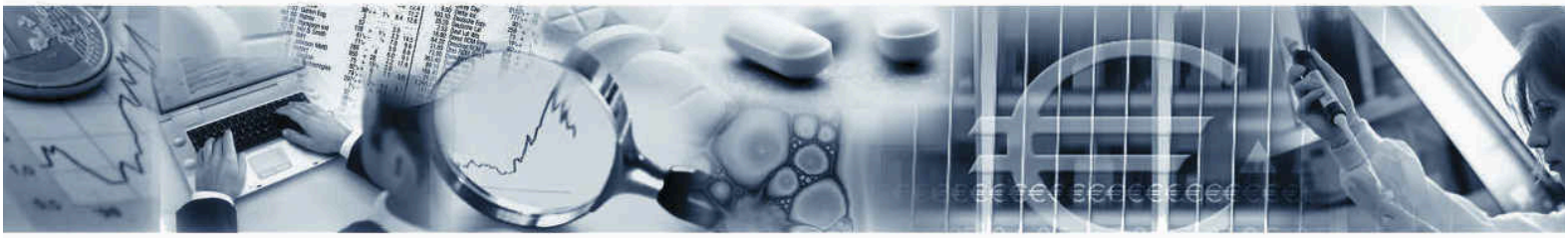

Research Note

Navidea Biopharmaceuticals

Driving growth with a clean slate

Chief Research Analyst

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Name:	**Navidea Biopharmaceuticals Inc.**
Country:	**United States**
Price:	**USD 0.39**
ISIN Code:	**US67066G1040**
Reuters Code:	**NAVB**
Market Cap (USD m):	**62.3**
EV (USD m):	**54.7**
Cash & cash eq. (USD m):	**7.6**
Shares outstanding (m):	**164.9**
Volume:	**333,792**
Free float:	**91%**
52-week Range:	**0.26-1.16**

USD million	2015A	2016A	2017E
Total Revenues	13.2	22.0	9.0
Net (Loss)/Profit	(27.6)	(14.3)	(2.5)
Net (loss)/profit ps (cents)	(0.19)	(0.09)	(0.02)
R&D costs	12.8	8.9	2.9
Cash increase/(decrease)	1.7	(5.6)	10.5
Cash and marketable sec.	7.2	1.5	12.0

Executive Summary

- Navidea Biopharmaceuticals is focused on the development and commercialization of precision immunodiagnostic agents and immunotherapeutics. Navidea is developing multiple precision-targeted products based on its proprietary Manocept™ platform to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making and targeted treatment.

- In 2015 the company formed a new division called Macrophage Therapeutics that develops the therapeutic drug delivery system Manocept. Manocept™ targets the CD206 mannose receptor expressed on macrophages. Macrophages play important roles in many disease states and are an emerging target in many disorders like RA, NASH and cancer

- The Manocept platform serves as the molecular backbone of Lymphoseek (technetium 99m tilmanocept), the first product developed by Navidea based on the platform. **Lymphoseek**, is a novel radiopharmaceutical diagnostic imaging agent approved by the FDA and EMA for Sentinel Lymph Node Biopsy (SLNB), Interoperative Lymphatic Mapping (ILM) , and lymph node imaging.. It is used to locate lymph nodes which may be draining from the tumour bed, and assist doctors in identifying those lymph nodes most likely to harbour disease.

- Building on the success of Tc 99m tilmanocept, Manocept platform acts as an engine for the design of purpose built molecules offering the potential to be utilized across a range of diagnostic modalities and therapeutic applications including single photon emission computed tomography ("SPECT"), positron emission tomography ("PET"), intra-

operative and/or optical-fluorescence detection in a variety of disease states and potential therapeutic uses.

