Navidea®
BIOPHARMACEUTICALS

Investor Presentation

May 2022

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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**.

Navidea BIOPHARMACEUTICALS

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.

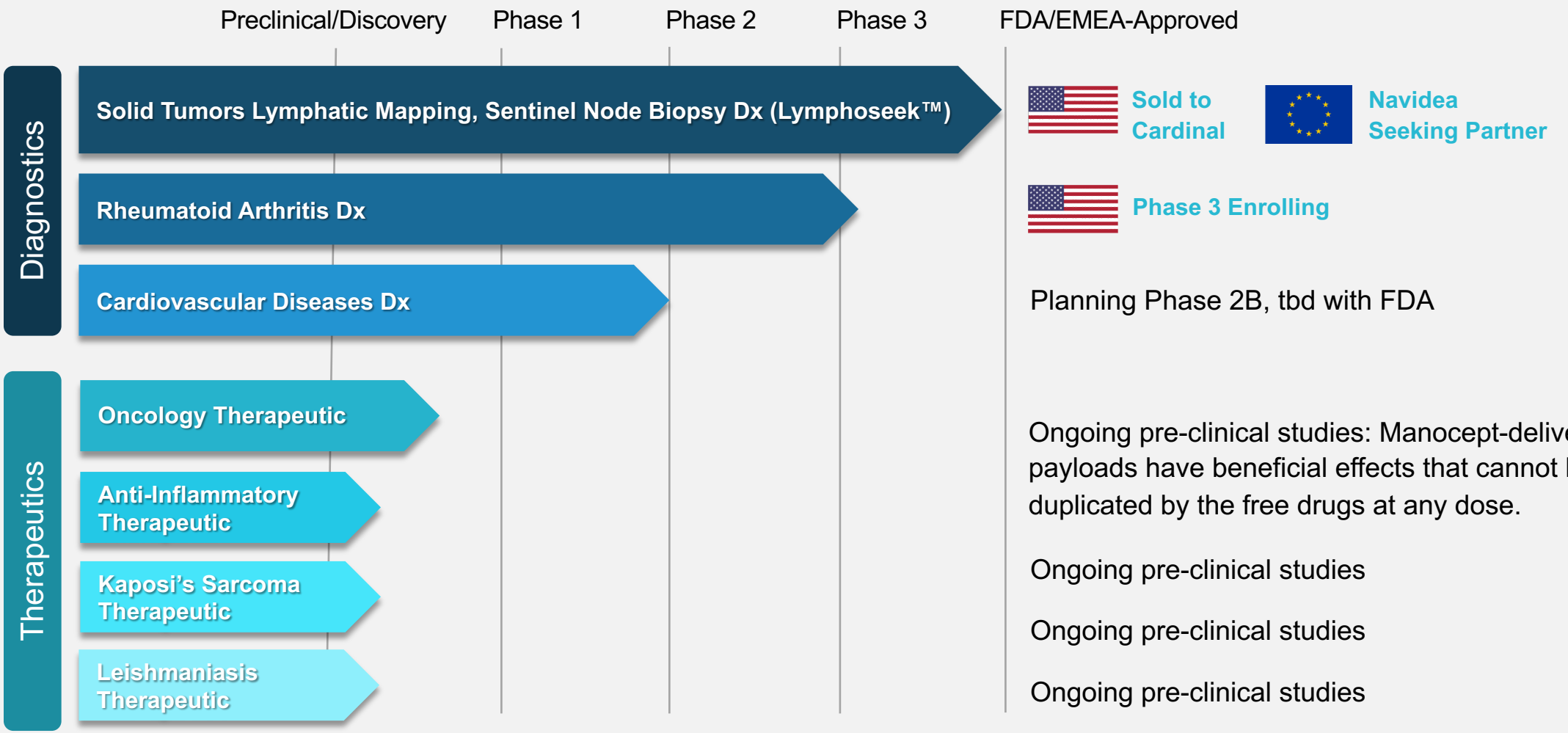
Lead pipeline product is a treatment response predictor enabling personalized rheumatoid arthritis disease management.

