NAVIDEA BIOPHARMACEUTICALS, INC.
Form 10-K
March 16, 2015

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

FORM 10-K

(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2014

or

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE EXCHANGE ACT

For the transition period from to to

Commission file number 001-35076

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

Delaware (State or other jurisdiction of incorporation or organization)	31-1080091 (I.R.S. Employer Identification No.)
5600 Blazer Parkway, Suite 200, Dublin, Ohio (Address of principal executive offices)	43017-7550 (Zip Code)

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

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

Common Stock, par value $.001 per share (Title of Class)	NYSE MKT (Name of Each Exchange on Which Registered)

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.
Yes ¨ No ý

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.
Yes ¨ No ý

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.
Yes ý No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).
Yes ý No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is a large accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer o	Accelerated filer x
Non-accelerated filer o	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12-b-2 of the Act.)
Yes ¨ No ý

The aggregate market value of shares of common stock held by non-affiliates of the registrant on June 30, 2014 was $220,518,363.

The number of shares of common stock outstanding on March 2, 2015 was 150,337,098.

DOCUMENTS INCORPORATED BY REFERENCE

None.

References in this report to Navidea Biopharmaceuticals, Navidea, the Company, we, our and us refer to Navidea Biopharmaceuticals, Inc. and its subsidiaries on a consolidated basis. In January 2012, we changed our name to Navidea Biopharmaceuticals, Inc. from Neoprobe Corporation. Navidea was chosen as the new name to reflect the Company's dedication to "NAVigating IDEAs" that translate cutting edge innovation and precision medicines technologies into novel products to advance patient care. Historical references within this Annual Report on Form 10-K to Neoprobe Corporation have therefore generally been revised to refer to our new name.

The Private Securities Litigation Reform Act of 1995 (the Act) provides a safe harbor for forward-looking statements made by or on behalf of the Company. Statements in this document 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, the ability to obtain, and timing of, regulatory approvals of the Company's products, the timing and anticipated results of commercialization efforts, and anticipated markets for the Company's products, are forward-looking statements within the meaning of the Act. The words "believe," "expect," "anticipate," "estimate," "project," and similar expressions identify forward-looking statements that speak only as of the date hereof. Investors 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, uncertainty of regulatory approvals for and 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, risks of development of new products, and other risks set forth below under Item 1A, "Risk Factors." The Company undertakes no obligation to publicly update or revise any forward-looking statements.

PART I

Item 1. Business

Development of the Business

Navidea Biopharmaceuticals, Inc., a Delaware corporation, is a precision medicine company focused on the development and commercialization of precision diagnostics, therapeutics and radiopharmaceutical agents. Navidea is developing multiple precision-targeted products based on the Manocept™ platform to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making, targeted treatment and, ultimately, patient care.

Navidea's Manocept platform is predicated on the ability of the chemical backbone of the tilmanocept molecule to specifically target the CD206 mannose receptor expressed on macrophages. The Manocept platform serves as the molecular backbone of Lymphoseek® (technetium Tc 99m tilmanocept) injection, the first product developed by Navidea based on the platform. Lymphoseek 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 the U.S. Food and Drug Administration (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 has also received European approval in imaging and intraoperative detection of sentinel lymph nodes in patients with melanoma, breast cancer or localized squamous cell carcinoma of the oral cavity.

Building on the success of Lymphoseek, the flexible and versatile 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, including single photon emission computed tomography (SPECT), positron emission tomography (PET), intra-operative and/or

optical-fluorescence detection in a variety of disease states.

Recent preclinical data being developed by the Company using tilmanocept linked to various therapeutic agents also suggest 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, cardiovascular, and central nervous system diseases. Thus, in January 2015, the Company formed a new subsidiary, Macrophage Therapeutics, Inc., to further explore therapeutic applications for the Manocept platform.

