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

# FORM 8-K

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

| | |
|---|---|
| Date of Report (date of earliest event reported): | December 13, 2021 |

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

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

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

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

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

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

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

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

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

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

Emerging growth company ☐

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

**Item 8.01 Other Events.**

On December 13, 2021, Navidea Biopharmaceuticals, Inc. (the "Company") provided an executive summary of a third-party asset valuation of its rheumatoid arthritis diagnostic product candidate on its corporate website, www.navidea.com.

Copies of the valuation report and the December 13, 2021 press release announcing the report are furnished as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K and are incorporated herein by reference.

**Item 9.01. Financial Statements and Exhibits.**

(a) Not applicable.

(b) Not applicable.

(c) Not applicable.

(d) Exhibits

| **Exhibit No.** | **Description** |
|---|---|
| 99.1 | Navidea Biopharmaceuticals, Inc. Valuation Report |
| 99.2 | Press Release dated December 13, 2021 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURES**

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

Navidea Biopharmaceuticals, Inc.

Date: December 13, 2021

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

EXHIBIT 99.1

**NAVIDEA BIOPHARMACEUTICALS, INC.**
**REPORT OF LIFESCI PARTNERS**
**EXPLANATORY NOTE**
**December 13, 2021**

Navidea Biopharmaceuticals, Inc. ("Navidea") is publicly disclosing the attached report (the "LifeSci Report") of LifeSci Partners (LifeSci Advisors, LLC), which has performed a U.S.-focused secondary market research valuation of Navidea's advanced pipeline product Tc99m tilmanocept for prediction of treatment efficacy of anti-TNFα therapy in Rheumatoid Arthritis ("RA"). Navidea is releasing the LifeSci Report to provide investors with information on Navidea's process for evaluating investments in its product pipeline.

*Cautionary Note Regarding Forward-Looking Statements.* Some of the statements made in the LifeSci Report 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. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things, the fact that the valuation by LifeSci Partners of Navidea's Tc99m tilmanocept pipeline product is subject to and based on numerous assumptions about the commercial success of the product, expected associated costs, and the outcome of various risks, including results of clinical trials, that could affect the timetable for revenues, among other assumptions, and that actual outcomes are likely to vary from such assumptions, which would result in variations from the possible results set forth in the LifeSci Report. Any such statements about possible outcomes for Navidea's product are subject to other risk factors detailed in Navidea's most recent Annual Report on Form 10-K and other SEC filings. You are urged to carefully review and consider the disclosures found in Navidea's SEC filings, which are available at http://www.sec.gov or at http://ir.navidea.com.

You are cautioned not to place undue reliance on any forward-looking statements, any of which could turn out to be incorrect. Navidea undertakes no obligation to update publicly or revise any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this report. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements.

LIFESCI PARTNERS

Partnering & Analytics | December 2021

Navidea Biopharmaceuticals
U.S. RA Diagnostics rNPV Valuation

# Executive Summary

As the first therapeutic-guiding RA diagnostic, Tc-Tilmanocept represents a potential multi-billion $ opportunity

| | |
|---|---|
| **Diagnostics Landscape** | • Tc-Tilmanocept is positioned to be the **first and only therapeutic-guiding diagnostic** in rheumatoid arthritis (RA), a disease that impacts ~1.9 M adult patients in the U.S.<br>• A novel RA radiopharmaceutical diagnostic may fall under **CMS's CPT code 78802** |
| **Tc-Tilmanocept Positioning** | • For the purpose of this assessment, we modeled Tc-Tilmanocept's opportunity for **adult RA patients in consideration for anti-TNF therapies** (i.e., 2L+ patients), though opportunity remains for label expansion to additional therapeutic classes, pediatrics, and primary diagnosis |
| **Base-case Valuation Outputs** | • Assuming ~45% share in 2L+ line-of-therapy switch patients, ~4.5% share in 2L+ prevalent follow-up patients, and a discount rate of 12%, **cumulative 2022 – 2036 revenue may reach ~$9.2 B with a PV of ~$3 B**<br>• With costs and a ~52% likelihood of success, **risk-adjusted net present value (rNPV) may reach ~$850 M** |
| **Upside Valuation Outputs** | • Upside scenario assumes **ACR guideline inclusion** boosts 2L+ switch share to ~78% and 2L+ prevalent share to ~7.8%, resulting in **~$15.9 B in cumulative revenue from 2022 – 2036 and a PV of ~$5.2 B**<br>• The upside scenario may result in an **rNPV of ~$1.5 B** after considering the program's costs and risks |
| **Future Opportunities** | • Multiple opportunities remain to unlock further Tc-Tilmanocept value in RA, including **label expansion** to additional therapeutic classes or pediatrics, **patient advocacy campaigns** to increase **patient compliance** and **diagnosis rates**, **marketing efforts** to **bolster preference share**, and **registration as a biomarker** |



