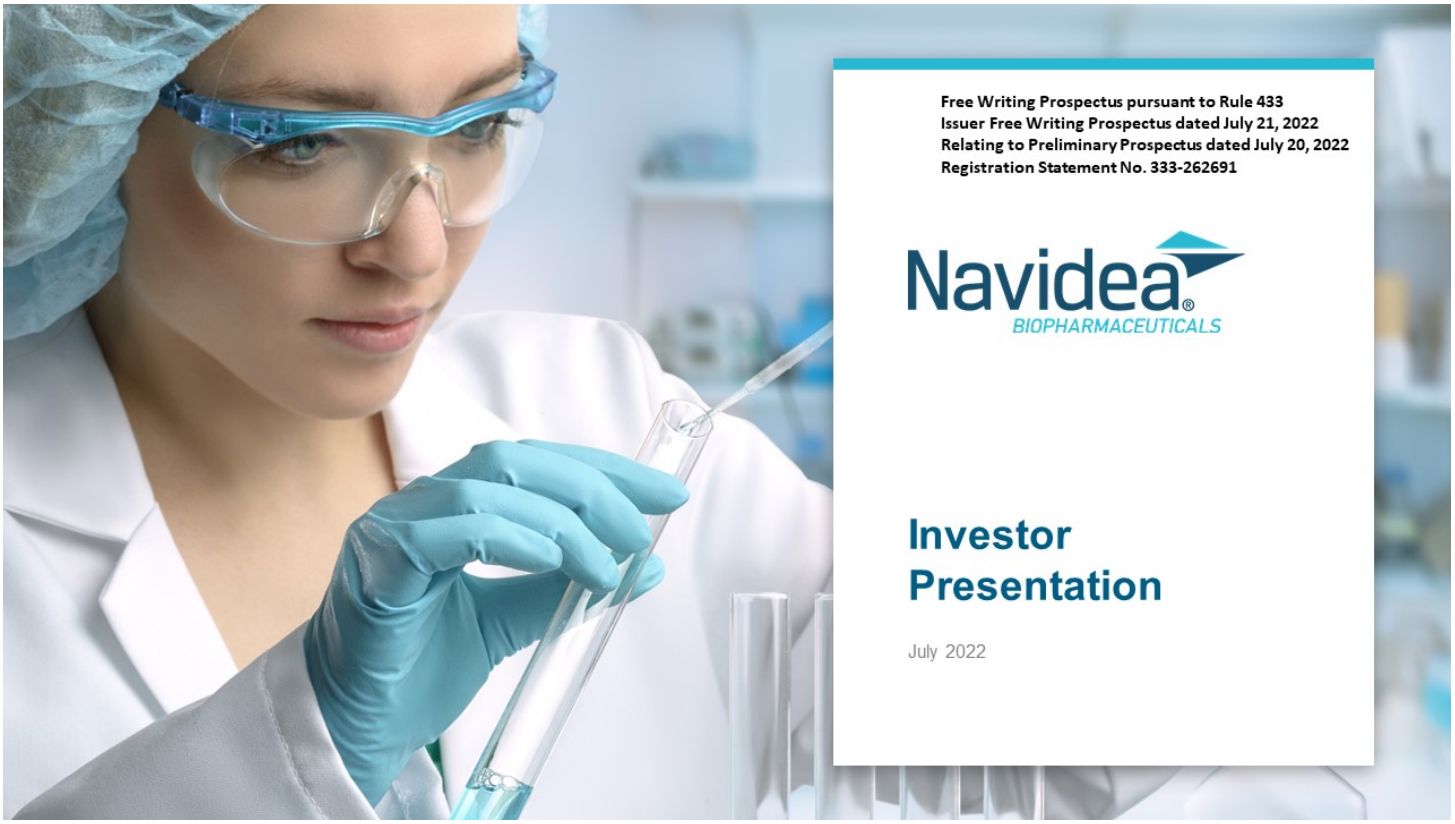

Free Writing Prospectus pursuant to Rule 433
Issuer Free Writing Prospectus dated July 21, 2022
Relating to Preliminary Prospectus dated July 20, 2022
Registration Statement No. 333-262691
Navidea
BIOPHARMACEUTICALS
Investor Presentation
July 2022

