Filed Pursuant to Rule 424(b)(3)
Registration No. 333-256093

2,173,913 Shares of
Common Stock

This prospectus relates to the disposition from time to time of up to 2,173,913 shares of our common stock, $0.001 par value per share (the "*Shares*"), issuable upon conversion of shares of 50,000 shares of Series E Redeemable Convertible Preferred Stock, par value $0.001 (the "*Series E Preferred*), which are held by the selling stockholder named in this prospectus. We issued the Shares to the selling stockholder pursuant to a Stock Purchase Agreement and Letter of Investment Intent, dated March 2, 2021 (the "*Stock Purchase Agreement*"). We are registering the resale of the Shares as required by the Registration Rights Agreement we entered into with the selling stockholder on March 2, 2021 (the "*Registration Rights Agreement*").

The selling stockholder may resell or dispose of the Shares, or interests therein, at fixed prices, at prevailing market prices at the time of sale or at prices negotiated with purchasers, to or through underwriters, broker-dealers, agents, or through any other means described in the section of this prospectus entitled "Plan of Distribution." The selling stockholder will bear all commissions and discounts, if any, attributable to the sale or disposition of the Shares, or interests therein, held by the selling stockholder. We will bear all costs, expenses and fees in connection with the registration of the Shares. We will not receive any of the proceeds from the sale of the Shares by the selling stockholder.

Our common stock is listed on the NYSE American under the symbol "NAVB." On May 7, 2021, the last reported sale price of our common stock on the NYSE American was $1.62 per share. You are urged to obtain current market quotations for our common stock.

You should read this prospectus and any prospectus supplement, together with additional information described under the headings "Incorporation of Certain Documents by Reference" and "Where You Can Find More Information," carefully before you invest in any of our securities.

Investing in our securities involves a high degree of risk. See "Risk Factors" on page 9 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 24, 2021

TABLE OF CONTENTS

You should read this prospectus, including all documents incorporated herein by reference, together with additional information described under "Where You Can Find More Information."

You may obtain the information incorporated by reference without charge by following the instructions under "Where You Can Find More Information."

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. The selling stockholder may offer to sell, and seek offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock.

In this prospectus, "we," "us," "our" and "Navidea" refer to Navidea Biopharmaceuticals, Inc. and its subsidiaries.

ABOUT THIS PROSPECTUS

You should rely only on the information we have provided or incorporated by reference into this prospectus, any applicable prospectus supplement and any related free writing prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the Shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

The selling stockholder is offering the Shares only in jurisdictions where such issuances are permitted. The distribution of this prospectus and the issuance of the Shares in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the sale of the Shares and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, the Shares offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission (the "*SEC*"), under which the selling stockholder may offer from time to time up to an aggregate of 2,173,913 Shares in one or more offerings. If required, each time the selling stockholder offers Shares, we will provide you with, in addition to this prospectus, a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to that offering. We may also use a prospectus supplement and any related free writing prospectus to add, update or change any of the information contained in this prospectus or in documents we have incorporated by reference. This prospectus, together with any applicable prospectus supplements, any related free writing prospectuses and the documents incorporated by reference into this prospectus, includes all material information relating to this offering. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in a prospectus supplement. Please carefully read both this prospectus and any prospectus supplement together with the additional information described below under the section entitled "Incorporation of Certain Information by Reference" before buying any of the securities offered.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled "Where You Can Find More Information."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The Private Securities Litigation Reform Act of 1995 (the "*PSLRA*") provides a safe harbor for forward-looking statements made by or on behalf of the Company. Statements in this document which relate to other than strictly historical facts, such as statements about the Company's plans and strategies, expectations for future financial performance, new and existing products and technologies, anticipated clinical and regulatory pathways, the ability to obtain, and timing of, regulatory approvals of the Company's products, the timing and anticipated results of commercialization efforts, and anticipated markets for the Company's products, are forward-looking statements within the meaning of the PSLRA. The words "anticipate," "believe," "estimate," "expect," "future," "intend," "plan," "project," and similar expressions identify forward-looking statements that speak only as of the date hereof. Investors are cautioned that such statements involve risks and uncertainties that could cause actual results to differ materially from historical or anticipated results due to many factors including, but not limited to, our history of operating losses and uncertainty of future profitability, accumulated deficit, future capital needs, the outcome of any pending litigation, uncertainty of capital funding, dependence on royalties and grant revenue, limited product line and distribution channels, competition, risks of development of new products, our ability to maintain effective control over financial reporting, our ability to comply with NYSE American continued listing standards, and other risks set forth in our Form 10-K under Item 1A, "Risk Factors" and beginning on page 9 of this prospectus. Navidea undertakes no obligation to publicly update or revise any forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the impact of the global COVID-19 pandemic on our business, financial condition or prospects, including a decline in the volume of procedures using our products, potential delays and disruptions to global supply chains, manufacturing activities, logistics, operations, employees and contractors, the business activities of our suppliers, distributors, customers and other business partners, as well as the effects on worldwide economies, financial markets, social institutions, labor markets and healthcare systems;
- our history of operating losses and uncertainty of future profitability;
- 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, including delays and additional costs related to the ongoing COVID-19 pandemic;
- our ability to successfully commercialize our drug candidates, including delays or disruptions related to the ongoing COVID-19 pandemic;
- our ability to raise capital sufficient to fund our development programs, including unavailability of funds or delays in receiving funds as a result of the ongoing COVID-19 pandemic;
- delays in receipt of anticipated proceeds from our capital funding transactions and other receivables;
- our dependence on royalties and grant revenue;
- our limited product line and distribution channels;
- advances in technologies and development of new competitive products;
- our ability to maintain effective control over financial reporting;
- the outcome of any pending litigation;
- our ability to comply with NYSE American continued listing standards;
- our ability to register and maintain the registration of the shares issuable upon conversion of the Series E Preferred; and
- other risk factors set forth in this report and detailed in our most recent Annual Report on Form 10-K and other SEC filings.