RA: Rheumatoid Arthritis; CMS: Centers for Medicaid and Medicare Services; CPT: Current Procedure Terminology; 2L: Second-line; PV: Present Value; ACR: American College of Rheumatology.

# Table of Contents

Navidea Biopharmaceuticals U.S. Rheumatoid Arthritis Diagnostic Valuation

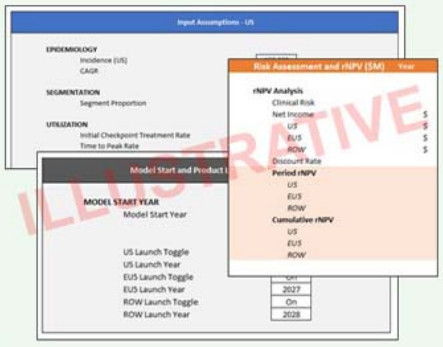
LIFESCI PARTNERS

# Valuation Model Architecture

# P&L Model Scope

LifeSci built an Excel model to calculate the risk-adjusted net present value (rNPV) of Navidea's RA diagnostic

*The LifeSci **P&L model** estimates the present value of the RA program*




**Context:** The P&L dynamically models the future commercial opportunity, costs, and rNPV of Navidea's RA diagnostic in the U.S. market

**Key Territory:**
**United States**

**Disease:**
**Rheumatoid Arthritis**

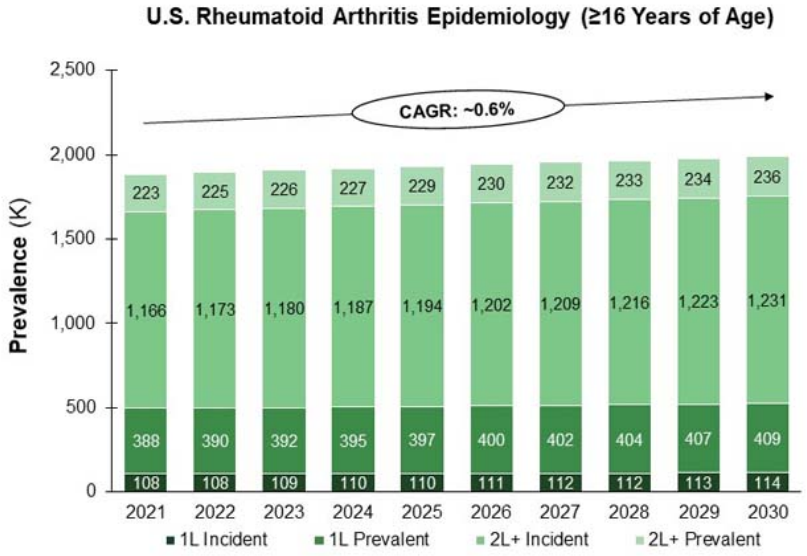
**Evaluated Label:**
*For the early prediction of Anti-TNFα response in patients with moderate to severe active rheumatoid arthritis*

**The P&L outputs revenue, expenses, probability of success, and net present value for the RA diagnostic based on inputs sourced from LifeSci secondary research and Navidea internal assumptions**


# Rheumatoid Arthritis Landscape

# U.S. Rheumatoid Arthritis Epidemiology (≥16 Years of Age)

Due to poor initial response rates and current therapies' attenuating efficacy, most RA patients are in the 2L+




In the U.S., rheumatoid arthritis (RA) has an **incidence of ~40 per 100 K** and a **prevalence of ~0.7%** of the population over 16 years of age