Disclaimer

The Private Securities Litigation Reform Act of 1995 (the "Act") provides a safe harbor for forward-looking statements made by or on behalf of Navidea Biopharmaceuticals. Inc. Statements in this presentation, 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, and markets for the Company's products are forward-looking statements within the meaning of the Act. The words "believe," "expect," "anticipate," "estimate," "project," "forecast", "goal" "future", "intent", "will", "may", "could" and similar expressions, as well as the negatives of these words or comparable words, identify forward-looking statements that speak only as of the date hereof. You 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, the Company's continuing operating losses and uncertainty of future profitability; uncertainty of market acceptance of its products; reliance on third party manufacturers; accumulated deficit; future capital needs; uncertainty of capital funding; dependence on limited product line and distribution channels; competition; limited marketing and manufacturing experience; our ability to successfully complete research and further development of our drug candidates; the timing cost, and uncertainty of obtaining any required regulatory approvals of our drug candidates; our ability to successfully commercialize our drug candidates; 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 risks detailed in the Company's most recent Annual Report on Form 10-K and other Securities and Exchange Commission filings. You are further cautioned that the foregoing list of important factors is not exclusive. The Company undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Navidea Biopharmaceuticals, Inc. has filed a registration statement with the Securities and Exchange Commission ("SEC") for the rights offering to which this presentation relates. Before you invest, you should read the prospectus in that registration statement and other documents the issuer has filed with the SEC for more complete information about the issuer and the rights offering. You may get these documents for free by visiting EDGAR on the SEC website at https://www.sec.gov. Alternatively, a copy of the prospectus and other documents may be obtained from Broadridge Corporate Issuer Solutions, Inc., the Company's information and subscription agent for the rights offering, by calling (888) 789-8409 (toll-free) or by emailing shareholder@broadridge.com.

We are a **precision immuno-diagnostics and therapeutics company** commercializing a powerful and adaptable platform technology, creating a **robust pipeline of products for cancer and inflammatory disorders**.

Corporate Overview

Adaptable Platform Technology to Target Diseases with Significant Unmet Need

FDA/EMA-approved diagnostic product demonstrates the features of the **proprietary** platform technology, the **Manocept Platform.**

Lymphoseek® (technetium Tc 99m tilmanocept) injection

The **Manocept Platform** enables **targeted delivery** of imaging agents or small molecule drug payloads to mannose receptors (CD206) on activated macrophages at sites of pathological inflammation.

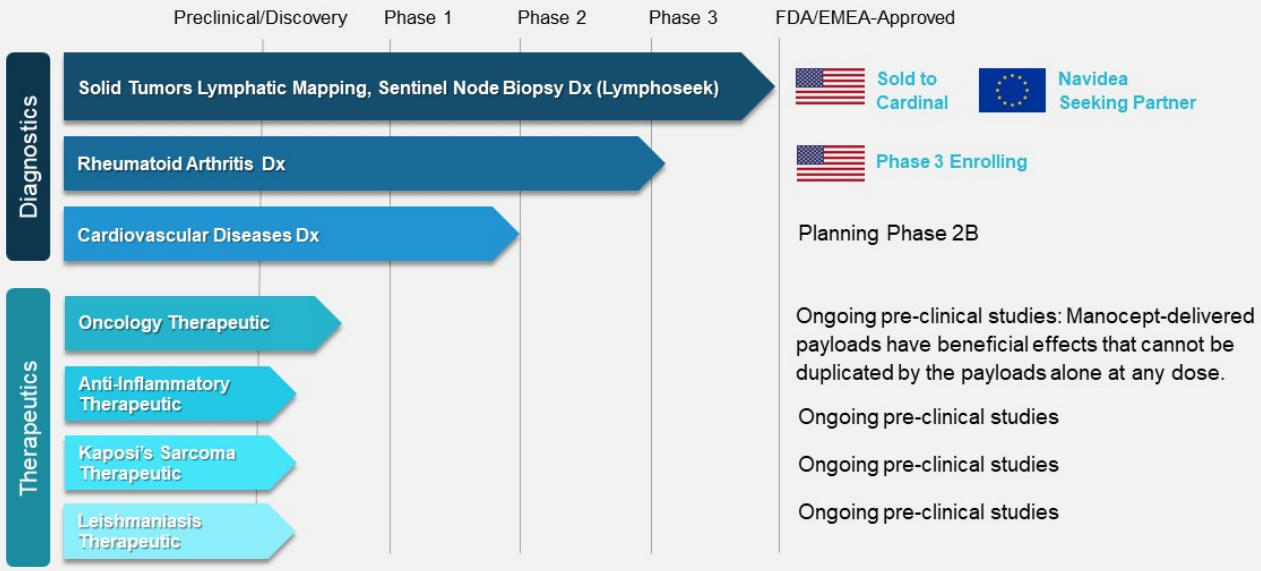
Lead pipeline product is a treatment response predictor enabling personalized rheumatoid arthritis disease management.

