Navidea Biopharmaceuticals, Inc. ("Navidea") is publicly disclosing the attached report (the "LifeSci Report") of LifeSci Partners (LifeSci Advisors, LLC), which has performed a primary U.S. market and secondary E.U. market research valuation of Navidea's advanced pipeline product Tc99m tilmanocept for prediction of treatment efficacy of anti-TNFα therapy in 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.

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Executive Summary

Tc-Tilmanocept represents a potential multi-billion opportunity to fill key unmet needs in RA for the U.S. and EU

- **Diagnostics Landscape**
  - Tc-Tilmanocept is positioned to be the first therapeutic-guiding diagnostic with **physician-perceived reliable predictive power** in RA, a disease that impacts ~1.9 M adult patients in the U.S. and ~3.7 M across Europe.
  - A novel RA radiopharmaceutical diagnostic is expected to **price between ~$850 (EU) and ~$1,300 (U.S.)**

- **Physician Feedback on Tc-Tilmanocept**
  - Physicians expressed **enthusiasm for Tc-Tilmanocept** in RA, particularly for **baseline prediction of response** to anti-TNF therapies, and anticipated use in the **majority of 2L+ patients** when initiating new lines of therapy; however, use in 5 week and annual follow-up settings may grow with increased data and comfort.

- **Base-case Valuation Outputs**
  - Assuming ~55% and ~8% share in 2L+ LoT switch and 1L incident patients, respectively, 5 week follow-up in ~35% of baseline patients, and annual follow-up in ~15% of baseline patients, **peak revenue may reach ~$1.2 B** in the U.S. and EU in 2036; considering costs and a ~52% POS, **rNPV may reach ~$1.1 B**

- **Upside Valuation Outputs**
  - Upside scenario assumes ACR / EULAR guideline inclusion boosts baseline use in **incident patients by ~45%**, **5 week testing to ~60%** of baseline patients, and **annual follow-up to ~40%** of baseline patients, resulting in **~$2.6 B in peak revenue (2036)** and an **rNPV of ~$2.2 B across the U.S. and EU**

- **Future Opportunities**
  - Multiple opportunities remain to unlock further Tc-Tilmanocept value in RA, including **label expansion, patient advocacy campaigns** to increase **diagnosis rates**, **marketing efforts to bolster preference share**, and **registration as a biomarker**

RA: Rheumatoid Arthritis; 1L: First-line; 2L: Second-line; 2L+: Second-line and Beyond; LoT: Line of Therapy; ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; POS: Probability of Success; rNPV: Risk-adjusted Net Present Value.
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Project Overview
Navidea Biopharmaceuticals Tc-Tilmanocept U.S. Valuation Assessment

Key Project Goals

• Conduct primary and secondary market research to characterize the current (and evolving) market environment, KOL feedback on Product X, and the expected revenue potential for Product X

• Evaluate KOL receptivity to Product X’s target product profile to gauge anticipated adoption and utilization within RA

• Bolster Navidea’s utilization assumptions for its commercial revenue forecast for Product X based on primary market research

Market Landscape
Develop insights on current market dynamics (e.g., patient journey, competitive landscape, etc.) for diagnostics in RA across the U.S. and EU

U.S. Primary Market Research
Understand the current & future RA diagnostic landscape and anticipated utilization of Product X based on primary research with academic and community physicians

Commercial Forecast
Develop a comprehensive Excel-based commercial forecast model to project the year-over-year commercial potential of Product X in the U.S. and EU
U.S. & EU Rheumatoid Arthritis Epidemiology (≥16 Years of Age)

RA has a prevalence of ~0.7% and ~0.6% of the population ≥16 years of age in the U.S. and EU, respectively.

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, with an annual growth rate of ~0.6%.

Similar to the U.S., EU-based secondary publications suggest RA has an incidence of ~35 per 100 K and a prevalence of ~0.6% of the population over 16 years of age, with an annual growth rate of ~0.1%.

Notably, these prevalence assumptions only include adult RA patients and not juvenile RA under the age of 16, which is estimated to impact ~300 K patients in the U.S. alone.
# Rheumatoid Arthritis Treatment Paradigm