You should carefully read this prospectus, the documents that we incorporate by reference into this prospectus and the documents we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this prospectus by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

PROSPECTUS SUMMARY

This summary highlights information contained in other parts of this prospectus or incorporated by reference into this prospectus from our filings with the U.S. Securities and Exchange Commission (the "SEC") listed in the section of the prospectus entitled "Incorporation of Certain Information by Reference." Because it is only a summary, it does not contain all of the information that should be consider before purchasing our securities in this offering and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere or incorporated by reference into this prospectus. You should read the entire prospectus, the registration statement of which this prospectus is a part, and the information incorporated by reference herein in their entirety, including the "Risk Factors" and our financial statements and the related notes incorporated by reference into this prospectus, before purchasing our securities in this offering. Unless the context requires otherwise, references in this prospectus to "the Company," "Navidea," "we," "us" and "our" refer to Navidea Biopharmaceuticals, Inc. together with its wholly owned subsidiaries, Navidea Biopharmaceuticals Europe Limited and Navidea Biopharmaceuticals Limited, and its majority-owned subsidiary, Macrophage Therapeutics, Inc.

The Company

Navidea Biopharmaceuticals, Inc. ("Navidea," the "Company," "we," "us" or "our"), a Delaware corporation (NYSE American: NAVB), is a biopharmaceutical company focused on the development and commercialization of precision immunodiagnostic agents and immunotherapeutics. Navidea is developing multiple precision-targeted products based on our Manocept™ platform to enhance patient care by identifying the sites and pathways of undetected 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. Other than Tc99m tilmanocept, which the Company has a license to distribute outside of Canada, Mexico and the United States, none of the Company's drug product candidates have been approved for sale in any market.

Our business is focused on two primary types of drug products: (i) diagnostic substances, including Tc99m tilmanocept and other diagnostic applications of our Manocept platform, and (ii) therapeutic development programs, including therapeutic applications of our Manocept platform. See Note 16 to the consolidated financial statements included in our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q for more information about our business segments.

Technology and Product Candidates

Our primary development efforts over the last several years were focused on diagnostic products, including Tc99m tilmanocept, which the Company has a license to distribute outside of Canada, Mexico and the United States. Our more recent initiatives have been focused on diagnostic and therapeutic line extensions based on our Manocept platform.

During the ongoing COVID-19 global pandemic, the Company's primary concern is the safety of its employees, the employees of its clinical trial sites, and the patients enrolled in its clinical trials. The Company is working hard to mitigate any safety risk along with any long-term impact on its clinical development programs. The spread of COVID-19 has impacted the global economy and our operations, including the interruption of our clinical trial activities in Europe. For example, the COVID-19 outbreak has delayed enrollment in our NAV3-32 clinical study in the United Kingdom due to national COVID-19-related shutdowns. Navidea has completed enrollment and imaging events in Arms 1, 2, and 3 of the Company's ongoing Phase 2b clinical trial (NAV3-31) and delivered interim data. The Company's pivotal Phase 3 trial for rheumatoid arthritis (NAV3-33) also remains on track for a second-half 2021 launch. The second Phase 2b trial (NAV3-32) correlating Tc99m tilmanocept uptake in rheumatoid arthritis ("RA")-involved joints with CD206 immunohistochemistry findings from synovial biopsies has received approval at both Northwestern University and in the United Kingdom and recruitment has begun at Northwestern University. In addition, the investigator-initiated Phase 2 cardiovascular ("CV") study is nearing completion at Massachusetts General Hospital. Results provided to date have paralleled data in our earlier published article, and these data are supportive of Navidea's hypothesis that tilmanocept can provide marked signal to background in a host of CV disease applications.

Manocept Platform - Diagnostics and Therapeutics Background

Navidea's Manocept platform is predicated on the ability to specifically target the CD206 mannose receptor expressed primarily on activated macrophages. This flexible and versatile platform serves as a molecular backbone for purpose-built targeted imaging molecules that may significantly impact patient care by providing enhanced diagnostic accuracy, clinical decision-making, and target-specific treatment. This CD206-targeted drug platform is applicable to a range of diagnostic modalities, including single photon emission computed tomography ("SPECT"), positron emission tomography ("PET"), gamma-scanning and intra-operative and/or optical-fluorescence detection, as well as delivery of therapeutic compounds that target macrophages, and their role in a variety of immune- and inflammation-involved diseases. The United States Food and Drug Administration ("FDA")-approved sentinel node/lymphatic mapping agent, Tc99m tilmanocept, is representative of the ability to successfully exploit this mechanism to develop powerful new products and to expand this technology into additional diagnostic and therapeutic applications.

Activated macrophages play important roles in many disease states and are an emerging target in many diseases where diagnostic uncertainty exists. Impairment of the macrophage-driven disease mechanisms is an area of increasing and proven focus in medicine. The number of people affected by all the inflammatory diseases combined is estimated at more than 40 million in the United States and up to 700 million worldwide, making macrophage-mediated diseases an area of remarkable clinical importance. There are many recognized disorders having macrophage involvement, including RA, atherosclerosis/vulnerable plaque, nonalcoholic steatohepatitis ("NASH"), inflammatory bowel disease, systemic lupus erythematosus, cancer generally including Kaposi's sarcoma ("KS"), leishmaniasis, and others that span general clinical areas in cancer immunology, autoimmunity, infectious diseases, cardiology, central nervous system ("CNS") diseases, and inflammation. For the near term, we have selected target diseases that may, if successfully developed, benefit from this technology.

The Company has developed processes for producing the first two therapeutic Manocept immuno-construct series, MT-1000 series, which is designed to specifically target and kill or modify activated CD206+ macrophages by delivering doxorubicin, and MT-2000 series, which is designed to inhibit the inflammatory activity of activated CD206+ macrophages by delivering a potent anti-inflammatory agent, dexamethasone. We have contracted with independent facilities to improve chemical syntheses and to produce sufficient quantities of the MT-1000 series and MT-2000 series agents along with the concomitant analytical standards, to provide material for current and planned preclinical animal studies and future clinical trials.