Manocept Platform addresses unmet diagnostic and therapeutic needs in many societally important diseases.

Navidea® BIOPHARMACEUTICALS

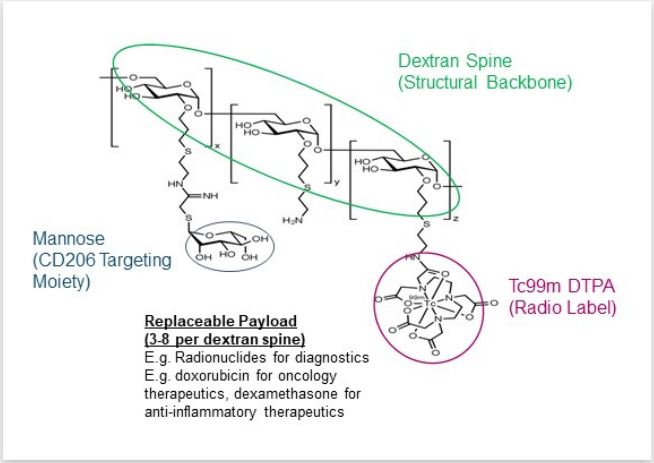
A precision targeted immuno-diagnostics and therapeutics company focused on inflammatory diseases and cancer for better patient outcomes

Our Diagnostics and Therapeutics Pipeline



Our Core Technology

Targeted Binding to Activated Macrophages

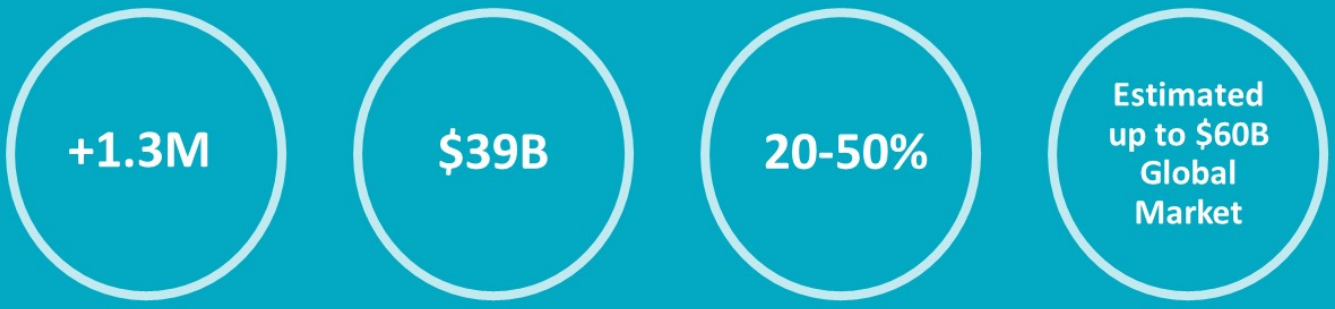


- Target CD206 receptor on **macrophages**- on the order of best-in-class affinity
- **Flexible Manocept platform** allows switching of payloads for diagnostics or therapeutics indications
- Macrophages are involved in many diseases
- FDA/EMA approved **(favorable regulatory pathway)**
- Over 600,000 injections with no SAEs **(safe core molecule)**

Key Features of the Manocept Platform

	Manocept	Key Differentiator
Target	Activated macrophages	Significant Unmet Need in Cancer, CVD, and RA
Chemistry	Cell-free synthetic chemistry	Scalable, low-cost production- high gross margins; Difficult to reverse engineer
Backbone (BB)	Made from natural carbohydrate polymers	Very low toxicity and antigenicity
Specificity	Targeted, high affinity binding to macrophages	Highly reduced off-target exposure and toxicity
Small size	10-22 kDa	Better tissue penetration
Drug loading	Can be loaded with nearly any small molecule payload	Highly adaptable and expandable drug delivery platform

Why Focus on Rheumatoid Arthritis?