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

Navidea® BIOPHARMACEUTICALS

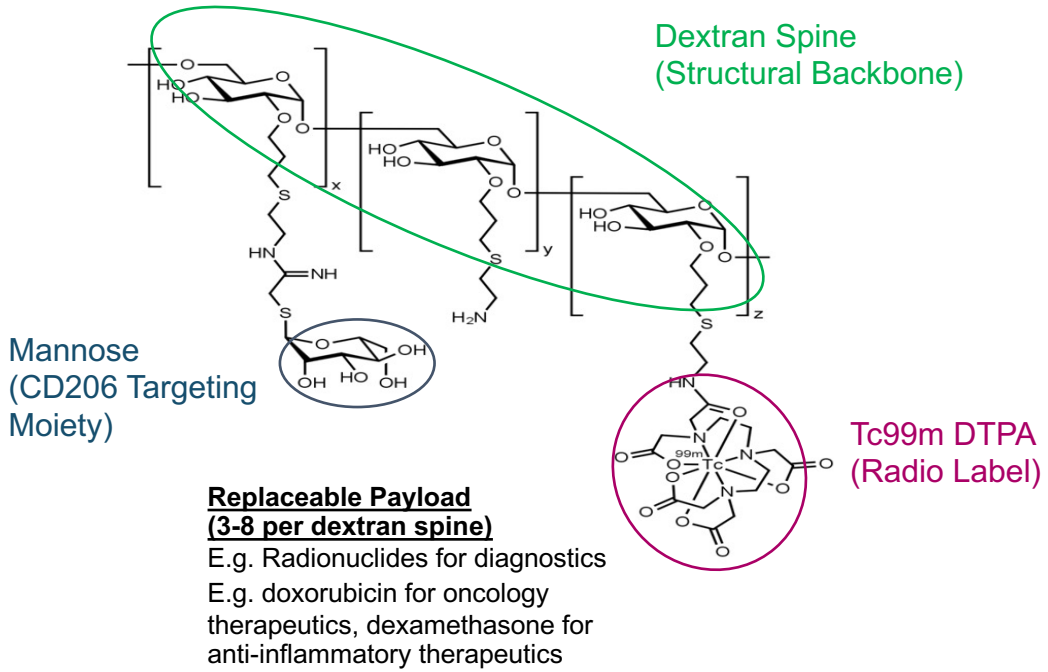
A precision targeted immuno-diagnostics and therapeutics company focused on inflammatory disorders and cancer for better patient outcomes

Our Diagnostics and Therapeutics Pipeline



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)**

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 or 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?

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)

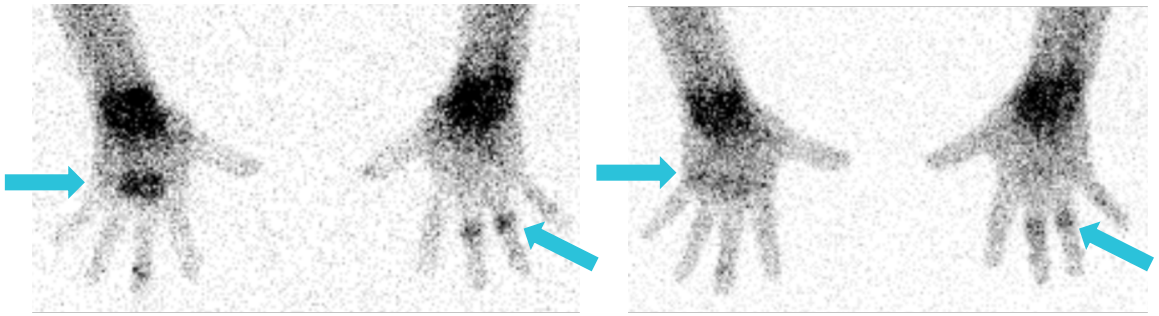
Correlate with Pathology- Ongoing
(NAV3-32 P2B)