Of incident patients who initiate 1L methotrexate therapy, **~30% will initially respond** with an average **duration on treatment of ~13 years**

Among 2L+ patients initiating a new line of therapy (i.e., "2L+ Incident" patients), **~20% and ~15% initially respond** for an average of **~4 and ~2 years** in the 2L and 3L+ setting, respectively



Source: Almutairi. Rheum Int. 2020; Novella-Navarro. Arth Res & Ther. 2020; Bluett. Arth Res & Ther. 2018; Aletha. JAMA. 2018; Eriksson. Arthritis Care Res. 2013; Myasoedova. Rheumatoid Arthritis Clinical Studies. 2010; Census Bureau International Data Base. LoT: Line of Therapy. Note: Epidemiology does not include the ~300 K Juvenile RA patients under the age of 16 in the U.S. (Prakken. The Lancet. 2011).

# Rheumatoid Arthritis Diagnostics Landscape and Pricing Potential

Tc-Tilmanocept is unlikely to face competition from other diagnostics

**Rheumatoid Arthritis Diagnostics Landscape**

| Current Availability of RA Diagnostic Capabilities | | |
|---|---|---|
| Diagnostic | Prognostic | Therapeutic-guiding |
| ✓ | ✓ | ✗ |

- There are **no therapeutic-guiding RA diagnostics** commercialized or in development that are expected to pose a direct competitive threat to Tc-Tilmanocept
- **Inflammatory blood markers** such as CRP levels, rheumatoid factor, and anti-CCP antibodies may be tested to **complement physicians' clinical diagnosis** of RA or **inform prognosis**
- Quest offers such **RA blood panels for ~$80**, though these panels are poor analogs for Navidea given **they do not provide therapeutic-guiding information**

**Radiopharmaceutical Diagnostic Price Range**

| Anticipated Tc-Tilmanocept Pricing and Reimbursement (2021) | CPT Code |
|---|---|
| | 78802 |

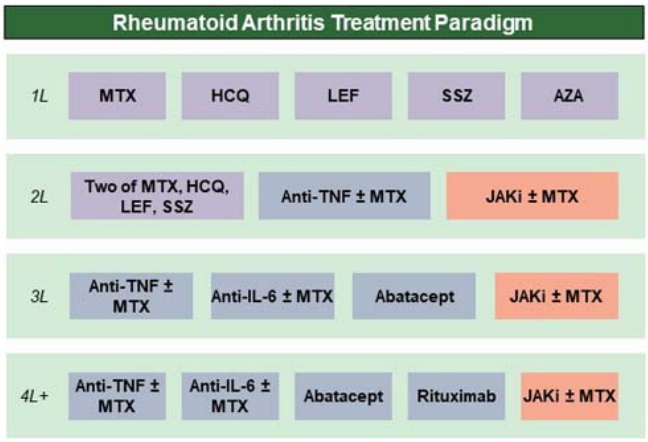
- CMS reimbursement for radiopharmaceutical diagnostics across therapeutic areas range from **$80 – 2,750 in 2021**
- **CPT code 78802** for "radiopharmaceutical localization of tumor, **inflammatory process** or **distribution of radiopharmaceutical agent(s),** (includes vascular flow and blood pool imaging when performed); planar, **whole body**, single day of imaging" may be appropriate for Tc-Tilmanocept in RA given its **coverage of inflammation and whole body imaging**



Source: SNMMI; Company Websites.
1. Annual reimbursement growth rate was 3.5% from 2019 – 2020, 2.6% from 2020 – 2021, and 2.1% from 2021 – 2022. CAGR of 2.1% was chosen to reflect the most recent and conservative rate.