Patients in the US are living with RA[1]

$39 billion cost to the US economy[2]

20-50% of patients respond adequately to RA treatment[3]

RA is one of the largest drug categories globally[4]

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

2 Birnbaum et al., Curr Med Res Opin. 2010 Jan;26(1):77-90.

3 Smolen JS, Aletaha D. Nat Rev Rheumatol. 2015 May;11(5):276-89.

4 https://www.precedenceresearch.com/rheumatoid-arthritis-drugs-market

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Why Focus on Rheumatoid Arthritis? A Large Unmet Need to Find the Best RA Tx for the Individual Patient

Hypothesis is that **tilmanocept imaging can quantify whether a drug is working or likely to work earlier than is currently possible- even before the patient has started an anti-TNFα** in some cases

- There are many patients living with RA in the US (>1.3M by most estimates)
- Current treatments might work for a time but then **typically fail**
- Almost all patients (~90%) are put on an **anti-TNFα biologic therapy** as first-line biologic treatment- this is our first focus
- **About half or more of these patients will fail to receive a clinically meaningful response!**
- ***Current methods of assessing efficacy are subjective and are performed up to 6 months after a patient has started a drug***
- In this time the disease **might be getting worse**, there are possible **serious side effects**, and the **costs are high** ($3,000 per month)
- When a drug is found to not be working, a **spin-the-wheel attempt with new drug is made- cycle repeats**
- There is a **large unmet need** for a reliable, early predictor of treatment efficacy- **tilmanocept imaging**
- **Macrophages are the key target of anti-TNFα tx** (and play a role in all RA types and all RA therapies), and **tilmanocept imaging can quantify levels of macrophage involvement**

The Goals of Our Completed and Ongoing RA Studies

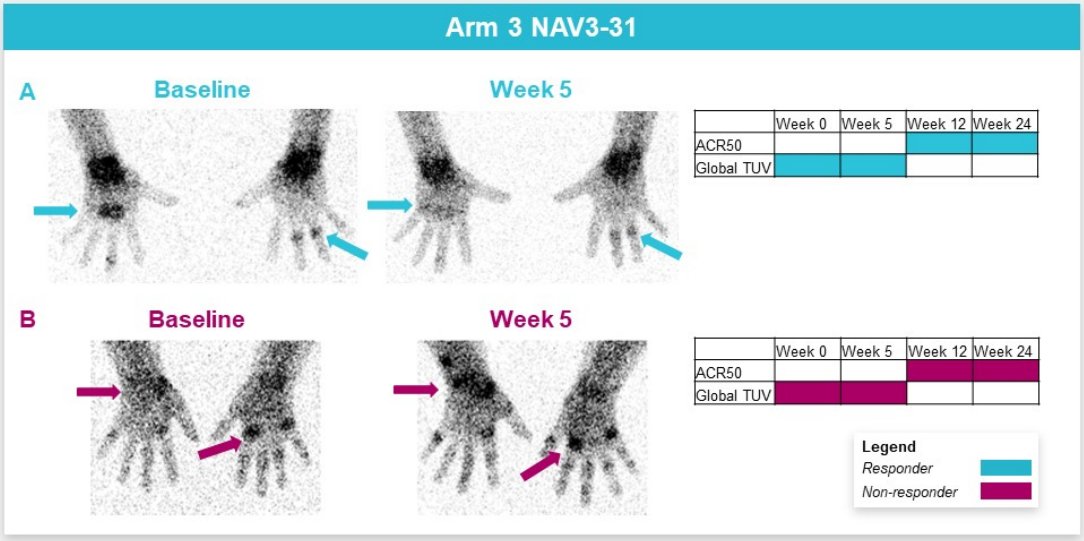
Confirm Reproducibility and Evaluate Predictive Capacity of Tx Response- Completed
(NAV3-31 P2B- 116 patients)

Establish Normative Database- Completed
(NAV3-35 P2B- 134 patients)

Correlate with Pathology- Ongoing
(NAV3-32 P2B- 12-24 patients)

Establish Predictive Capacity of Tx Response- Ongoing
(NAV3-33 P3- 198-672 patients)

Tc99m Tilmanocept Prediction of Treatment Response



Tc99m tilmanocept imaging can provide early prediction of treatment efficacy

Tc99m Tilmanocept Prediction of Treatment Response

NAV3-31 Arm 3

Tilmanocept Imaging	Clinical Efficacy- ACR50 Week 12	Clinical Efficacy- ACR50 Week 24
Total Predicted Correctly	27	24
Total Predicted Incorrectly	3	4