In addition, over the last year, the company's Board of Directors made the decision to reduce our support while seeking to partner or out-license two of our development programs:

- NAV4694 is a fluorine-18 (F-18) radiolabeled PET imaging agent being developed as an aid in the diagnosis of patients with signs or symptoms of Alzheimer's disease (AD) and mild cognitive impairment (MCI). NAV4694 is in Phase 3 clinical development.
- NAV5001 is an iodine-123 (I-123) radiolabeled SPECT imaging agent being developed as an aid in the diagnosis of Parkinson's disease (PD) and other movement disorders, with potential use as a diagnostic aid in dementia. NAV5001 is in Phase 3 clinical development.

The company is in discussions with potential parties interested in sublicensing and/or assuming financial responsibility for the ongoing development of these two neuro tracer compounds and is currently evaluating term sheets.

Other than Lymphoseek, none of the Company's drug product candidates have been approved for sale in any market.

A Brief Look at Our History

We were originally incorporated in Ohio in 1983 and reincorporated in Delaware in 1988. From inception until January 2012, we operated under the name Neoprobe Corporation. In January 2012, we changed our name to Navidea Biopharmaceuticals, Inc. in connection with both the sale of our medical device business and our strategic repositioning as a precision medicines company focused on "NAVigating IDEAs" that result in the development and commercialization of precision diagnostic and therapeutic pharmaceuticals.

Since our inception, the majority of our efforts and resources have been devoted to the research and clinical development of radiopharmaceutical technologies primarily related to the intraoperative diagnosis and treatment of cancers. From the late 1990's through 2011, we also devoted substantial effort towards the development and commercialization of medical devices, including a line of handheld gamma detection devices which was sold in 2011 and a line of blood flow measurement devices which we operated from 2001 through 2009.

From our inception through August 2011, we manufactured a line of gamma radiation detection medical devices called the neoprobe® GDS system (the GDS Business). From October 1999 through July 2010, the GDS products were marketed throughout most of the world through a distribution arrangement with Ethicon Endo-Surgery, Inc. (EES), a Johnson & Johnson company, and from July 2010 through August 2011 through a distribution arrangement with Devicor Medical Products, Inc. (Devicor). We sold the GDS Business to Devicor in August 2011. In exchange for the assets of the GDS Business, Devicor made net cash payments to us totaling $30.3 million, assumed certain liabilities of the Company associated with the GDS Business, and agreed to make royalty payments to us of up to an aggregate maximum amount of $20 million based on the net revenue attributable to the GDS Business through 2017. To date, we have not received any such royalty payments.

Following the sale of the GDS business and the subsequent strategic repositioning as a precision medicines company, the Company in-licensed the two neuro tracer product candidates, NAV4694 and NAV5001. The Company progressed the development of both product candidates over the course of 2012 through 2014, moving both into Phase 3 clinical trials. However, in May 2014, the Navidea Board announced that, based on its belief that the public markets were not giving appropriate value to its Phase 3 pipeline products and was likely penalizing the Company for allocating resources to these programs, the Company would be restructuring its development efforts to focus on cost effective development of the Manocept platform while it sought development partners for NAV4694 and NAV5001.

In December 2014, we announced the formation of a new business unit, Macrophage Therapeutics, to further explore therapeutic applications for the Manocept platform, which was incorporated as Macrophage Therapeutics, Inc. in January 2015.

Our Technology and Product Candidates

Our primary development efforts over the last few years have been focused on our now-approved Lymphoseek product, as well as more recently on our other pipeline programs, including NAV4694, NAV5001, and our Manocept platform. In May 2014, the Board of Directors made the decision to refocus the Company's resources to better align the funding of our pipeline programs with the expected growth in Lymphoseek revenue. This realignment has primarily involved reducing our near-term support for our two neurological product candidates, NAV4694 and NAV5001, as we seek to secure a development partner or partners for these programs.

Navidea remains committed to realizing the full potential of Lymphoseek. We intend to deploy our own sales team and strategy to accelerate the strong growth of this important product. The Company believes that the resources being devoted to drive Lymphoseek sales will lead to positive cash flows and profitability. The Company is focused on expanding the market for Lymphoseek in all relevant markets.

