Some of the statements made in this presentation represent forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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 Acts. The words “believe,” “expect,” “anticipate,” “estimate,” “project,” “forecast”, “goal” “future”, “intent”, “will”, “may”, ”could” and similar expressions, as well as the negatives of thee 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, 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.
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.

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.

A precision targeted immuno-diagnostics and therapeutics company focused on inflammatory disorders and cancer for better patient outcomes.
Our Diagnostics and Therapeutics Pipeline

Diagnostics
- Solid Tumors Lymphatic Mapping, Sentinel Node Biopsy Dx (Lymphoseek™)
- Rheumatoid Arthritis Dx
- Cardiovascular Diseases Dx

Therapeutics
- Oncology Therapeutic
- Anti-Inflammatory Therapeutic
- Kaposi's Sarcoma Therapeutic
- Leishmaniasis Therapeutic

Preclinical/Discovery Phase 1 Phase 2 Phase 3 FDA/EMEA-Approved

- Ongoing pre-clinical studies: Manocept-delivered payloads have beneficial effects that cannot be duplicated by the free drugs at any dose.

Planning Phase 2B, tbd with FDA

- Ongoing pre-clinical studies
- Ongoing pre-clinical studies
- Ongoing pre-clinical studies

- Sold to Cardinal
- Navidea Seeking Partner
Our Core Technology

Targeted Binding to Activated Macrophages

- Target CD206 receptor on macrophages - best-in-class affinity
- Flexible Manocept platform allows switching of payloads for diagnostics or therapeutics indications
- Macrophages are involved in a very large number of diseases
- FDA/EMA approved (favorable regulatory pathway)
- Over 600,000 injections with no drug-related serious adverse events (safe core molecule)

- Mannose (CD206 Targeting Moiety)
- Dextran Spine (Structural Backbone)
- Tc99m DTPA (Radio Label)
- Replaceable Payload (3-8 per dextran spine)
  - E.g. Radionuclides for diagnostics
  - E.g. doxorubicin for oncology therapeutics, dexamethasone for anti-inflammatory therapeutics
# Key Features of the Manocept™ Platform

<table>
<thead>
<tr>
<th>Manocept™</th>
<th>Key Differentiator</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>Activated macrophages</td>
</tr>
<tr>
<td><strong>Chemistry</strong></td>
<td>Cell-free synthetic chemistry</td>
</tr>
<tr>
<td><strong>Backbone (BB)</strong></td>
<td>Made from natural carbohydrate polymers</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>Targeted, high affinity binding to macrophages</td>
</tr>
<tr>
<td><strong>Small size</strong></td>
<td>10-22 kDa</td>
</tr>
<tr>
<td><strong>Drug loading</strong></td>
<td>Can be loaded with nearly any small molecule payload</td>
</tr>
</tbody>
</table>
Why Focus on Rheumatoid Arthritis?
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 at some point in their treatment path- 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
- During this time the disease might be getting worse, there are possible serious side effects, and the costs are high (~$3,000 per month)
- When drug is found to not be working, a “spin-the-wheel” attempt with new drug is made- cycle repeats
- A reliable, early predictor of treatment efficacy is needed- tilmanocept imaging
- Macrophages are the key target of anti-TNFα tx (and play a role in RA types and 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)
- **Establish Normative Database** - COMPLETED (NAV3-35 P2B)
- **Correlate with Pathology** - Ongoing (NAV3-32 P2B)
- **Establish Predictive Capacity of Tx Response** - Ongoing (NAV3-33 P3)
Tc99m Tilmanocept Prediction of Treatment Response

Tc99m tilmanocept imaging can provide early prediction of treatment efficacy
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
RA Path to NDA Submission

- FDA discussion & review of Phase 3 meeting held September 1
- Began Phase 3
- 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
**Tc-Tilmanocept Base-case Revenue Projections* (U.S. and EU)**

*Tc-Tilmanocept may generate ~$735 M and ~$500 M in annual revenue by 2036 in the U.S. and EU, respectively*

**Base-case U.S. and EU Projected Net Revenue ($M)**

<table>
<thead>
<tr>
<th>Year</th>
<th>U.S. Sales</th>
<th>EU Sales</th>
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<tbody>
<tr>
<td>2022</td>
<td>$41</td>
<td>$134</td>
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<tr>
<td>2023</td>
<td>$42</td>
<td>$176</td>
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<tr>
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<td>2036</td>
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</table>

U.S. and EU Base-case Outputs:
- **2036 Peak Sales:** $1.2 B
- **Aggregate Sales (2022 – 2036):** $11.7 B
- **Probability Of Success:** 52%
- **rNPV (2022 – 2036):** $1.1 B

*Third-party valuation*
If Tc-Tilmanocept is incorporated into ACR/EULAR guidelines, 2036 U.S. / EU sales may approach ~$2.6 B

```
2036 Peak Sales: $2.6 B
Aggregate Sales (2022 – 2036): $24.0 B
Probability Of Success: 52%
rNPV (2022 – 2036): $2.2 B
```

*Third-party valuation
Therapeutics Optionality

Leveraging our core Manocept Platform to deliver targeted therapeutics.
Therapeutics Concept

Platform for Therapeutics that target CD206+ (and CD209 dendritic cells) Activated Macrophages

GPS

Mannose Moiety With One Hardwired Address - CD206 Activated Macrophages

Delivery

Manocept™ Backbone

Targeted Payload

Immune-modulators, Chemotherapeutics, Tc⁹⁹, Other Isotopes
Fibrosis
Overactive M2 macrophages are a key driver of fibrosis (NASH, Nephropathies, Fibrotic Disorders)

Cardiovascular
Lipid-containing macrophages can exacerbate atherosclerosis, an inflammatory condition

Infectious Disease
The macrophage acts as an incubator in certain infectious diseases - Leishmaniasis

Therapeutics Pipeline

Oncology - almost all cancers
Flipping Tumor Associated Macrophages & Altering the Tumor Microenvironment to Enhance Immunotherapies
Targeted therapeutics convert M2-like (pro-tumor) TAMs to M1 (anti-tumor) macrophages, stimulating immune response against tumors

Depleting Myeloid Derived Suppressor Cells

Anti-inflammatory - ARDS
Altering Activated Macrophage Function & Treating the Mechanism of Disease
Inhibiting Inflammatory Activity
Targeted steroid converts M1 to M2

Pipeline Expansion
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 Nov 16 to Dec 18, 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 from May 16 to Nov 16, and CSO of MediLumine, Inc. from Oct 2015 to May 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 Mgmt 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.