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

Tc99m Tilmanocept Prediction of Treatment Response

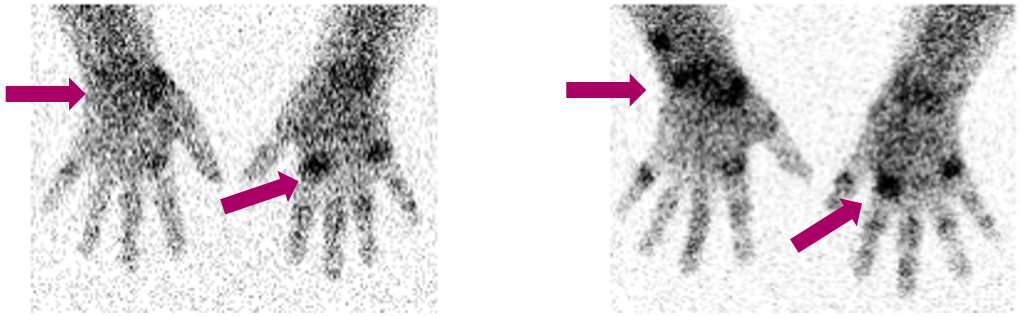
Arm 3 NAV3-31

A Baseline Week 5



	Week 0	Week 5	Week 12	Week 24
ACR50				
Global TUV				

B Baseline Week 5



	Week 0	Week 5	Week 12	Week 24
ACR50				
Global TUV				

Legend
Responder
Non-responder

~90% accuracy at early prediction of ACR50 response (90% at week 12 and 86% at week 24)

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

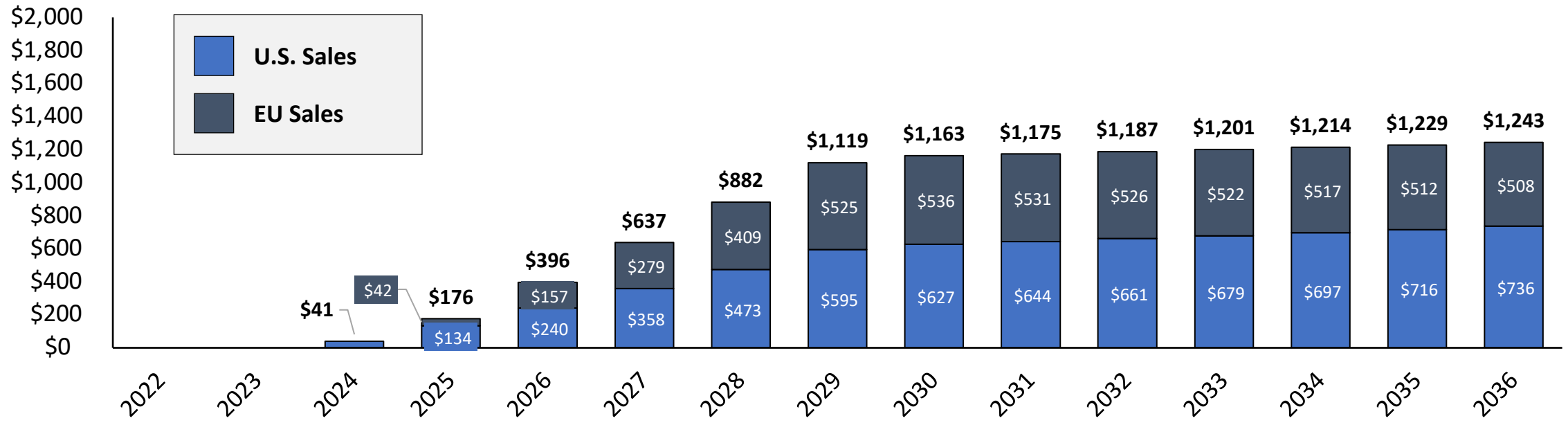
  Not on critical path for FDA approval, supports adoption and biomarker designation, proof of MoA

- 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)