- In March, the company completed sale of the North American rights to Lymphoseek® to Cardinal Health 414, receiving approximately USD 82 million at closing. Navidea will have the opportunity to earn up to USD 227 million of additional consideration through 2026, with USD 17.1 million guaranteed over the next three years. The deal improves its financial position considerably. By the end of 2017Q1 the company has a cash position of USD 13.4 million

- The application of intraoperative lymphatic mapping ("ILM") and SLNB are well established in breast cancer. Breast cancer is the second leading cause of death from cancer among all women in the U.S. According to the ACS, over 255,000 new cases of breast cancer are expected to be diagnosed during 2017 in the U.S. alone. The use of ILM is also common in melanoma. The ACS estimates that approximately 87,000 new cases of melanoma will be diagnosed in the US during 2017. In addition to breast cancer and melanoma, we estimate that Navidea's oncology products may have utility in other cancer types with another 786,000 new cases expected during 2017 in the US.

- **Given the NPV-based valuation, we believe that Navidea Biopharmaceuticals is substantially undervalued at the current share price of USD 0.41. Using our valuation model and taking into account the future revenues from its Manocept** platform**, the company's current total value should be USD 200 million, or USD 1.20 per share. This represents a substantial upside from the current share price.**

Company Profile & Technology Platform

Navidea Biopharmaceuticals (NYSE: NAVB) is a biopharmaceutical company focused on the development and commercialization 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 based on the ability to specifically target the CD206 mannose receptor expressed on activated macrophages. The Manocept platform serves as the molecular backbone of technetium 99m tilmanocept (Lymphoseek), the first product developed and commercialized by Navidea based on the platform.

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Its technology is applied across various indications being:

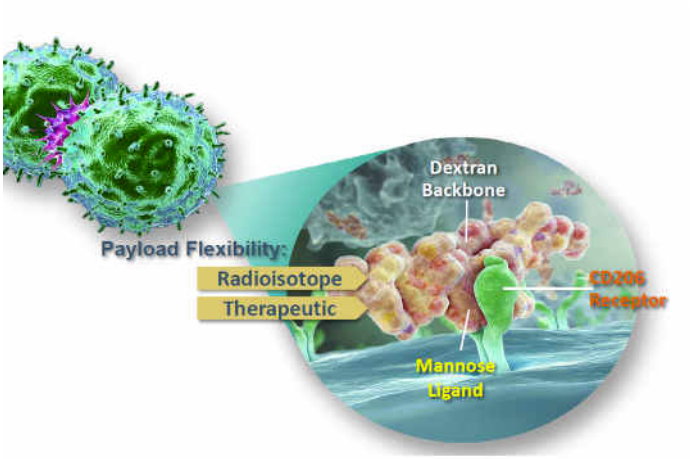
- Lymph nodes in cancer
- Intraoperative Lymphatic Mapping (ILM)
- Sentinel Lymph Node Biopsy

Furthermore, Navidea is developing a pipeline of immunodiagnostic applications beginning with rheumatoid arthritis, Kaposi's sarcoma and cardiovascular disease with an addressable market that is substantial.

Technology Platform: Manocept

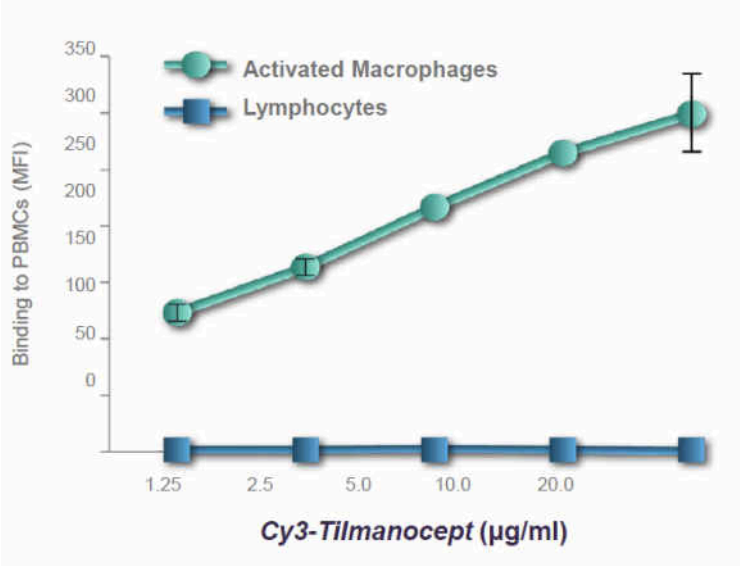
Navidea's Manocept platform is based on the ability to specifically target the CD206 mannose receptor expressed on activated macrophages. Activated macrophages play important roles in