Tilmanocept Imaging	Clinical Efficacy- ACR50 Week 12	Clinical Efficacy- ACR50 Week 24
Negative Predictive Value	.92	.88
Positive Predictive Value	.75	.67

N=30 patients up to week 12;
28 patients up to week 24

~90% accuracy at early prediction

Our First Rheumatoid Arthritis Indications

Quantitative Imaging with Tc 99m Tilmanocept for candidates of Anti-TNF Therapy

- **Early prediction of RA treatment response to a new or first time anti-TNFα therapy.**
  Imaging shortly after initiation of a new Tx
- **Identify RA patients with low level of localization who are less likely to respond to anti-TNFα therapy.**
  Imaging before treatment (low localization= low macrophage= no anti-TNF)
- **Planned NDA submission 2024**

NAV3-32 P2B Preliminary Results
Two distinct, non-overlapping classes

To date:

11 patients with both imaging and biopsy
- 7 fibroid
- 3 diffuse myeloid
- 1 lympho-myeloid

Tilmanocept imaging is **11/11** at identifying fibroid vs. non-fibroid

Why this is important:
- *Patients with the fibroid pathotype of RA have been shown to be much less responsive to anti-TNF therapies*
- *If we can identify fibroid patients at baseline the physician can recommend a different class of therapy with a better chance of success*

Subject	Global TUV	Pathotype
32-03-002	12.26	LM
32-03-005	2.67	Fibroid
32-03-003	5.77	Fibroid
32-01-002	25.74	Diffuse Myeloid
32-03-006	1.81	Fibroid
32-01-003	3.89	Fibroid
32-03-007	11.51	Diffuse Myeloid
32-01-001	3.99	Fibroid
32-03-011	10.52	Diffuse Myeloid
32-03-009	5.04	Fibroid
32-03-014	3.52	Fibroid
Average		
Fibroid	3.81	
DM	15.92	
LM	12.26	

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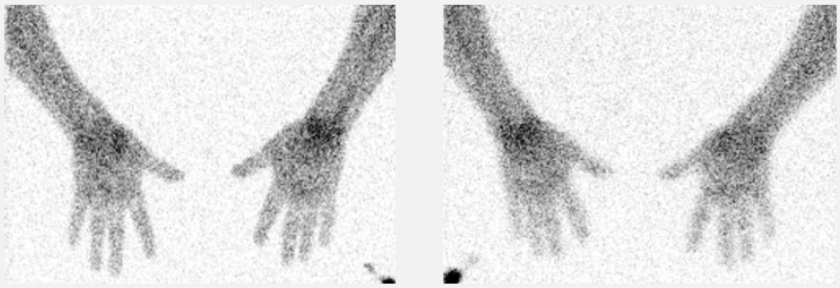
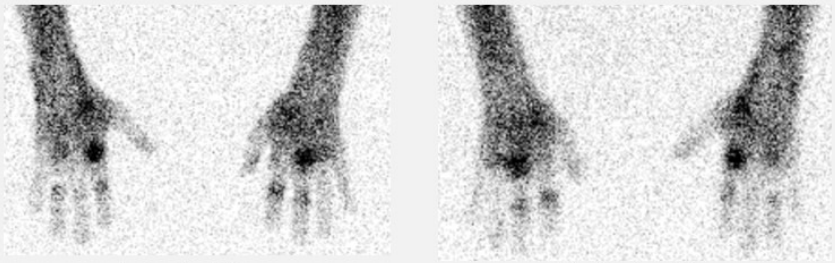
NAV3-32 P2B example images

32-03-014 (Fibroid)



32-03-007 (Diffuse Myeloid)