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

## U.S. Rheumatoid Arthritis Treatment Paradigm

<table>
<thead>
<tr>
<th>Line (L)</th>
<th>Treatment Options</th>
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</thead>
<tbody>
<tr>
<td><strong>1L</strong></td>
<td>MTX, HCQ, LEF, SSZ, AZA</td>
</tr>
<tr>
<td><strong>2L</strong></td>
<td>Two of MTX, HCQ, LEF, SSZ, Anti-TNF ± MTX, JAKi ± MTX</td>
</tr>
<tr>
<td><strong>3L</strong></td>
<td>Anti-TNF ± MTX, Anti-IL-6 ± MTX, Abatacept, JAKi ± MTX</td>
</tr>
<tr>
<td><strong>4L</strong></td>
<td>Anti-TNF ± MTX, Anti-IL-6 ± MTX, Abatacept, Rituximab, JAKi ± MTX</td>
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- **MTX** often prescribed with NSAIDs / GCs for rapid symptom relief; ineligible patients receive alternative single-agent csDMARDs.
- **The ~70% of patients who do not achieve remission after 3 – 6 mo. often progress to anti-TNFs/-JAKs or a combo of two csDMARDs.**
- **The ~80% of patients who fail 2L often receive alternative anti-TNFs/JAKs; select patients receive IL-6 inhibitors or abatacept.**
- **The ~85% of patients refractory to 3L progress to 4L, where prescribing is guided by treatment history and highly variable.**

Tc-Tilmanocept is likely to be used in 2L+ as 1L patients are rarely considered for anti-TNFs (i.e., csDMARDs are generic and often mandated in 1L by payers).

## EU-Specific Findings

- **EU treatment guidelines (i.e., EULAR) outline a very similar treatment progression to that of the U.S. (i.e., csDMARD utilized alone for all 1L patients, adding a bDMARD or tsDMARD in combo if refractory).**
- **EU patients are even less likely to get a 1L biologic given increased cost-sensitivity vs. the U.S.**

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Source: LifeSci Physician Interviews (N=15); ACR Guidelines; EULAR Guidelines; UpToDate; GlobalData. DMARD: Disease-modifying Antirheumatic Drug; b: Biological; cs: Conventional Synthetic; ts: Targeted Synthetic; GC: Gluco-corticoid; MTX: Methotrexate; HCQ: Hydroxychloroquine; LEF: Leflunomide; SSZ: Sulfasalazine; AZA: Azathioprine.

Key:
- csDMARD
- bDMARD
- tsDMARD

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Clinical Unmet Needs
KOLs are most interested in biomarkers for prediction of response to therapy and disease severity

Key Unmet Needs

1. **Predictive Treatment Response**: A predictive test that can determine a patient’s response to therapy, to help inform prescribing decision making across multiple available therapeutic classes in RA

   “Predicting response to treatment is currently a black box. All we can do is cycle through therapies, which takes time. For RA patients, time is cartilage and bone.”

2. **Prognostic Biomarkers**: Physicians desire a highly specific test (e.g., predictive biomarkers) that can distinguish more severe forms of RA to help inform management

   “I would love to see biomarkers that can categorize who is more at risk for more severe RA, especially those who are at risk for progressive lung disease.”

3. **Novel Therapeutics**: KOLs note interest in a novel therapies that can provide benefit to refractory RA patients (e.g., new MOA, non-immunosuppressive, and/or orally administered)

   “There are patients who have failed every line of therapy. It would be nice if there was a new class of drugs that was safe and could help these patients.”

U.S. Physician Feedback on Tc-Tilmanocept
Summary of Physician TPP Feedback

Rheums were interested in Product X, citing its predictive power and exceptional safety as key highlights

- Physicians were enthusiastic about using Product X in RA patients considered for biologics, most often patients in the 2L+
- They expressed greater interest in Product X as a predictor of response at baseline, rather than early response at 5 weeks

- Specificity was identified as a key endpoint to ensure beneficial therapies are not withheld
- Respondents perceived Product X's specificity and sensitivity to be clinically meaningful

- Rheumatologists were unfamiliar with CD206 expressing activated macrophages in RA, suggesting a need for physician education
- ROA was considered less convenient than other diagnostic modalities, but convenience would only limit use if more convenient options exhibited similarly strong predictive power

- Rheumatologists were most enthusiastic about Product X’s safety and tolerability profile
- Physicians were impressed by Product X’s real-world safety record in cancer, indicating safety would be no issue in implementing Product X in RA
Product X Patient Eligibility

Rheums viewed most 2L+ switch patients as eligible for Product X, along with select 1L and prevalent patients

1L Incident Pts. Considered for Anti-TNFs: Physicians estimated ~10% of 1L patients exhibit particularly severe disease or are MTX ineligible (e.g., women of childbearing age, those who refuse alcohol cessation) and therefore considered for anti-TNFs and Product X

“Anti-TNFs may be used in a small percentage of 1L patients, mostly due to contraindications to MTX, though I also consider patients with particularly inflammatory disease if insurance will cover it.”