Manocept Platform – Immuno-Diagnostics Clinical Data

Rheumatoid Arthritis

Two Tc99m tilmanocept dose escalation studies in RA have been completed. The first study was completed and included 18 subjects (nine with active disease and nine healthy subjects) dosed subcutaneously ("SC") with 50 and 200 µg/2mCi Tc99m tilmanocept (ClinicalTrials.gov NCT02683421). The results of this study were presented at five international meetings, including Biotechnology Innovation Organization, Society of Nuclear Medicine and Molecular Imaging ("SNMMI"), and The American College of Rheumatology ("ACR"). In addition, based on completion of extensive preclinical dosing studies pursuant to our dialog with the FDA, we have completed a Phase 1/2 study involving intravenous ("IV") dosing of 39 subjects with IV-administered Tc99m tilmanocept (ClinicalTrials.gov NCT02865434). In conjunction with this study, we have completed pharmacokinetic, pharmacodynamics and radiation dosimetry phases in human subjects as well. The majority of the costs of these studies have been supported through a Small Business Innovation Research ("SBIR") grant (NIH/NIAMSD Grant 1 R44 AR067583-01A1). Results of this Phase 1/2 study were presented at the June 2018 and June 2019 SNMMI meetings, the 2018 European League Against Rheumatism ("EULAR") meeting and the 2018 ACR meeting. These studies have been combined and submitted for peer review publication and full published results will follow.

In June 2019, the results of the Company's NAV3-21 clinical study were presented at the SNMMI Annual Meeting in Anaheim, California. The presentation, titled "A Phase 1/2 Study of Intravenously Administered Tc99m Tilmanocept to Determine Safety, Tolerability, Optimal Clinical Dose Selection, and Imaging Timepoint in Patients Clinically Diagnosed with Rheumatoid Arthritis," was delivered by Arash Kardan, M.D. In addition, an abstract of the presentation was published in the *Journal of Nuclear Medicine* (2019, Volume 60, Supplement 1). The NAV3-21 study enrolled subjects with active, moderate-to-severe RA, and healthy controls. Results from the completed trial demonstrate that Tc99m tilmanocept is well-tolerated with no serious adverse events, adverse drug reactions, or drug-related adverse events observed. Additionally, static planar images revealed joint-specific Tc99m tilmanocept localization in RA subjects to disease-involved joints of the shoulders, knees, hands, and feet, but no joint-specific localization in healthy control subjects, revealing potentially significant immunodiagnostic information about CD206-expressing synovial macrophage involvement in RA. An optimal imaging time window post-Tc99m tilmanocept IV administration, as well as optimal dosing, were also determined.

In April 2019, the Company received feedback from the FDA regarding the Company's planned clinical studies that will evaluate joint disease in patients with RA and monitor patient response to therapy. The Company's proposed RA studies were discussed with the FDA during an in-person meeting and through follow-up collaborative efforts. The FDA communicated that the first study, a Phase 2b trial, is aligned with expectations for the studies and that they will continue to work with Navidea as we progress into a second Phase 2b trial correlating Tc99m tilmanocept uptake in RA-involved joints with CD206 immunohistochemistry findings from synovial biopsies and into the planned Phase 3 clinical trial. In May 2019, we began enrolling patients into the first Phase 2b study, entitled "Evaluation of the Precision and Sensitivity of Tilmanocept Uptake Value ("TUV") on Tc99m Tilmanocept Planar Imaging" (ClinicalTrials.gov MCT03938636). This study will provide confirmatory support necessary to initiate Navidea's Phase 3 study program.

In October 2019, the Company performed its first interim analysis of this trial, covering subjects enrolling into Arms 1 and 2. The results of this interim analysis were in line with the Company's hypotheses that Tc99m tilmanocept can provide robust, stable imaging in healthy subjects as well as in patients with active RA, and provide the fundamental information needed to keep moving forward into the Phase 3. A summary of these results was presented at the 2020 EULAR meeting. In May 2020, the Company announced the results of its second interim analysis, covering Arm 3 of the trial. This Arm mirrors the upcoming Phase 3 in design and provided information relevant for sample size calculation for the Phase 3 as well as support for the hypothesis that Tc99m tilmanocept imaging can provide an early indicator of treatment efficacy of anti-tumor necrosis factor ("TNF") alpha therapeutics. These interim results were presented at the 2020 ACR meeting. In June 2020, the Company announced full enrollment into this trial, with imaging events now completed in each patient enrolled in Arm 3. In February 2021, the Company submitted its formal briefing book to the FDA, containing detailed analysis and discussion of the Company's ongoing Phase 2b study (NAV3-31) and prior studies in RA as well as the design and statistical analysis plan for the proposed Phase 3 for FDA comment. Following the feedback received from the FDA at the end of March 2021, the Company continues to work toward completing the analysis of the full trial dataset in preparation for the standard End of Phase 2 Type B meeting. The pivotal Phase 3 study program will assess joint disease status and monitor patient response to therapy.

Cardiovascular Disease

In collaboration with researchers at Massachusetts General Hospital, Navidea has completed one and has initiated a second investigator-initiated clinical study evaluating Tc99m tilmanocept's ability to enable imaging of atherosclerotic plaques. Results of these studies provide strong preliminary evidence of the potential of Tc99m tilmanocept to accumulate specifically in and enable imaging of non-calcified atherosclerotic plaques. Non-calcified atherosclerotic plaques include plaques with morphologies indicating a high risk of rupture. Rupture of such plaques causes myocardial infarctions (heart attacks) and a significant portion of ischemic strokes. The studies compared aortic Tc99m tilmanocept uptake imaged by SPECT/CT in clinically asymptomatic subjects with intermediate Framingham Risk Scores ("FRS") who were infected with Human Immunodeficiency Virus ("HIV") as compared to healthy, uninfected, FRS and age-matched subjects. Tc99m tilmanocept SPECT/CT images were compared to aortic images of the same subjects obtained by contrast enhanced coronary computed tomography angiography and/or [18F]NaF PET/CT.

A nine-subject study to evaluate diagnostic imaging of emerging atherosclerosis plaque with the Tc99m tilmanocept product dosed SC was performed (ClinicalTrials.gov NCT02542371). The results of this study were presented at two major international meetings (Conference on Retroviruses and Opportunistic Infections and SNMMI, 2017) and published in early release in the *Journal of Infectious Diseases* in January 2017 (published in the circulated version,*Journal of Infectious Diseases* (2017) 215 (8): 1264-1269), confirming that the Tc99m tilmanocept product can both quantitatively and qualitatively target non-calcified plaque in the aortic arch of Acquired Immunodeficiency Syndrome ("AIDS") patients (supported by NIH/NHLBI Grant 1 R43 HL127846-01). This study was later expanded to include up to 31 participants, and enrollment is nearly complete, with full image analysis to follow.

