibroid pathotype of RA, and those with higher levels of localization are representative of one of the other two pathotypes.

Dr. Michael Rosol, Chief Medical Officer for Navidea, said, “We are encouraged by these preliminary results. They support one of our main hypotheses- that the joints of patients with the pathotype of RA involving low levels of synovial macrophages, the fibroid pathotype, have low levels of Tc99m tilmanocept uptake, while those with the other pathotypes have relatively higher levels.” Dr. Rosol continued, “We believe that this Phase 2B study is critical for establishing the definitive relationship of our imaging readout to the underlying pathobiology of an RA-involved joint, as well as to assess our hypothesis that we can use Tc99m tilmanocept imaging to classify RA subtype. This information may further assist physicians to determine what type of therapy might be most beneficial for a given patient earlier and more noninvasively than is currently possible. This study will also be important for us as we seek to achieve qualification with the FDA of CD206 as a biomarker for RA.”

The Company will hold a business update conference call today, Wednesday, April 20, 2022, at 5:00 p.m. (EDT). Chief Medical Officer Dr. Michael Rosol will host the call and webcast.

To participate in the first call and webcast, please refer to the information below:

Event: Navidea Business Update – Company Strategy and Clinical Update

Date: Wednesday, April 20, 2022

Time: 5:00 p.m. (EDT)

U.S. & Canada Dial-In: 877-407-0312

International Dial-In: +1 201-389-0899

Conference ID: 13729076

Webcast Link: <https://www.webcast-eqs.com/navidbioph20220420/en>

A live audio webcast of the conference call will also be available on the investor relations page of Navidea’s corporate website at [www.navidea.com](http://www.navidea.com). In addition, the recorded conference call can be replayed and will be available for 90 days following the call on Navidea’s website.

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

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](http://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 ability to obtain additional financing; our ability to continue as a going concern; 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>.

These forward-looking statements include, but are not limited to, statements about preliminary data from Navidea's ongoing clinical trials. Data from the NAV3-32 Phase 2B clinical trial are preliminary and will require confirmation in additional patients as well as further analyses to draw any clinical conclusion. Preliminary data from Navidea's clinical trials that it announces or publishes from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in

material changes in the final data.

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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