many disease states and are an emerging target in many diseases where diagnostic uncertainty exists. This flexible and versatile platform serves as an engine for purpose-built molecules that may significantly impact patient care by providing enhanced diagnostic accuracy, clinical decision-making, and target-specific treatment. This disease targeted drug platform provides the capability to utilize a breadth of diagnostic modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection, as well as delivery of therapeutic compounds that target macrophages, and their role in a variety of immune and inflammation-based disorders. The FDA-approved sentinel lymph node biopsy/lymphatic mapping agent, Tc 99m tilmanocept, is representative of the ability to successfully exploit this mechanism to develop powerful new products.



Preclinical data using tilmanocept linked to a therapeutic agent indicate that tilmanocept's binding affinity to CD206 receptors demonstrates the potential for this technology to be useful in treating diseases linked to the over-activation of macrophages. This includes various cancers as well as autoimmune, infectious, CV, and central nervous system ("CNS") diseases. To date, the Company has developed two lead families of therapeutic products. The MT1000 class is designed to deplete activated macrophages via apoptosis. The MT2000 class is designed to modulate activated macrophages from a classically activated phenotype to the alternatively activated phenotype. From

its ongoing preclinical studies it was confirmed that tilmanocept selectively binds only to activated macrophages without targeting lymphocytes (non-activated macrophages), or non-activated tissue resident macrophages (kupfer cells, microglial cells, etc.)



Manocept versus Monoclonal Antibodies

	Manocept	**Monoclonal Antibodies**
Molecular Weight	~2-20 kilo daltons	~150 kilo daltons
Backbone (BB)	Natural and synthetic polymers	Complex proteins
Cost	Negligible	$$$$
Half life	Hours	Weeks
Binding affinity	$10^{-9} – 10^{-13}$	$10^{-5} – 10^{-7}$
Antigenic	Highly unlikely	Antibodies must by humanized
Delivery options	IV, SC, oral, topical	IV
Drug loading	Multiple copies per BB	Antibody drug conjugates being developed to deliver proprietary agents

License deal Lymphoseek with Cardinal Health

In November 2016 Navidea entered into an asset purchase agreement with Cardinal Health for the purchase of its product Lymphoseek for lymphatic mapping, lymph node biopsy and the diagnosis of metastatic spread to lymph nodes for the staging of cancer in North America. Navidea received USD 80 million at closing, plus the opportunity to earn up to USD 230 million of contingent consideration based on certain milestones through 2026, with USD 20.1 million of that amount guaranteed over the next 3 years. As part of the transaction, Cardinal Health also licensed a portion of the acquired intellectual property back to Navidea to allow Navidea to develop and sell new immunodiagnostic and immunotherapeutic products for specific purposes in North America, and to continue to produce and sell Lymphoseek, mostly under a different brand, outside of North America.

Norgine

Navidea entered into an exclusive sublicense agreement with SpePharm, a subsidiary of Norgine, in exchange Navidea received an upfront payment, milestone payments and will receive royalties on all European net sales. The territory covered by the agreement includes all 28 member states of the European Economic Union in addition to extended territories such as Switzerland and Australia. Norgine is a leading European specialist pharmaceutical company with a direct commercial presence in all major European markets. In 2016, Norgine's total revenue was EUR 368 million. Norgine employs over 1,000 people across its commercial, development and manufacturing operations and manages all aspects of product development, production, marketing, sale and supply. Norgine specialises in gastroenterology, hepatology, cancer and supportive care.