# Rheumatoid Arthritis Treatment Paradigm

Anti-TNFs are used in the 2L+, but patients may switch TNFs and receive them across multiple lines of therapy




| | |
|---|---|
| 1L | **MTX is often prescribed** in conjunction with NSAIDs and GCs for rapid symptomatic relief; patients ineligible for MTX **receive alternative single-agent csDMARDs** |
| 2L | For the **~70% of patients** who do not achieve remission after **3 – 6 months of 1L therapy**, physicians most often prescribe **anti-TNFs with or without MTX** or a combination of two csDMARDs |
| 3L | Of the **~80% of patients** who fail 2L, most will receive **alternative anti-TNFs** or JAKis, while patients with severe inflammation may receive IL-6 inhibitors and elderly patients may receive abatacept |
| 4L | **~85% of 3L patients are refractory and progress to the fourth line**, where prescribing behavior is guided by patients' treatment history and highly variable; rituximab may be considered |

**We anticipate Tc-Tilmanocept to be used in the 2L+ as 1L patients are rarely considered for anti-TNF therapies given csDMARDs represent generic, lower-cost options (often stepped-through by payers)**



Source: ACR Guidelines; UpToDate; GlobalData. csDMARD: Conventional Synthetic Disease-modifying Antirheumatic Drug; GC: Glucocorticoid; MTX: Methotrexate; HCQ: Hydroxychloroquine; LEF: Leflunomide; SSZ: Sulfasalazine; AZA: Azathioprine.

Key: csDMARD bDMARD tsDMARD


# Summarized Valuation Assumptions

# Revenue and Cost Assumptions Summary

## Select Revenue Assumptions

- **Addressable Patients:** Adults >16 years with diagnosed RA
- **Overall RA Treatment Rate:** ~94%
- **Prevalent Patients (2024):** ~1.9 M
- **Preference Share:** 45% in 2L patients switching therapies in base case scenario
  *(Note: Based on secondary research only, pending upcoming physician interviews)*

  78% in upside scenario
- **Annual Tests per Patient:** 1 – 2
- **Compliance:** 40 – 60%
- **Launch Year (U.S.):** 2024

## Select Cost Assumptions

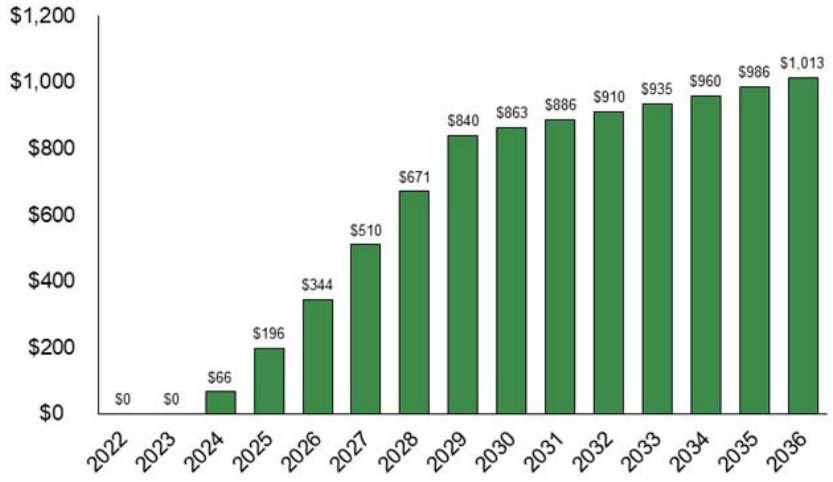
- **R&D and Regulatory Expenses:** Ongoing P2B & upcoming P3; NDA filing
- **SG&A:** high 20% range
- **CAPEX:** low single digit % of sales
- **Corporate tax rate:** 21%
- **Discount rate:** 12% (*Cost of capital estimates assume Navidea partners with a mid-to-large size company for RA commercialization)*
- **Probability of Technical and Regulatory Success (PTRS)**: Phase II: 100% Phase III: 68.4% Approval: 80.3% Commercialization: 95% (*Development risk assumptions based on historical precedence by stage for NMEs in autoimmune diseases reported in published literature (Hay. Nature. 2014). Assumes Tc-Tilmanocept has already succeeded Phase 2 based on data to-date.)*


# Tc-Tilmanocept Commercial Opportunity and Valuation

# Tc-Tilmanocept Base-case Revenue Projections (U.S.)

With base-case assumptions, Tc-Tilmanocept may generate ~$1 B in annual U.S. revenue by 2036