A second Phase 1/2 investigator-initiated study in cooperation with Massachusetts General Hospital in subjects with HIV was initiated that expanded the original study in both the scope of the drug administration as well as the diagnostic assessment of the subjects. This study enrolled both AIDS subjects and healthy controls in imaging non-calcified plaque using IV and SC-administered Tc99m tilmanocept and will expand the initial investigation to the assessment of aortic plaque as well as carotid and coronary arteries. Initial analysis suggested that the SC route of administration led to superior signal-to-background in areas of non-calcified plaque. These results are being further assessed.

Navidea has also been awarded a $225,000 phase 1 Small Business Technology Transfer grant (1R41HL147640-01A1) entitled*Gallium 68 Tilmanocept for PET Imaging of Atherosclerosis Plaques*. This grant will support a research collaboration between Navidea and Dr. Suzanne Lapi of the University of Alabama Birmingham. These efforts will evaluate [68]gallium tilmanocept for imaging plaques in an animal model of atherosclerosis and began activities in the fourth quarter of 2019.

Kaposi's Sarcoma

We initiated and completed a study of KS in 2015 (ClinicalTrials.gov NCT022201420) and received additional funding from the National Institutes of Health ("NIH") in 2016 to continue diagnostic studies in this disease. The new support not only continues the imaging of the cutaneous form of this disease but expands this to imaging of visceral disease via IV administration of Tc99m tilmanocept (NIH/NCI 1 R44 CA192859-01A1; ClinicalTrials.gov NCT03157167). This now-escalated study includes a pathology/biopsy component as well as an imaging component to determine pathology concordance with image assessment. We received Institutional Review Board approval of the clinical protocol and initiated a Phase 1/2 clinical study in KS in 2017. This trial has completed enrollment and imaging. Data and image analysis for this study are ongoing.

Tuberculosis ("TB")

In April 2019, we announced that Professor Mike Sathekge, MBChB, M. Med (Nuclear Medicine), PhD, Professor and Head of the Department of Nuclear Medicine in the Faculty of Health Sciences at the University of Pretoria/Steve Biko Academic Hospital, planned to initiate a comparative study evaluating the use of tilmanocept in patients with TB. The purpose of this ongoing study is to explore using 68Ga tilmanocept as an aid in TB patient management while contributing to the better understanding of the biology of TB granulomas. CD206+ macrophages constitute one of the most abundant cell types in TB granulomas. Therefore, a molecular probe such as 68Ga-labeled tilmanocept targeting mannose receptor CD206 expressed on macrophages holds great promise not only in understanding the biology of TB granulomas, but may also support future development of a tilmanocept-like drug delivery vehicle for delivering therapeutic interventions to TB granulomas. Navidea has provided tilmanocept for use in this study, and several subjects have been injected and imaged to date. Successful completion of this study could support an extended claim of 68Ga-tilmanocept.

Biomarker Application and Qualification

In November 2017, the Company commenced the qualification of the biomarker CD206 with the FDA Biomarker Section of The Center for Drug Evaluation and Research ("CDER"). As per FDA protocol, Navidea submitted a draft letter of intent ("LOI") to CDER prior to the November 2017 meeting. According to the CDER directive, "the Biomarker Qualification Program was established to support the CDER's work with external stakeholders to develop biomarkers that aid in the drug development process. Through the FDA's Biomarker Qualification Program, an entity may request regulatory qualification of a biomarker for a particular context of use ("COU") in drug development." Following the meeting with the FDA, and because of Navidea's data sets and the general external publication database, Navidea, in conjunction with FDA, is now reviewing the LOI with the FDA's recommended consultants. Navidea has revised the LOI draft strategy in order to expedite the application process. In March 2018, Navidea had a follow-up meeting with the FDA's assigned strategist, during which the potential to further narrow the LOI elements was reviewed. Navidea is continuing the process of finalizing the COU LOI and providing the background data sets for qualification review with the FDA/CDER. Additional meetings have taken place and the pursuit of this qualification is ongoing.

Manocept Platform – In-Vitro and Pre-Clinical Immunotherapeutics Data

The Company has been developing Manocept platform drug delivery constructs that carry various payloads including doxorubicin and dexamethasone. Chemical synthesis techniques have advanced considerably, resulting in more robust and reproducible synthesis protocols that provide products with chemical attributes indicative of enhanced in vivo activity. The most advanced drug delivery construct carries a doxorubicin payload and is now in its third generation of chemical synthesis protocol design. This third generation doxorubicin carrying construct has been extensively evaluated in human macrophage cell culture assays and in three experiments using syngeneic mouse cancer models. These experiments show that at treatment doses below what is required to kill macrophages, the doxorubicin carrying constructs dramatically alters the immunological behavior of macrophages, making them more proinflammatory. In one of the syngeneic mouse tumor experiments, the Manocept doxorubicin construct significantly synergized the activity of another anticancer therapy producing anti-tumor activity that was greater than either treatment alone. Results from this study will be presented at the New York Academy of Sciences Frontiers in Cancer Immunotherapy 2021 conference on May 14, 2021. Near-term experiments with the Manocept doxorubicin construct include further studies in macrophage cell culture, additional syngeneic mouse tumor models, and a toxicity study in rats. Work involving a second generation Manocept dexamethasone carrying construct and efforts developing Manocept constructs with different payloads is ongoing.

Kaposi's Sarcoma

The novel MT-1000 class constructs are designed to specifically deliver doxorubicin, a chemotoxin, which can kill KS tumor cells and their tumor-associated macrophages, potentially altering the course of cancer. We have received additional funding to continue therapeutic studies in this disease with the goal of completing an investigational new drug ("IND") submission for a Manocept construct (MT-1000 class of compounds) consisting of tilmanocept linked to doxorubicin for the treatment of KS. The first part of the grant, now complete, supported analyses including *in vitro* and cell culture studies, to be followed by Parts 2 and 3 FDA-required preclinical animal testing studies. The information from these studies can be combined with other information in an IND application that can be submitted to the FDA requesting permission to begin testing the compound in selected KS subjects (supported by NIH/NCI 1 R44 CA206788-01).

Other Immunotherapeutic Applications

The Company continues to evaluate emerging data in other disease states to define areas of focus, development pathways and partnering options to capitalize on the Manocept platform, including ongoing studies in KS, RA and infectious diseases. The immuno-inflammatory process is remarkably complex and tightly regulated with indicators that initiate, maintain and shut down the process. Macrophages are immune cells that play a critical role in the initiation, maintenance, and resolution of inflammation. They are activated and deactivated in the inflammatory process. Because macrophages may promote dysregulation that accelerates or enhances disease progression, diagnostic and therapeutic interventions that target macrophages may open new avenues for controlling inflammatory diseases. There can be no assurance that further evaluation or development will be successful, that any Manocept platform product candidate will ultimately achieve regulatory approval, or if approved, the extent to which it will achieve market acceptance.