2L+ LoT Switch Patients: Respondents identified 2L+ LoT switch patients as the key patient population for Product X, given the vast majority of 2L+ patients are considered for anti-TNFs aside from the few with history of infections, organ dysfunction, or cancer

“Almost all patients are considered for anti-TNFs after failing MTX. It’s only those with renal or liver issues, past infections, or fear over a family history of cancer who may go elsewhere.”

Prevalent RA Patients: While incident / LoT switch patients were identified as the key eligible population, select physicians expressed interest in annual follow-up among prevalent patients who originally received it in the incident / LoT switch setting (N=3)

“I like the idea of imaging for sub-clinical synovitis over time. Even if patients feel good, the disease can progressively damage their joints.”

MTX: Methotrexate; LoT: Line of Therapy.
Product X Preference Share

Physician-stated preference share estimates suggest a majority of 2L+ incident patients may receive Product X

Product X Baseline Preference Share
(Represents Patients Ordered At Least 1 Diagnostic Annually)

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<tr>
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<th>Preference Share</th>
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<tbody>
<tr>
<td>1L Incident</td>
<td>5.5%</td>
</tr>
<tr>
<td>1L Prevalent</td>
<td>1%</td>
</tr>
<tr>
<td>2L+ Incident</td>
<td>55%</td>
</tr>
<tr>
<td>2L+ Prevalent</td>
<td>8.5%</td>
</tr>
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</table>

5 Week Early Prediction of Response Testing:
Physicians estimated ~35% of patients initially ordered Product X would repeat testing at 5 weeks, predominantly in severe patients and/or those with no sign of response

Annual Follow-up Testing:
~15% of patients originally ordered Product X at baseline may receive annual follow-up testing, with most physicians desiring additional data in the follow-up setting to support use

- Preference share assumptions are based off physician-stated estimates and reactions to Product X’s base-case TPP
- Physician willingness to order Product X was highest for 2L+ incident patients, though physicians noted interest in Product X among the minority of 1L patients considered for anti-TNFs
- Of those who receive Product X at baseline, ~35% of patients may receive a 5-week follow-up test and ~15% may receive annual follow-up testing based on the presented TPP, though additional data in the follow-up setting and experience with Product X may boost follow-up utilization over time
U.S. 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 U.S.(2024)/EU (2025):** ~1.9 M/~ 3.7 M
- **Preference Share:** 55% in 2L patients switching therapies in base case scenario  
  *(Note: Based on U.S. primary research)*  
  80% in upside scenario
- **Annual Tests per Patient:** 1 – 2
- **Compliance:** 90%
- **Launch Year U.S./EU:** 2024/2025

### Select Cost Assumptions

- **R&D and Regulatory Expenses:** Ongoing P2B & 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.)*
Valuation Output and Strategic Considerations
Tc-Tilmanocept may generate ~$735 M and ~$505 M in 2036 annual revenue in the U.S. and EU, respectively.
Tc-Tilmanocept Base-case Revenue Projections (U.S. only)

With base-case assumptions, Tc-Tilmanocept may generate ~$735 M in annual U.S. revenue by 2036.
Tc-Tilmanocept Base-case Revenue Projections (EU only)

With base-case assumptions, Tc-Tilmanocept may generate >$500 M in annual EU revenue by 2029

Base-case EU Projected Net Revenue ($M)

EU Base-case Outputs

- 2030 Peak Sales: ~$535 M
- Aggregate Sales (2022 – 2036): ~$5.1 B
- Probability of Success (PoS): ~52%
- rNPV (2022 – 2036): ~$450 M
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 U.S. and EU 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.
Aggregate rNPV for Tc-Tilmanocept in RA (U.S. and EU)

Accounting for revenue, costs, and risk, base-case rNPV may reach ~$1.1 B with upside potential of ~$2.2 B

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<tr>
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<th>Base-case rNPV</th>
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<th>Upside rNPV</th>
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<tbody>
<tr>
<td>1L Incident Preference Share</td>
<td>5.5% (U.S. and EU)</td>
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<td>8% (U.S. and EU)</td>
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<tr>
<td>1L Prevalent Preference Share</td>
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<td></td>
<td>3.5% (U.S. and EU)</td>
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</tr>
<tr>
<td>2L+ Incident Preference Share</td>
<td>55% (U.S. and EU)</td>
<td></td>
<td>80% (U.S. and EU)</td>
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<tr>
<td>2L+ Prevalent Preference Share</td>
<td>8.5% (U.S. and EU)</td>
<td></td>
<td>35% (U.S. and EU)</td>
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~$1.1 B ~$2.2 B
Opportunities to Expand Future Commercial Potential

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

Expansion to Juvenile RA in the U.S.
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 Follow-up Testing
Increasing comfort with Tc-Tilmanocept and additional data to support follow-up testing may boost the number of tests patients receive over time

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/EMA registration for 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

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