The Company is also working to establish new sources of non-dilutive funding, including collaborations and grant funding that can augment the balance sheet as the Company works to reduce spending to levels that can be increasingly offset by growing Lymphoseek revenue. In particular, substantial progress on the Manocept platform has resulted in several promising opportunities, including our R-NAV venture beginning in July 2014, and the formation of Macrophage Therapeutics, Inc. in January 2015, which we believe may further expand the Company's pipeline but which require less near-term funding from Navidea than the two ongoing Phase 3 neurological development programs.

Lymphoseek – Regulatory Background

Lymphoseek is a lymph node targeting radiopharmaceutical agent intended for use in intraoperative lymphatic mapping procedures and lymphoscintigraphy employed in the overall diagnostic assessment of certain solid tumor cancers. Lymphoseek has the potential to provide oncology surgeons with information to identify key predictive lymph nodes that may harbor cancer and to help avoid the unnecessary removal of non-cancerous lymph nodes and the surrounding tissue in patients with a variety of solid tumor cancers. Lymphoseek was approved and indicated for use in lymphatic mapping for breast cancer and melanoma by the FDA in March 2013. In June 2014, the FDA approved a supplemental New Drug Application (sNDA) for the expanded use of Lymphoseek indicated for guiding sentinel lymph node biopsy in head and neck cancer patients with squamous cell carcinoma of the oral cavity. In September 2014, the FDA granted Orphan Drug Designation for use in sentinel lymph node detection in patients with cancer of the head and neck. This designation provides for a seven-year market exclusivity period in this indication as well as certain incentives, including federal grants, tax credits and a waiver of PDUFA filing fees. As a result of the designation, Navidea received a refund of the previously paid filing fees of $1.1 million in the fourth quarter of 2014. In October 2014, the FDA approved a second sNDA for lymphatic mapping in solid tumors and added sentinel lymph node detection for breast cancer and melanoma to the approved indications. The FDA also allowed expanded utilization of Lymphoseek with or without scintigraphic imaging, known as lymphoscintigraphy, to enable pre-operative imaging and mapping of lymph nodes to facilitate node localization during surgical procedures. Lymphoseek is now the first and only FDA-approved radiopharmaceutical agent for sentinel lymph node detection and is the only FDA-approved agent for lymphatic mapping of solid tumors. Additional trials, including an ongoing trial in colorectal cancer, and others in various stages of execution, planning or consideration, are anticipated to provide additional data to potentially support expansion of the Lymphoseek opportunity.

We submitted our Marketing Authorization Application (MAA) for Lymphoseek to the EMA in December 2012. In September 2014, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending marketing authorization for Lymphoseek for use in the EU in imaging and intraoperative detection of sentinel lymph nodes draining a primary tumor in adult patients with breast cancer, melanoma, or localized squamous cell carcinoma of the oral cavity. The CHMP's positive opinion was reviewed by the European Commission (EC), which has the authority to approve medicinal products for use in the 28 countries of the EU and generally follows the recommendations of the CHMP. The EC granted marketing authorization for Lymphoseek in the EU in November 2014.

Lymphoseek - Clinical Data and Licensing Background

In March 2014, we announced results of a three-year, voluntary follow-up study of Lymphoseek conducted in patients who participated in a Phase 3 clinical trial (NEO3-05) of the product. The primary objective of the follow-up study

was to determine the regional recurrence-free rate (RRFR) after sentinel lymph node biopsy with Lymphoseek. Results of the follow-up study indicated that in patients who were confirmed to be node-negative after sentinel lymph node biopsy (n=88; 49 breast cancer, 39 melanoma) the RRFR was 98.8% (100% in breast cancer; 97.4% in melanoma) and the disease-specific survival rate was 98.6% (97.8% in breast cancer; 100% in melanoma) at three years.

