UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 12 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (date of earliest event reported): December 14, 2021

NAVIDEA BIOPHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-35076	31-1080091
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

4995 Bradenton Avenue, Suite 240, Dublin, Ohio	43017
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code (614) 793-7500

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, par value $.001 per share	NAVB	NYSE American

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934.

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 1.02 Termination of a Material Definitive Agreement.

On December 15, 2021, Navidea Biopharmaceuticals, Inc. (the "Company") issued a press release announcing that it had terminated that certain Stock Purchase Agreement, dated August 30, 2020, by and between the Company and each of the investors named therein, effective December 14, 2021. A copy of the Company's December 15, 2021 press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 8.01 Other Events.

On December 15, 2021, the Company issued a press release announcing that it had achieved full enrollment in its NAV3-35 Phase 2b normative database clinical study. A copy of the Company's December 15, 2021 press release is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

On December 16, 2021, the Company issued a press release announcing that it had received approval to launch its pivotal NAV3-33 Phase 3 clinical study in rheumatoid arthritis. A copy of the Company's December 16, 2021 press release is furnished as Exhibit 99.3 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(a) Not applicable.

(b) Not applicable.

(c) Not applicable.

(d) Exhibits

Exhibit No.	**Description**
99.1	Press Release dated December 15, 2021
99.2	Press Release dated December 15, 2021
99.3	Press Release dated December 16, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Navidea Biopharmaceuticals, Inc.

Date: December 16, 2021

By: */s/ Michael S. Rosol*
Michael S. Rosol, Ph.D.
Senior Vice President and Chief Medical Officer

Exhibit 99.1

Navidea Biopharmaceuticals Terminates Stock Purchase Agreement

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 it has terminated the Stock Purchase Agreement that was executed on August 30, 2020.

On August 30, 2020, the Company entered into a Stock Purchase Agreement with each of the investors named therein (the "Investors"), pursuant to which the Investors agreed to purchase from the Company up to $25.0 million in shares of the Company's common stock, par value $0.001 per share ("Common Stock"). The initial closings of the sale and purchase of the Common Stock (collectively, the "Initial Closing") were to occur within forty-five (45) business days after the date on which the Company's application to the NYSE American for the listing of the Common Shares for trading thereon was approved by the NYSE American. The Investors agreed to purchase an aggregate of 1,000,000 shares of Common Stock at the Initial Closing at a purchase price of $5.00 per share. To date, we have received only $25,000 of the $5.0 million that was due at the Initial Closing. On December 14, 2021, the Company notified the Investors that it was terminating the Stock Purchase Agreement in accordance with its terms.

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.

Investor Relations Contact

Navidea Biopharmaceuticals, Inc.
Jeffrey Smith
Vice President of Operations
614-822-2365
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Navidea Biopharmaceuticals Completes Full Enrollment in Phase 2b Normative Database Study to Support its Rheumatoid Arthritis Program

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 it has achieved full enrollment in its NAV3-35 Phase 2b clinical study titled "Development of a Normative Database for Rheumatoid Arthritis (RA) Imaging with Tc99m Tilmanocept."

Establishing a healthy subject database is necessary to create a quantitative method for determining RA-involved inflammation in joints. The NAV3-35 Phase 2b clinical trial accomplishes this goal. The trial has two arms, with Arm 1 designed to acquire hand and wrist planar (two-dimensional) images from healthy subjects that were age and sex-matched to the RA population and injected with Tc99m tilmanocept. Arm 2 is a pilot feasibility study to examine the potential of three-dimensional SPECT/CT imaging of the hands and wrists of healthy subjects and patients with RA injected with Tc99m tilmanocept. The main objective of the trial is to complete the healthy subject (normative) database in support of the Company's RA imaging commercial product development. A total of 120 healthy volunteers were enrolled in Arm 1. Enrollment is also finalized in Arm 2 of the study.

Tc99m tilmanocept attaches to mannose receptors (CD206) on macrophages that are frequently involved in RA joint inflammation. Relatively smaller numbers of CD206-expressing macrophages normally reside in the joints of healthy people without RA. An integral part of the ability to quantitatively discriminate RA-inflamed joints from those that do not have inflammation using Tc99m tilmanocept imaging is the knowledge of the distribution of Tc99m tilmanocept localization in healthy joints. The establishment of this database will enable improved accuracy of discrimination of RA-involved joints from non-RA inflamed joints and should have a positive impact on the ability to predict treatment response early, the primary indication the Company is pursuing in RA in the upcoming Phase 3 trial.

This database will also be used in the training of automated image analysis software to further improve the accuracy of the quantification of Tc99m tilmanocept localization in joints as well as the workflow for later commercialization in RA.

Dr. Michael Rosol, the Company's Chief Medical Officer, said, "We are pleased to have reached this important milestone in our RA program pipeline. This healthy subject normative database will allow us to define the parameters of what a normal joint looks like with Tc99m tilmanocept, and with that information we can improve upon the quantitative determination of RA-inflamed joints." Dr. Rosol continued, "This database will play an essential part in both the Phase 3 data analysis as well as commercial product. It will not only enable us to more accurately quantitate RA-involved inflammation but, along with the proprietary algorithm we use to read the images, it will serve as an additional barrier to entry for possible long-term competition. This is a critical step forward in the advancement of our RA program into the upcoming Phase 3 trial."

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Investor Relations Contact

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Exhibit 99.3

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 Tc 99m 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."

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