Risks Associated with Our Business and this Offering

Our business and our ability to implement our business strategy are subject to numerous risks, as more fully described in the section of this prospectus entitled "Risk Factors" and under similarly titled headings of the documents incorporated herein by reference. You should read these risks before you invest in our securities. We may be unable, for many reasons, including those that are beyond our control, to implement our business strategy. In particular, risks associated with our business and this offering include:

- The global COVID-19 pandemic may continue to impact our business, financial condition or prospects, including a decline in the volume of procedures using our products, potential delays and disruptions to global supply chains, manufacturing activities, logistics, operations, employees and contractors, the business activities of our suppliers, distributors, customers and other business partners, as well as the effects on worldwide economies, financial markets, social institutions, labor markets and healthcare systems.

- There is substantial doubt about our ability to continue as a going concern, which may affect our ability to obtain future financing and may require us to curtail our operations. We will need to raise additional capital to support our operations.

- We have incurred losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future, and our future profitability is uncertain.

- Our product candidates must undergo rigorous clinical testing, such clinical testing may fail to demonstrate safety and efficacy and any of our product candidates could cause undesirable side effects, which would substantially delay or prevent regulatory approval or commercialization.

- We are dependent on patents and proprietary technology. If we fail to adequately protect this intellectual property or if we otherwise do not have exclusivity for the marketing of our products, our ability to commercialize products could suffer.

- If our competitors are able to develop and market products that are more effective, safer or more affordable than ours, or obtain marketing approval before we do, our commercial opportunities may be limited.

Corporate Information

Our corporate headquarters are located at 4995 Bradenton Avenue, Suite 240, Dublin, Ohio 43017-3552, and our telephone number is (614) 793-7500. We maintain a website at www.navidea.com, to which we regularly post copies of our press releases as well as additional information about us. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "*Exchange Act*"), are available free of charge through the investor relations page of our internet website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

The Offering

Common stock offered by selling stockholder	This prospectus covers the resale of 2,173,913 shares of common stock issuable upon conversion of outstanding shares of Series E Preferred.
Offering price	The selling stockholder will sell its Shares at prevailing market prices or privately negotiated prices.
Common stock outstanding	29,025,412 shares (as of May 7, 2021). The number of outstanding shares does not include shares issuable upon conversion of outstanding shares of our Series E Preferred.
Use of proceeds	We will not receive any proceeds from the sale of the Shares in this offering. See "Use of Proceeds."
Dividend policy	We have not declared or paid any cash or other dividends on our common stock, and we do not expect to declare or pay any cash or other dividends in the foreseeable future.
Risk factors	Investing in our common stock involves a high degree of risk. You should carefully read and consider the information on page 9 of this prospectus set forth under the headings "Risk Factors" and all other information set forth in this prospectus and the documents incorporated herein by reference before deciding to invest in our common stock.
Market for our shares	Our common stock is traded on the NYSE American under the symbol "NAVB."

As of May 7, 2021, there were 29,025,412 shares of our common stock outstanding (20,695,281 shares held by non-affiliates). If all of 2,173,913 shares of our common stock offered hereby were issued and outstanding as of the date hereof, such shares would represent 7.0% of the total common stock outstanding or 9.5% of the non-affiliate shares of common stock outstanding as of the date hereof. The number of shares of our common stock ultimately offered for sale by the selling stockholder is dependent upon the number of shares acquired by the selling stockholder upon conversion of the Series E Preferred.

RISK FACTORS

Investing in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the specific risk factors discussed in the sections entitled "Risk Factors" contained in our annual report on Form 10-K for the fiscal year ended December 31, 2020 under the heading "Item 1A. Risk Factors," and as described or may be described in any subsequent quarterly report on Form 10-Q under the heading "Item 1A. Risk Factors," as well as in any applicable prospectus supplement and contained or to be contained in our filings with the SEC and incorporated by reference in this prospectus, together with all of the other information contained in this prospectus, or any applicable prospectus supplement. For a description of these reports and documents, and information about where you can find them, see "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." If any of the risks or uncertainties described in our SEC filings or any prospectus supplement or any additional risks and uncertainties actually occur, our business, financial condition and results of operations could be materially and adversely affected. In that case, the trading price of our securities could decline and you might lose all or part of the value of your investment.

The issuance of common stock to the selling stockholder may cause substantial dilution to our existing stockholders and the sale of such Shares acquired by the selling stockholder could cause the price of our common stock to decline.

We are registering for sale up to 2,173,913 shares of common stock issuable upon conversion of shares of our Series E Preferred. The number of Shares ultimately offered for sale by the selling stockholder under this prospectus is dependent upon the number of Shares issued to the selling stockholder upon conversion of the Series E Preferred. Depending on a variety of factors, including market liquidity of our common stock, the issuance of Shares to the selling stockholder may cause the trading price of our common stock to decline.

The sale of a substantial number of Shares of our common stock by the selling stockholder in this offering, or anticipation of such sales, could cause the trading price of our common stock to decline or make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise desire.

Because we do not expect to pay dividends on our common stock in the foreseeable future, stockholders will only benefit from owning common stock if it appreciates.

We have paid no cash dividends on any of our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, with respect to our common stock, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our Board of Directors. Furthermore, we are subject to various laws and regulations that may restrict our ability to pay dividends and we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Due to our intent to retain any future earnings rather than pay cash dividends on our common stock and applicable laws, regulations and contractual obligations that may restrict our ability to pay dividends on our common stock , the success of your investment in our common stock will likely depend entirely upon any future appreciation and there is no guarantee that our common stock will appreciate in value.

THE SERIES E PREFERRED TRANSACTION

Series E Preferred Purchase Agreement

On March 2, 2021, we entered into a Stock Purchase Agreement and Letter of Investment Intent (the "*Purchase Agreement*") with an existing accredited investor, John K. Scott, Jr. ("*Investor*") pursuant to which we issued to Investor in a private placement transaction 50,000 shares of newly-designated Series E Redeemable Convertible Preferred Stock, par value $0.001 (the "*Series E Preferred*) for an aggregate purchase price of $5,000,000. The shares of Series E Preferred have the rights set forth in the Certificate of Designation of Preferences, Rights and Limitations of Series E Preferred (the "*Series E Preferred Certificate*").