In June 2014, the Company announced results from combined analyses of Phase 3 clinical trials that evaluated Lymphoseek efficacy in lymphatic mapping for identifying pathology-positive lymph nodes across multiple solid tumor types: melanoma, breast cancer and head and neck squamous cell carcinoma. The results indicated that Lymphoseek sensitivity for sentinel lymph node mapping was consistent across the tumor type studies, regardless of whether surgery was conducted on the same day as, or on the day after, injection of Lymphoseek. Additionally, for patients with head and neck cancer, Lymphoseek demonstrated a low false negative rate (FNR) of 2.6% (4.6% for same day injection before surgery and 0.0% FNR in patients injected the day prior to surgery). Results from the study comprise part of an sNDA filing for Lymphoseek which is under review by the FDA.

Also in June 2014, we announced results from a post-hoc analysis of patient data from the Company's Phase 3 clinical trial (NEO3-06) of Lymphoseek in head and neck cancer. In the NEO3-06 Phase 3 study, Lymphoseek localization to lymph nodes showed a strong correlation with a full regional lymph node dissection and pathology analysis with a low false negative rate, a priority in identifying sentinel nodes. Lymphoseek was also observed to home preferentially to pathology-positive nodes at a higher rate than pathology-negative nodes. These results suggest that Lymphoseek not only effectively targets sentinel lymph nodes, but further that its ability to highlight tumor-positive lymph nodes may be augmented mechanistically by the recruitment of macrophages to cancer-harboring lymph nodes.

In January 2015, we announced that an analysis comparing sentinel lymph node (SLN) biopsy procedures using Lymphoseek (TcTM) + vital blue dye (VDB) to filtered [99mTc] sulfur colloid (fTcSC) + VBD in breast cancer patients was published in the Annals of Surgical Oncology. Results demonstrated that (i) Lymphoseek patients had significantly fewer SLNs removed per procedure (mean TcTM: 1.85 vs. fTcSC: 3.24, $p < 0.0001$); (ii) proportionally fewer nodes were necessary to detect cancer spread; and (iii) nodes removed using Lymphoseek held greater predictive value for diagnosing the spread of breast cancer to lymph nodes. The study, "Comparison of [99mTc]Tilmanocept and Filtered [99mTc]Sulfur Colloid for Identification of SLNs in Breast Cancer Patients," authored by Anne Wallace, M.D., et. al., at the UC San Diego School of Medicine was published in the January print issue of the journal Annals of Surgical Oncology.

In February 2015, we announced the peer-reviewed publication of results from a Phase 3 clinical trial of Lymphoseek in patients with certain head and neck cancer in the journal Annals of Surgical Oncology. The trial assessed the performance of Lymphoseek-guided sentinel node biopsy against the standard of care, nodal pathology, in planned elective neck dissection. Results demonstrated that Lymphoseek met the primary efficacy endpoint of accurately identifying sentinel lymph nodes in subjects with node-negative squamous cell carcinoma of the oral cavity, as compared to the removal of all lymph nodes during multiple level nodal dissection surgery of the head and neck. Pathology assessment of lymph nodes from the multiple-level nodal dissection surgery is considered the "gold standard" to determine the presence and extent of cancer spread. The study, "[99mTc]Tilmanocept Accurately Detects Sentinel Lymph Nodes and Predicts Pathology Status in Patients with Oral Squamous Cell Carcinoma of the Head and Neck: Results of a Phase III Multi-Institutional Trial" was published as an Online First article in the journal Annals of Surgical Oncology. Data from this study were previously presented in part at the 2013 Society of Nuclear Medicine and Molecular Imaging Annual Meeting (Vancouver, British Columbia), at the 2013 American College of Surgeons Clinical Congress (Washington, DC), and at the 6th European Congress on Head and Neck Oncology-2014 (Liverpool, UK).

An investigator-initiated study is currently underway at the University of California, San Diego (UCSD) to evaluate injection site pain between Lymphoseek and an alternative radiopharmaceutical that is commonly used in lymphatic mapping procedures. The study is designed to determine if patients receiving Lymphoseek experience the same or less pain following injection compared to radiolabeled sulfur colloid, and to measure the amount of discomfort that patients report during and after injection, as well as other characteristics of performance.