U.S. and EU Base-case Outputs

2036 Peak Sales:	Aggregate Sales (2022 – 2036):	Probability Of Success:	rNPV (2022 – 2036):
$1.2 B	$11.7 B	52%	$1.1 B

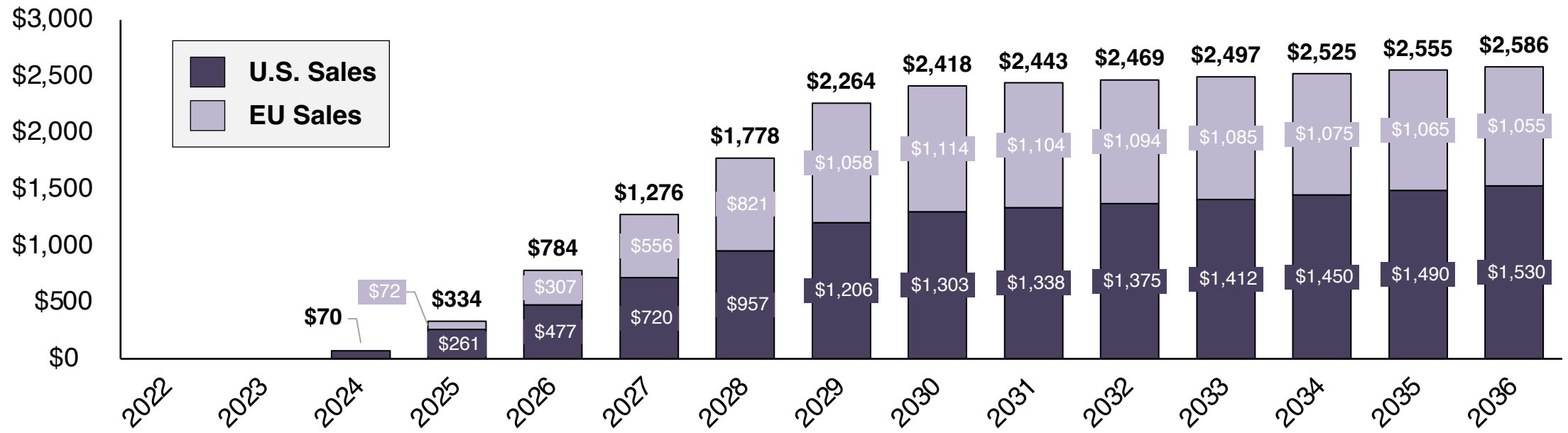
rNPV: Risk-Adjusted Net Present Value.

*Third-party valuation

Tc-Tilmanocept Upside Revenue Projections* (U.S. and EU)

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

Upside Projected Net Revenue ($M)



U.S. and EU Upside Outputs

2036 Peak Sales: $2.6 B

Aggregate Sales (2022 – 2036): $24.0 B

Probability Of Success: 52%

rNPV (2022 – 2036): $2.2 B

rNPV: Risk-Adjusted Net Present Value.

*Third-party valuation

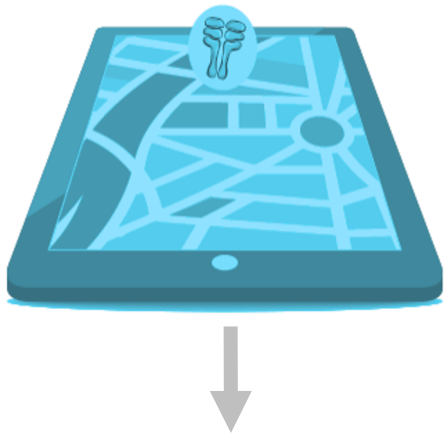
Therapeutics Optionality

Leveraging our core Manocept Platform to deliver targeted therapeutics.

Therapeutics Concept

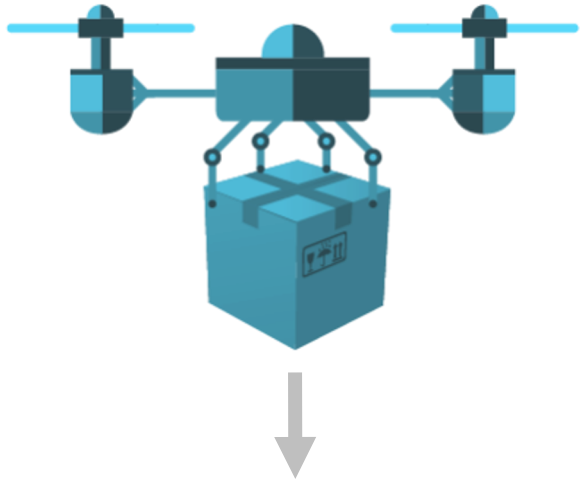
Platform for Therapeutics that target CD206+ (and CD209 dendritic cells) Activated Macrophages

GPS



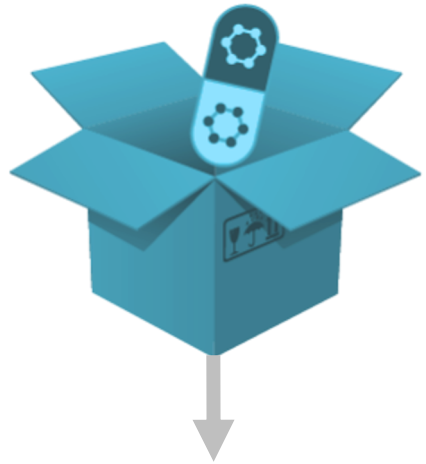
Mannose Moiety
With One Hardwired Address -
CD206 Activated Macrophages

Delivery



Manocept™
Backbone

Targeted Payload



Immune-modulators,
Chemotherapeutics, Tc^{99},
Other Isotopes

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

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

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.