**Base-case Projected Net Revenue** ($M)

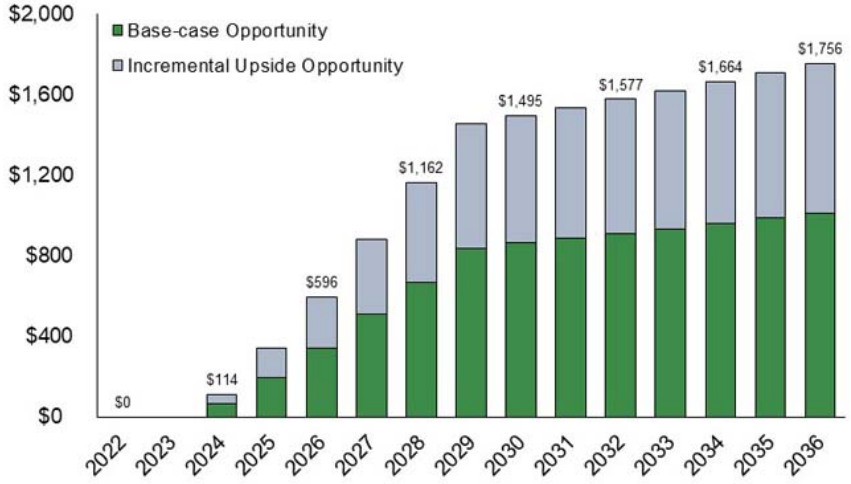



| Base-case PV Valuation Outputs | |
|---|---|
| **Present Value** (PV) | **~$3.0 B** |
| **Risk-adjusted PV** (rPV) | **~$1.6 B** |
| **Probability of Success (PoS)** | **~52%** |
| **U.S. Peak Sales** | **~$1.0 B** |
| **U.S. Cumulative Sales** (2022 – 2036) | **~$9.2 B** |

# Tc-Tilmanocept Upside Revenue Projections (U.S.)

Assuming American College of Rheumatology guideline inclusion boosts share to 78%, peak sales may approach ~$1.8 B

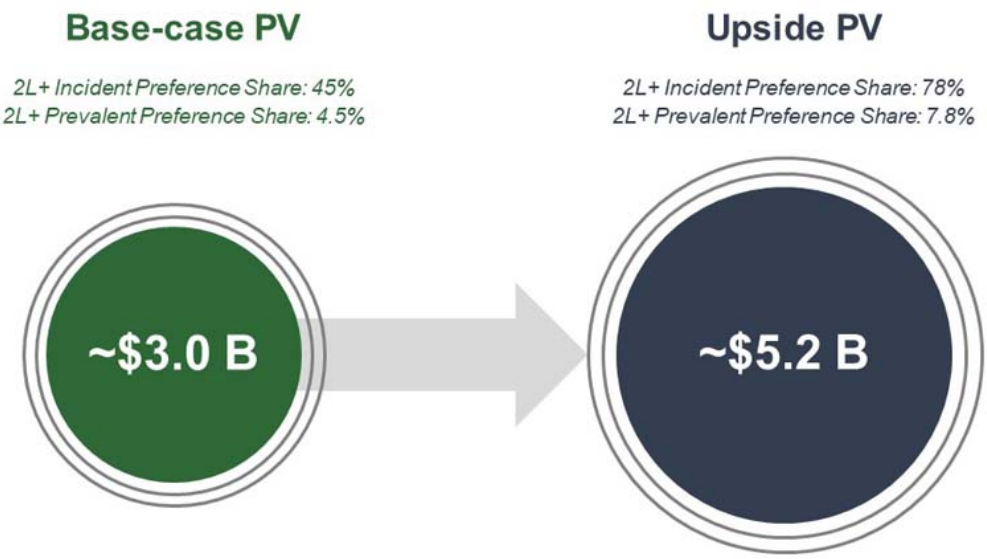
**Upside Projected Net Revenue** ($M)




| Upside PV Valuation Outputs | |
|---|---|
| **Present Value** (PV) | **~$5.2 B** |
| **Risk-adjusted PV** (rPV) | **~$2.7 B** |
| **Probability of Success (PoS)** | **~52%** |
| **U.S. Peak Sales** | **~$1.8 B** |
| **U.S. Cumulative Sales** (2022 – 2036) | **~$15.9 B** |