In July 2014, we amended our license agreement with UCSD for the exclusive world-wide rights to Lymphoseek. The amended license agreement is effective until the third anniversary of the expiration date of the longest-lived underlying patent. Under the terms of the license agreement, UCSD has granted us the exclusive rights to make, use, sell, offer for sale and import licensed products as defined in the agreement and to practice the defined licensed methods during the term of the agreement. We may also sublicense the patent rights, subject to certain sublicense terms as defined in the agreement. In consideration for the license rights, we agreed to make payments to UCSD upon successfully reaching certain clinical, regulatory and cumulative sales milestones, and a royalty on net sales of licensed products subject to a $25,000 minimum annual royalty. We also agreed to reimburse UCSD for all patent-related costs and to meet certain diligence targets.

In September 2014, Navidea received a notice of award for a Fast Track Small Business Innovation Research (SBIR) grant providing for up to $1.67 million from the National Cancer Institute National Institutes of Health (NIH), to fund evaluation of Lymphoseek in women with cervical cancer. The multicenter clinical study in patients with early cervical cancer will seek to assess and provide data in support of the use of Lymphoseek in sentinel lymph node biopsy procedures which identify and evaluate the lymph nodes most likely to harbor additional cancer. The SBIR grant is awarded in two parts with the potential for total grant money up to $1.67 million over two and a half years. The first six-month funding segment of $165,917, which has already been awarded, is expected to enable Navidea to identify and qualify trial sites and secure necessary contracts and institutional review board approvals. The second funding segment could provide for up to an additional $1.5 million to be used to accrue participants, perform the sentinel lymph node procedures and pathology evaluations, and perform data analyses to confirm the safety and effectiveness of Lymphoseek.

Manocept Platform - Diagnostics and Therapeutics Background

Navidea's Manocept platform is predicated on the ability to specifically target the CD206 mannose receptor expressed on macrophages. 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 enhance diagnostic accuracy, clinical decision-making and ultimately patient care, while offering the potential to utilize a breadth of diagnostic modalities, including SPECT, PET, intra-operative and/or optical-fluorescence detection, as well as potentially in the delivery of therapeutic compounds targeting macrophages and their role in a variety of immune- and inflammation-based disorders. The Company's FDA-approved sentinel node/lymphatic mapping agent, Lymphoseek, is representative of the ability to successfully exploit this mechanism to develop powerful new products.

Impairment of the macrophage-driven disease mechanisms is an area of increasing focus in medicine. The number of people affected by all the inflammatory diseases combined is estimated at more than 40 million in the United States and perhaps 700 million worldwide, making these macrophage-mediated diseases an area of remarkable clinical importance. There are many recognized disorders having macrophage involvement, including rheumatoid arthritis (RA), atherosclerosis/vulnerable plaque, Crohn's disease, tuberculosis (TB), systemic lupus erythematosis, Kaposi's Sarcoma (KS), and others that span clinical areas in oncology, autoimmunity, infectious diseases, cardiology, and inflammation. Data from studies using agents from the Manocept platform in RA, KS and TB were published in a special supplement, Nature Outlook: Medical Imaging, in Nature's October 31, 2013 issue. The supplement included a White Paper by Navidea entitled "Innovations in receptor-targeted precision imaging at Navidea: Diagnosis up close and personal," focused on the Manocept platform.

In February 2014, data utilizing compounds from our Manocept platform in models of RA were presented by representatives from The Ohio State University at a Keystone Symposia on Molecular Cell Biology of Macrophages in Human Disease. The studies demonstrate the ability of fluorescent Cy3-tilmanocept to identify and localize to disease-state macrophages when administered intravenously, enabling detection of immune-mediated arthritis in affected joints in vivo in mice. Results were confirmed using histopathology. The data highlighted the identification of immune-mediated inflammation seen in arthritic joints of arthritis-affected mice but not in control mice or un-affected joints within arthritis-affected mice. The imaging results in this study showed preferential localization of macrophages by Cy3-tilmanocept in affected joints with little to no localization in unaffected joints.