The Series E Preferred have not been registered under the Securities Act, and until so registered the securities may not be offered or sold absent registration or availability of an applicable exemption from registration.

Right of First Offer and Preemptive Right

Under the Purchase Agreement, Investor was granted a right of first offer with respect to future issuances of our securities (the "*Right of First Offer*"); *provided*, *however*, that in no event shall Investor have such right if the acquisition of any of such securities would result in Investor beneficially holding more than thirty three and one-third percent (33.33%) of our outstanding common stock on an as-converted basis, as determined in accordance with Section 13(d) of the Exchange Act, and the rules thereunder (the "*Share Cap*"). In the event that Investor does not exercise the Right of First Offer, we will then be entitled to offer and sell the new securities to any third party at a price not less than, and upon terms no more favorable to the offeree than, those offered to Investor (a "*Third Party Offering*").

Pursuant to the Purchase Agreement, Investor also has the option to purchase up to thirty three and one-third percent (33.33%) of the new securities offered in a Third-Party Offering at the same price and upon the terms available to the other purchaser(s) (the "*Preemptive Right*"); *provided*, *however*, that in no event may Investor acquire new securities in a Third-Party Offering to the extent the acquisition thereof would violate the Share Cap.

The Right of First Offer and the Preemptive Right will expire upon the earlier of (i) December 31, 2021 or (ii) upon the voluntary or involuntary liquidation, dissolution, or winding up of the Company.

Registration Rights Agreement

In connection with the sale of the Series E Preferred, we entered into a registration rights agreement (the "*Registration Rights Agreement*"), pursuant to which, among other things, we agreed to prepare and file with the Commission one or more registration statements to register for resale the maximum number of shares of common stock issuable upon conversion of the Series E Preferred. In the event that both (i) the number of shares of common stock beneficially held by Investor falls below twenty percent (20%) of the outstanding common stock on an as-converted basis, as determined in accordance with Section 13(d) of the Exchange Act and the rules thereunder and (ii) Investor is an affiliate (as that term is defined under Rule 144) at the time of the Reload Request (as defined below), we, upon written request from Investor (the "*Reload Request*"), will be required to prepare and file with the Commission one, and only one, additional registration statement covering the resale of those shares of common stock owned by Investor as of the date of the Reload Request that, as of such time, are not registered for resale under the Securities Act.

Description of Series E Preferred

On March 2, 2021, we filed with the Series E Preferred Certificate Secretary of State of the State of Delaware. The Series E Preferred Certificate authorizes 50,000 shares of Series E Preferred and establishes the rights and preferences of the Series E Preferred, including as follows:

- Except with respect to transactions which may adversely affect any right, preference, privilege or voting power of the Series E Preferred Stock, the Series E Preferred Stock has no voting rights.

- Whenever our Board declares a dividend on common stock, each record holder of a share of Series E Preferred Stock on the record date set by the Board will be entitled to receive an amount equal to such dividend declared on one share of common stock multiplied by the number of shares of common stock ("*Conversion Shares*") into which such share of Series E Preferred Stock could be converted on the record date, without regard to any conversion limitations in the Series E Preferred Certificate.

- Holders of the Series E Preferred Stock may convert some or all of the Series E Preferred Stock into Conversion Shares at a fixed price of $2.30 per Conversion Share, *provided* that the aggregate number of Conversion Shares issued pursuant to the Series E Preferred Certificate cannot exceed the Share Cap without stockholder approval, which we are not required to seek.

- We have the right to redeem any outstanding shares of Series E Preferred Stock at a price of $110 per share at any time on or prior to the one-year anniversary of the issuance date, payable in cash.

No Short-Selling or Hedging

Investor has agreed that neither it nor any of its affiliates acting on its behalf or pursuant to any understanding with it, will execute any "short sales" of our common stock as defined in Rule 200 of Regulation SHO under the Exchange Act until the later to occur of (A) Investor, or any affiliate of his acting on his behalf or pursuant to any understanding with him, no longer holds any of the Shares, or (B) December 31, 2021.

Effect of Performance of the Purchase Agreement on Our Stockholders

The Purchase Agreement does not limit the ability of Investor to convert the Series E Preferred, except with respect to the Share Cap, or to sell any or all of the 2,173,913 Shares registered in this offering. The sale by Investor of a significant number of Shares registered in this offering at any given time could cause the market price of our common stock to decline and/or to be highly volatile. Investor may ultimately acquire all, some or none of the 2,173,913 Shares not yet issued but registered for resale in this offering. After it has acquired such Shares, it may sell all, some or none of such Shares. Therefore, the issuance of the Shares to Investor by us pursuant to the Purchase Agreement also may result in substantial dilution to the interests of other holders of our common stock.

USE OF PROCEEDS

This prospectus relates to Shares of our common stock that may be offered and sold from time to time by the selling stockholder. We will not receive any proceeds upon the sale of Shares by the selling stockholder.

The selling stockholder will pay any discounts, commissions, and fees of underwriters, selling brokers, dealer managers or similar securities industry professionals incurred by such selling stockholder in disposing of the Shares covered by this prospectus. We will bear all other costs, fees and expenses incurred in effecting the registration of the Shares covered by this prospectus and any accompanying prospectus supplement, including, without limitation, all registration and filing fees, NYSE American listing fees and fees and expenses of our counsel and our accountants.

SELLING STOCKHOLDER

We have prepared this prospectus to allow the selling stockholder or its pledgees, donees, transferees or other successors in interest, to sell or otherwise dispose of, from time to time, up to 2,173,913 Shares.

On March 2, 2021, we entered into the Purchase Agreement with the Investor pursuant to which we issued to Investor in a private placement transaction 50,000 shares of newly-designated Series E Convertible Preferred for an aggregate purchase price of $5,000,000. Holders of the Series E Preferred Stock may convert some or all of the Series E Preferred Stock into Conversion Shares at a fixed price of $2.30 per Conversion Share, *provided* that the aggregate number of Conversion Shares issued pursuant to the Series E Preferred Certificate cannot exceed the Share Cap without stockholder approval, which we are not required to seek.