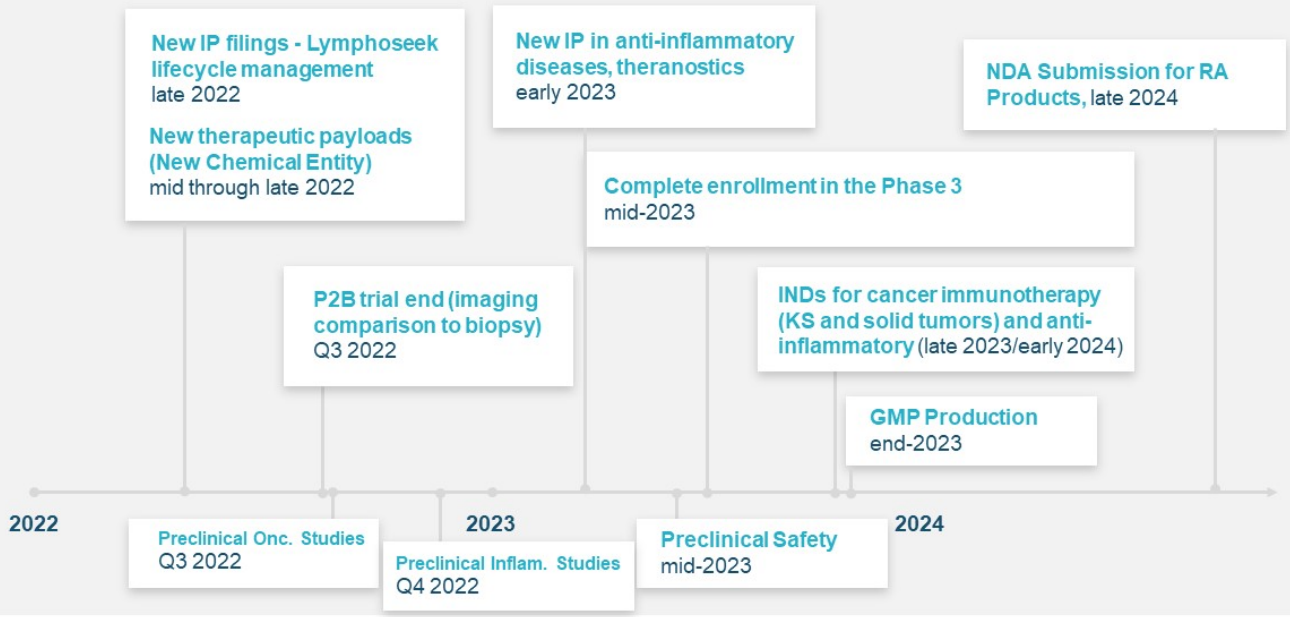


Anterior View | Posterior View

RA Path to NDA Submission

- **FDA discussion & review of Phase 3 meeting held September 1, 2021**
- Began Phase 3 Fourth Quarter 2021
- NAV3-32 Phase 2b correlation of imaging to biopsy readout ongoing
  - Not on critical path for FDA approval, supports adoption and biomarker designation, proof of MoA
- Aim for completion of Phase 3 by end of 2023 (Complete Enrollment by mid-2023)
- **NDA submission targeted 2024**

Milestones in the Next 12-24 Months



Key Management

Michael Rosol

Chief Medical Officer

Prior to Navidea, Dr. Rosol served as Associate Director in the Clinical and Translational Imaging Group at Novartis Institutes for BioMedical Research from 2016 to 2018, and as Head of its Translational Imaging Group from 2012-2015.

He was also Senior Director of Business Development at Elucid Bioimaging, Inc. where he drove adoption of its Computer-Aided Phenotyping applications in 2016 and CSO of MediLumine, Inc. from 2015 to 2016.

Dr. Rosol holds a Ph.D. from the Boston University School of Medicine.

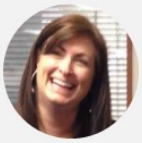
Jeffrey Smith

Vice President, Operations

Prior to joining Navidea in 2012, Mr. Smith held FP&A leadership roles at Cardinal Health, where he completed several M&A deals in expansion of the company's PET manufacturing and radiopharmacy footprint.

His professional career began in Operations Management at Bunge Ltd and General Mills Inc.

Mr. Smith earned a Chemical Engineering degree and Economics minor from The Ohio State University, and an MBA with Financial Management emphasis from Ashland University.



Erika Eves

Vice President, Finance & Administration

Erika has served as Vice President, Finance and Administration of Navidea since November 2020. Ms. Eves has served the Company in several roles of increasing responsibility beginning in March 1992, including Accounting Clerk, Staff Accountant, Senior Accountant, Controller and Director, Finance and Administration. In addition to directing the financial operations of the Company, she is responsible for internal and external financial reporting including all SEC filings, maintaining a system of internal controls, and managing banking and vendor relationships.

Ms. Eves earned a B.S.B.A. in Accounting from The Ohio State University and is a Certified Public Accountant.

Use of Funds

- Continue RA program through NDA submission
  - Complete Phase 3 (NAV3-33)
  - Complete imaging to biopsy trial (NAV3-32)
- Advance therapeutics pipeline to IND
- General SG&A