Pipeline: Late Stage Diagnostics vs Preclinical Therapeutics

With the sale of the North American rights to Lymphoseek® to Cardinal Health, Navidea is now focused on clinical stage development of diagnostic agents and therapeutic uses for rheumatoid arthritis (RA), cardiovascular diseases (CV), Kaposi's Sarcoma (KS), and non-alcoholic steatohepatitis (NASH).

Source: Navidea

Cardiovascular Disease ("CV")

Navidea has completed a study with nine patients to evaluate diagnostic imaging of emerging atherosclerosis plaque with the Tc 99m tilmanocept product dosed subcutaneously. The results of this study were recently published in the Journal of Infectious Diseases, confirming that the Tc 99m

tilmanocept product can both quantitatively as well as qualitatively target non-calcified plaque in the aortic arch (NIH/NHLBI Grant 1 R43 HL127846-01). The company has applied for follow-on NIH/NHLBI support to fund additional clinical studies. These studies are currently under development and design for both Phase I and Phase II trials.

Rheumatoid Arthritis ("RA")

One of the largest defined market opportunities in early diagnosis and disease monitoring is Rheumatoid Arthritis (RA). RA can be difficult to detect because it may begin with subtle symptoms such as achy joints or joint stiffness. Further, many diseases behave like RA early on; for example, gout and lupus. There is no single test that confirms an RA diagnosis and even combinations of tests provide little specificity for RA. Current diagnostic tools such as x-rays, ultrasound and MRI fall short of being able to quantitatively measure inflammation and the underlying macrophage inflammatory component, which is a key driver of RA progression. Misdiagnosis results in billions of dollars being spent each year unnecessarily on therapies, which may also result in significant side effects. In our primary market research, two aspects of the current unmet medical needs identified were early diagnosis and monitoring of disease progression and/or drug response. Early diagnosis and treatment improves outcomes. In patients with RA, joint damage occurs early, often within the first two years of the disease, and is irreversible. Additionally, once treatment is started, it becomes necessary to objectively monitor progression and measure how well a treatment is working or not. Approximately 10 million patients in economically advantaged countries alone are diagnosed with RA, of which approximately half are misdiagnosed due in large part to a lack of an accurate and cost-effective means for early detection and differential diagnosis. More succinctly, our primary market research suggests that early detection alone in the U.S. could add up to 300,000 procedures per year and disease monitoring could add as many as 700,000 procedures per year.

Navidea has initiated two dose escalation studies in RA. The first study was completed and included 18 patients (12 with active disease and 6 controls) who were dosed subcutaneously. In

addition, based on completion of extensive preclinical dosing studies pursuant to the company's dialog with the FDA, Navidea has initiated and partially completed a study dosing the Tc 99m tilmanocept product intravenously ("IV"). These studies have been supported through a Small Business Innovation Research ("SBIR") grant.

Lymphoseek

Lymphoseek (technetium Tc 99m tilmanocept) injection is the first and only FDA- and EMA-approved receptor-targeted lymphatic mapping agent. It is a novel, receptor-targeted, small-molecule radiopharmaceutical used in the evaluation of lymphatic basins that may have cancer involvement in patients. Lymphoseek is designed for the precise identification of lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. Lymphoseek is approved by FDA for use in solid tumor cancers where lymphatic mapping is a component of surgical management and for guiding sentinel lymph node biopsy in patients with clinically node negative breast cancer, melanoma or squamous cell carcinoma of the oral cavity. Lymphoseek also received EMA European approval in imaging and intraoperative detection of sentinel lymph nodes draining a primary tumor in patients with melanoma, breast cancer or localized squamous cell carcinoma of the oral cavity. Accurate diagnostic evaluation of cancer is critical, as results guide therapy decisions and determine patient prognosis and risk of recurrence. Overall in the U.S., solid tumor cancers may represent up to 1.2 million cases per year. The sentinel node label in the U.S. and Europe may address approximately 600,000 new cases of breast cancer, 160,000 new cases of melanoma and 100,000 new cases of head and neck/oral cancer diagnosed annually.