# Aggregate PV for Tc-Tilmanocept in RA (U.S.)

Cumulative revenue from 2022 – 2036 suggests a base-case PV of ~$3.0 B and upside potential of ~$5.2 B



# Aggregate rNPV for Tc-Tilmanocept in RA (U.S.)

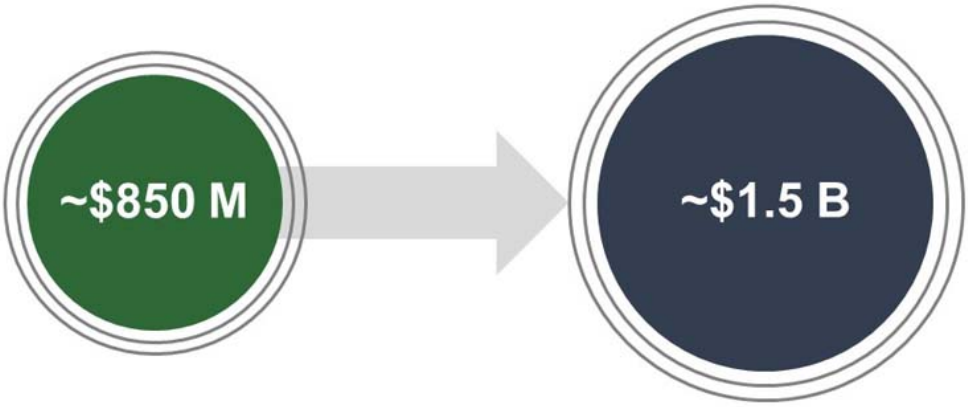
Accounting for revenue, costs, and risk, base-case rNPV may reach ~$850 M with upside potential of ~$1.5 B

## Base-case rNPV

*2L+ Incident Preference Share: 45%*
*2L+ Prevalent Preference Share: 4.5%*

## Upside rNPV

*2L+ Incident Preference Share: 78%*
*2L+ Prevalent Preference Share: 7.8%*



# Opportunities for Value Add

Multiple levers remain to unlock further Tc-Tilmanocept value in RA

### Expansion to Juvenile RA

Label expansion to Juvenile RA in patients <16 years of age may increase total diagnosed prevalence by ~300 K patients in the U.S.

### Increased RA Diagnosis Rate

Patient advocacy campaigns and clinical breakthroughs may improve RA's diagnosis rate and increase the diagnosed prevalence

### Increased Patient Compliance

Patient advocacy campaigns and increasing comfort with Tc-Tilmanocept over time may bolster patient compliance

### Increased Adoption

Marketing campaigns may drive adoption of Tc-Tilmanocept through guideline inclusion and physician preference

### Label Expansion to Other RA Drugs

Label expansion for therapeutic-guiding information across RA therapeutic classes will likely drive increased preference share

### Registration as a Biomarker

FDA registration for Tc-Tilmanocept's use as a biomarker of CD206 expression in RA joints may spur its use in clinical trials with pharma partners and support its inclusion in guidelines

Source: Prakken. The Lancet. 2011.

**Exhibit 99.2**

# Navidea Biopharmaceuticals Announces Third-Party Asset Valuation of Tc99m Tilmanocept for Indications in Rheumatoid Arthritis

DUBLIN, Ohio--(BUSINESS WIRE)--Navidea Biopharmaceuticals, Inc. (NYSE American: NAVB) ("Navidea" or the "Company"), a company focused on the development of precision immunodiagnostic agents and immunotherapeutics, today announced the results of a third-party asset valuation of its Rheumatoid Arthritis ("RA") diagnostic product candidate.

The Company engaged the independent third-party valuation firm, LifeSci Partners (LifeSci Advisors, LLC), to perform a U.S.-focused market research valuation of its advanced pipeline product Tc99m tilmanocept for prediction of treatment efficacy of anti-TNFα therapy in RA. A summary of the valuation report and the assumptions on which it is based is available on the Company's website, www.navidea.com.