The table below presents information regarding the selling stockholder and the Shares that the selling stockholder may offer and sell from time to time under this prospectus. Neither the selling stockholder nor any of its affiliates, officers, directors or principal equity holders have held any position or office or had any other material relationship with us or our affiliates within the past three years.

This table is prepared based on information supplied to us by the selling stockholder, and reflects beneficial ownership as of May 7, 2021. As used in this prospectus, the term "selling stockholder" includes the selling stockholder set forth below and any donees, pledgees, transferees or other successors-in-interest selling Shares received after the date of this prospectus from the selling stockholder as a gift, pledge, or other non-sale related transfer. Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Exchange Act of and includes Shares with respect to which the selling stockholder have voting and investment power, or rights to acquire beneficial ownership through conversion.

The number of shares in the column "Maximum Number of Shares of Common Stock that may be Offered Pursuant to this Prospectus" represents all of the Shares that the selling stockholder may offer under this prospectus. The fourth column assumes the sale of all the Shares offered by the selling stockholder pursuant to this prospectus and that the selling stockholder does not acquire any additional shares of common stock before the completion of this offering. However, because the selling stockholder may sell all or some of the Shares under this prospectus from time to time, or in another permitted manner, we cannot assure you as to the actual number of Shares that will be sold by the selling stockholder or that will be held by the selling stockholder after completion of any sales. The selling stockholder may sell some, all or none of its Shares in this offering. We do not know how long the selling stockholder will hold the Shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale of any of the Shares.

	Beneficial Ownership of Common Stock Prior to the Offering		Maximum Number of Shares of Common Stock that May Be Offered Pursuant to this Prospectus	Beneficial Ownership of Common Stock After the Offering	
Name of Selling Stockholder	**Number of Shares**	**Percent of Class (%)**		**Number of Shares (1)**	**Percent of Class (%)**
John K. Scott, Jr.	10,231,214	32.8%	2,173,913	8,057,301	27.8%
TOTAL:	10,231,214	32.8%	2,173,913	8,057,301	27.8%

(1) Assumes that all the Shares of the selling stockholder covered by this prospectus are sold, and that the selling stockholder does not acquire any additional shares of common stock before the completion of this offering. However, because the selling stockholder can offer all, some, or none of its common stock, no definitive estimate can be given as to the number of Shares that the selling stockholder will ultimately offer or sell under this prospectus.

PLAN OF DISTRIBUTION

The selling stockholder, including its pledgees, donees, transferees, distributees, beneficiaries or other successors in interest, may from time to time offer some or all of the Shares by this prospectus. We will not receive any of the proceeds from the sale of the Shares covered by this prospectus by the selling stockholder. We will bear all fees and expenses incident to our obligation to register the Shares covered by this prospectus.

The selling stockholder may sell all or a portion of the Shares beneficially owned by it and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the Shares are sold through underwriters or broker-dealers, the selling stockholder will be responsible for underwriting discounts or commissions or agent's commissions in connection with the Shares held by the selling stockholder. The Shares may be sold on any national securities exchange or quotation service on which the Shares may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at privately negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions.

The selling stockholder may use any one or more of the following methods when disposing of Shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the Shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an over-the-counter distribution;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the effective date of the registration statement of which this prospectus is a part;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with a selling stockholder to sell a specified number of such Shares at a stipulated price per share;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholder may, from time to time, pledge or grant a security interest in some or all of the Shares owned by it and, if it defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the Shares, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of the selling stockholder to include the pledgee, transferee, or other successors in interest as a selling stockholder under this prospectus. The selling stockholder also may transfer the Shares in other circumstances, in which case the transferees, pledgees or other successors in interest will be the beneficial owners for purposes of this prospectus.

In connection with the sale of Shares, or interests therein, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions it assumes. The selling stockholder may also sell Shares short and deliver the Shares to close out its short positions, or loan or pledge the Shares to broker-dealers that in turn may sell these securities. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of Shares offered by this prospectus, which Shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

Broker-dealers engaged by a selling stockholder may arrange for other broker-dealers to participate in sales. If a selling stockholder effects certain transactions by selling Shares to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from such selling stockholder or commissions from purchasers of the Shares for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with applicable rules of the Financial Industry Regulatory Authority ("*FINRA*"); and in the case of a principal transaction a markup or markdown in compliance with applicable FINRA rules.

The aggregate proceeds to a selling stockholder from the sale of the Shares offered by it will be the purchase price of the Shares less discounts or commissions, if any. The selling stockholder reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of Shares to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholder also may resell all or a portion of the Shares (or other shares of the Company's common stock that he owns) in open market transactions in reliance upon Rule 144 under the Securities Act, provided that it meets the criteria and conforms to the requirements of that rule.

The selling stockholder and any underwriters, broker-dealers or agents that participate in the sale of the Shares, or interests therein, may be deemed to be "underwriters" within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the Shares may be underwriting discounts and commissions under the Securities Act. The selling stockholder is subject to the prospectus delivery requirements of the Securities Act.

To the extent required pursuant to Rule 424(b) under the Securities Act, the Shares to be sold, the name of the selling stockholder, the purchase price and public offering price, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Shares may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Shares may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The selling stockholder and any other person participating in a sale of the Shares registered under this prospectus will be subject to applicable provisions of the Exchange Act, and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the Shares by the selling stockholder and any other participating person. All of the foregoing may affect the marketability of the Shares and the ability of any person or entity to engage in market-making activities with respect to the Shares. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholder for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholder may indemnify any broker-dealer that participates in transactions involving the sale of the Shares against certain liabilities, including liabilities arising under the Securities Act.

PRINCIPAL STOCKHOLDERS

The following table sets forth, as of May 7, 2021, certain information with respect to the beneficial ownership of shares of our Common Stock by: (i) each person known to us to be the beneficial owner of more than 5% of our outstanding shares of Common Stock, (ii) each director or nominee for director of our Company, (iii) each of the Named Executive Officers, and (iv) our directors and executive officers as a group.