In November 2016, Navidea entered into an agreement with Cardinal Health 414 for the sale of Lymphoseek in North America. See details of the agreement on page 8.

Cardiovascular Disease (CV)

Navidea has initiated and completed a study of CV in nine patients to evaluate diagnostic imaging of emerging atherosclerosis plaque with the Tc 99m tilmanocept product dosed subcutaneously. The study examined the ability of Tc 99m tilmanocept to localize in high-risk atherosclerotic plaques. These specific plaques are rich in CD206-expressing macrophages and are at high risk for near term rupture resulting in myocardial infarctions, sudden cardiac death and strokes. The consequences of atherosclerosis and the cardiovascular disease that atherosclerosis causes, while severe in all populations of people, are particularly concentrated in human immunodeficiency virus-positive ("HIV+") patients. Recently, it has been observed that CD206 expressing macrophages densely populate vulnerable plaques or thin cap fibroatheromas but not other kinds (i.e., calcified plaques) of atherosclerotic plaques. The results of this study were published in the Journal of Infectious Diseases, confirming that the Tc 99m tilmanocept product can both quantitatively as well as qualitatively target non-calcified plaque in the aortic arch. The company has applied for follow-on NIH/NHLBI support to fund additional clinical studies. These studies are currently under development and design for both Phase I and Phase II trials.

Kaposi's Sarcoma ("KS")

Navidea has initiated and completed a study of KS in 2015. Nonetheless, it received additional funding from the National Institutes of Health ("NIH") in 2016 to continue studies in this disease. The new support not only continues the imaging of cutaneous elements of this disease but expands this to imaging of visceral disease via IV administration of Tc99m tilmanocept. Navidea also received funding to support the therapeutic initiative for KS employing a select form of the class 1000 agent under current evaluation. The company has already completed part of the Phase I. Based on performance in these very large imaging market opportunities Navidea anticipates continued investment in these programs including initiating studies designed to obtain new approvals for the Tc 99m tilmanocept product.

Recent News Flow 2017Q2

Financials

Recently, the company published its 2017Q2 figures. Total revenues for the first six months amounted to USD 1.2 million (2016H1: USD 2.1 million). Net loss attributable to common stockholders was USD 5.2 million. Net revenues do not include the guaranteed payments from Cardinal Health 414, LLC (Cardinal Health 414) because those are represented on the balance sheet in accounts receivable. Navidea ended the quarter with USD 7.6 million in cash and investments, not including the quarterly guaranteed earnout payment of USD 1.67 million from Cardinal Health 414 which was received after the quarter ended.

In the past quarter, Navidea continued to enrol patients for its multi-center Phase I/II RA trial with Tc-99m tilmanocept. The trial was initiated in February and will be completed in 2017Q4. Another trial with Tc-99m tilmanocept in patients with colon cancer and liver metastases also started in 2017Q1. This trial is expected to show interim results before year end. In June, Lymphoseek was launched in several European countries (Denmark, Netherlands and UK)

Expected Milestones for Remainder 2017

In the coming months we expect a number of important mile stones that can drive the stock price upwards. These are:

Imaging

- Completion IV dosing RA study *(17 dosed, 6 yet to dose)*
- Initiate IV dosing CV study *(IRB protocol pending)*
- Initiate IV dosing NASH study *(protocol draft in review)*

Therapeutics

- Complete development plan for treating active M1mediated inflammation *(extension of imaging study RA, same population)*
- Complete development plan for orphan disease indication
- Complete animal testing by 2 pharmaceutical companies for possible partnering
- New backbone efforts including lower molecular weights and new backbone polymers *(first synthesis in progress)*

Analyst: Marcel Wijma MSc
Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.

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