The Company is advancing its program evaluating Tc99m tilmanocept imaging, a radiopharmaceutical that selectively targets the CD206 receptor expressed on activated macrophages, for indications in RA. A previously completed Phase 2B study demonstrated results in support of the hypotheses that Tc99m tilmanocept imaging can provide robust, quantitative imaging in healthy controls and in patients with active RA, and that this imaging can provide an early indicator of treatment efficacy in patients with active RA. The planned Phase 3 trial will evaluate the ability of Tc99m tilmanocept imaging to serve as an early predictor of treatment response in RA patients switching to an anti-TNFα therapy.

The valuation report used cited research and assumptions believed to conform to industry best practices. Under base-case assumptions that are discussed in the report, peak U.S. sales could reach $1 billion annually, and in the upside scenario peak annual U.S. sales could reach $1.8 billion. Opportunities for added value include possible indication expansion to other classes of RA therapeutics, registration of Tc99m tilmanocept imaging as a biomarker of activated macrophages in the joints of patients with RA, and expansion into additional geographic areas.

Dr. Michael Rosol, Navidea's Chief Medical Officer, said, "This report provides a third-party assessment of the potential commercial value of Tc99m tilmanocept in the U.S. market. We have released this in the spirit of transparency, while also giving investors a view into the company's internal rigor in evaluating investments in the product pipeline." Dr. Rosol continued, "We believe we are on the right path to bringing a valuable tool to bear to meet a large unmet medical need in patients with RA. Success would mean that we can provide rheumatologists and those suffering with RA a noninvasive, quantifiable, early indicator of whether or not an anti-TNFα treatment is working. This could bring enormous benefit to these patients by assisting physicians in putting them on the right course of treatment earlier than is possible today."

**About Navidea**

Navidea Biopharmaceuticals, Inc. (NYSE American: NAVB) is a biopharmaceutical company focused on the development of precision immunodiagnostic agents and immunotherapeutics. Navidea is developing multiple precision-targeted products based on its Manocept™ platform to enhance patient care by identifying the sites and pathways of disease and enable better diagnostic accuracy, clinical decision-making, and targeted treatment. Navidea's Manocept platform is predicated on the ability to specifically target the CD206 mannose receptor expressed on activated macrophages. The Manocept platform serves as the molecular backbone of Tc99m tilmanocept, the first product developed and commercialized by Navidea based on the platform. Navidea's strategy is to deliver superior growth and shareholder return by bringing to market novel products and advancing the Company's pipeline through global partnering and commercialization efforts. For more information, please visit www.navidea.com.

**Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements include our expectations regarding pending litigation and other matters. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: our history of operating losses and uncertainty of future profitability; the fact that the valuation by LifeSci Partners of our Tc99m tilmanocept pipeline product is subject to and based on numerous assumptions about the commercial success of the product, expected associated costs, and the outcome of various risks, including the outcome of clinical trials, that could affect the timetable for revenues, among other assumptions, that actual outcomes are likely to vary from such assumptions, resulting in variations from the possible results set forth in the valuation report; the final outcome of any pending litigation; our ability to successfully complete research and further development of our drug candidates; the timing, cost and uncertainty of obtaining regulatory approvals of our drug candidates; our ability to successfully commercialize our drug candidates; dependence on royalties and grant revenue; our ability to implement our growth strategy; anticipated trends in our business; our limited product line and distribution channels; advances in technologies and development of new competitive products; our ability to comply with the NYSE American continued listing standards; our ability to maintain effective internal control over financial reporting; the impact of the current coronavirus pandemic; and other risk factors detailed in our most recent Annual Report on Form 10-K and other SEC filings. You are urged to carefully review and consider the disclosures found in our SEC filings, which are available at http://www.sec.gov or at http://ir.navidea.com.

Investors are urged to consider statements that include the words "will," "may," "could," "should," "plan," "continue," "designed," "goal," "forecast," "future," "believe," "intend," "expect," "anticipate," "estimate," "project," and similar expressions, as well as the negatives of those words or other comparable words, to be uncertain forward-looking statements.

You are cautioned not to place undue reliance on any forward-looking statements, any of which could turn out to be incorrect. We undertake no obligation to update publicly or revise any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this report. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements.

**Investor Relations Contact**

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jsmith@navidea.com