Beneficial Owner	Number of Shares Beneficially Owned (*)		Percent of Class (**)	
Amit Bhalla	—	(a)	—	(j)
Claudine Bruck, Ph.D.	17,550	(b)	—	(j)
Joel H. Kaufman	54,093	(c)	—	(j)
Jed A. Latkin	147,590	(d)	—	(j)
Michael S. Rosol, Ph.D.	28,247	(e)	—	(j)
S. Kathryn Rouan, Ph.D.	18,350	(f)	—	(j)
Malcolm G. Witter	57,000	(g)	—	(j)
All directors and executive officers as a group (7 persons)	322,831	(h)(k)	—	(j)
John K. Scott, Jr.	10,231,214	(i)	32.8 %	

(*) Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission which generally attribute beneficial ownership of securities to persons who possess sole or shared voting power and/or investment power with respect to those securities. Unless otherwise indicated, voting and investment power are exercised solely by the person named above or shared with members of such person's household.

(**) Percent of class is calculated on the basis of the number of shares outstanding on February 28, 2021, plus the number of shares the person has the right to acquire within 60 days of February 28, 2021.

(a) This amount does not include 2,500 shares of unvested restricted stock and 2,500 shares issuable upon exercise of options which are not exercisable within 60 days.

(b) This amount includes 7,500 shares issuable upon exercise of options which are exercisable within 60 days, but does not include 2,500 shares of unvested restricted stock and 2,500 shares issuable upon exercise of options which are not exercisable within 60 days.

(c) This amount includes 19,800 shares issuable upon exercise of options which are exercisable within 60 days and 9,648 shares in Mr. Kaufman's account in the 401(k) Plan, but does not include 49,800 shares issuable upon exercise of options which are not exercisable within 60 days.

(d) This amount includes 16,667 shares of unvested restricted stock which will vest within 60 days, 69,919 shares issuable upon exercise of options which are exercisable within 60 days and 10,600 shares in Mr. Latkin's account in the 401(k) Plan, but does not include 33,000 shares of unvested restricted stock and 333,331 shares issuable upon exercise of options which are not exercisable within 60 days.

(e) This amount includes 14,584 shares issuable upon exercise of options which are exercisable within 60 days and 6,816 shares in Dr. Rosol's account in the 401(k) Plan, but does not include 41,666 shares issuable upon exercise of options which are not exercisable within 60 days.

(f) This amount includes 7,500 shares issuable upon exercise of options which are exercisable within 60 days, but does not include 2,500 shares of unvested restricted stock and 2,500 shares issuable upon exercise of options which are not exercisable within 60 days.

(g) This amount does not include 2,500 shares of unvested restricted stock and 2,500 shares issuable upon exercise of options which are not exercisable within 60 days.

(h) This amount includes 16,667 shares of unvested restricted stock which will vest within 60 days, 119,303 shares issuable upon exercise of options which are exercisable within 60 days, and 27,064 shares held in the 401(k) Plan on behalf of certain officers, but it does not include 43,333 shares of unvested restricted stock and 434,797 shares issuable upon the exercise of options which are not exercisable within 60 days. The Company's Chief Executive Officer, Chief Operating Officer and Chief Financial Officer, Jed A. Latkin, is the trustee of the Navidea Biopharmaceuticals, Inc. 401(k) Plan and may, as such, share investment power over Common Stock held in such plan. Mr. Latkin disclaims any beneficial ownership of shares held by the 401(k) Plan. The 401(k) Plan holds an aggregate total of 69,780 shares of Common Stock.

(i) The number of shares beneficially owned is based on a Schedule 13D filed by John K. Scott, Jr. with the SEC on April 5, 2021. The address of John K. Scott, Jr. is 30 Blue Heron Drive, Greenwood Village, CO 80121.

(j) Less than one percent.

(k) The address of all directors and executive officers is c/o Navidea Biopharmaceuticals, Inc., 4995 Bradenton Avenue, Suite 240, Dublin, OH 43017.

All of our employees and directors, or any of their designees, are prohibited from (i) purchasing financial instruments (including prepaid variable forward contracts, equity swaps, collars, and exchange funds), or (ii) otherwise engaging in transactions (including "short sales" and arrangements involving a non-recourse pledge of securities), that hedge or offset, or are designed to hedge or offset, any decrease in the market value of shares of our common stock granted to such employee or director, or any of their designees, as part of their compensation, or held (directly or indirectly) by such employee or director, or any of their designees.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, has been passed upon for us by Thompson Hine LLP, 335 Madison Avenue, 12th Floor, New York, New York 10017-4611.

EXPERTS

The financial statements for the years ended December 31, 2020 and 2019 incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2020, have been so incorporated in reliance on the report of Marcum LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the securities being offered by this prospectus. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the securities offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference. The SEC maintains an internet website that contains reports, proxy statements, and other information about registrants, like us, that file electronically with the SEC. The address of that website is www.sec.gov. The information contained in, or that can be accessed through, the SEC's website is not incorporated by reference in, and is not part of, this prospectus or any prospectus supplement.

We are subject to the information and periodic reporting requirements of the Exchange Act, and we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information are available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at https://www.navidea.com/. You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus.

We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-37544):

- our annual report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 26, 2021;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2021, filed with the SEC on May 13, 2021;
- our current reports on Form 8-K and all amendments thereto, filed with the SEC on March 4, 2021, March 17, 2021, April 5, 2021, May 5, 2021 and May 11, 2021; and
- the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on February 8, 2011, including all amendments and reports filed for the purpose of updating such description.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the termination of the offering (excluding any information furnished rather than filed) shall be deemed to be incorporated by reference into this prospectus.

We will provide to each person, including any beneficial owners, to whom a prospectus is delivered, a copy of any or all of the reports or documents that have been incorporated by reference in the prospectus contained in the registration statement but not delivered with the prospectus. We will provide these reports or documents upon written or oral request at no cost to the requester. You should direct any written requests for documents to Navidea Biopharmaceuticals, Inc., Attention: Chief Financial Officer, 4995 Bradenton Avenue, Suite 240, Dublin, Ohio 43017-3552. You may also telephone us at (614) 793-7500.

You may also access these documents, free of charge, on the SEC's website at www.sec.gov or on our website at https://ir.navidea.com/sec-filings. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus or any accompanying prospectus supplement.

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference into this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such an offer or solicitation.

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Our directors and officers are indemnified to the fullest extent permitted under Delaware law. We also maintain insurance which protects our officers and directors against any liabilities incurred in connection with their service in such a capacity.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing, or otherwise, we have been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by us of expenses incurred or paid by a director, officer or controlling person of ours in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

2,173,913

Shares of Common Stock

PROSPECTUS