In April 2014, collaborators from the University of California, San Francisco presented results at the 2014 American Association for Cancer Research conference, highlighting the potential utility of imaging agents derived from the Manocept platform in identifying affected tissues and lymph nodes in patients with KS. The investigators concluded that, based on the results obtained, labeled imaging agents from the CD206-targeting Manocept platform provide potential avenues to enhance diagnosis and staging in this disorder.

In July 2014, Navidea announced that it formed a joint enterprise with Essex Woodlands-backed Rheumco, LLC, to develop and commercialize radiolabeled diagnostic and therapeutic products for rheumatologic and arthritic diseases. The joint enterprise, called R-NAV, LLC (R-NAV), will combine Navidea's proprietary Manocept CD206 macrophage targeting platform and Rheumco's proprietary Tin-117m radioisotope technology to focus on leveraging the platforms across several indications with high unmet medical need.

Also in July 2014, the Company completed a license agreement with UCSD for the exclusive world-wide rights in all diagnostic and therapeutic uses of tilmanocept. The license agreement is effective until the third anniversary of the expiration date of the longest-lived underlying patent. Under the terms of the license agreement, UCSD has granted us the exclusive rights to make, use, sell, offer for sale and import licensed products for all diagnostic and therapeutic uses as defined in the agreement and to practice the defined licensed methods during the term of the agreement. We

may also sublicense the patent rights, subject to certain sublicense terms as defined in the agreement. In consideration for the license rights, we agreed to pay UCSD a license issue fee of $25,000 and license maintenance fees of $25,000 per year. We also agreed to make payments to UCSD upon successfully reaching certain clinical, regulatory and cumulative sales milestones, and a royalty on net sales of licensed products subject to a $25,000 minimum annual royalty. We also agreed to reimburse UCSD for all patent-related costs and to meet certain diligence targets.

Over the course of the last few years, management has provided periodic updates regarding the status of the NAV1800 development program we previously referred to as the RIGS program, or radio-immuno-guided surgery. RIGS was originally intended to use a monoclonal antibody as an aid in identifying a primary tumor, ascertaining tumor margins, or determining the extent and location of occult and metastatic tumor in patients with solid tumor cancers, such as colorectal cancer, ovarian cancer, prostate cancer, lung cancer and other cancers of epithelial origin. The detection of clinically occult tumor is intended

to provide the surgeon with a more accurate assessment of the extent and location of disease, and therefore may impact the surgical and therapeutic management of the patient.

Our most recent comments regarding NAV1800 had indicated the lower prioritization of this program relative to our other development activities and comments to the effect that we would not be spending on this program beyond the boundaries of the $1.5 million grant we were awarded in September 2012. Part of our ongoing consideration of the RIGS program has involved an evaluation of the manufacturability of the monoclonal antibody known as CC49 and its humanized derivative, and ultimately their clinical and commercial viability. In recent years, these evaluations have caused us to question the viability of the monoclonal antibody initiative as it was originally envisioned. During the same time period, we've learned more about tilmanocept, the underlying Manocept backbone, and the potential utility of tilmanocept in identifying tumor-associated macrophages (TAMs), and their consequent potential utility in identifying tumor itself. To that end, we petitioned the NIH to repurpose the grant we were previously awarded towards the study of TAMs in colorectal cancer. We recently received confirmation of the acceptance of this repurposing. We expect this repurposed grant will now support the collaboration we entered into in November 2013 with investigators at the University of Alabama at Birmingham (UAB) to assess diagnostic approaches in colorectal cancer patients. We recognize this repurposing represents a major refocusing of the original RIGS initiative, but we are confident that this change represents the best course of action at this time towards benefiting patients afflicted with colorectal cancer and is one which is consistent with the excitement we're seeing on many fronts related to our work on the Manocept platform. However, we cannot assure you that if further clinical trials for this product proceed, that they will be successful, that the product will achieve regulatory approval, or if approved, that it will achieve market acceptance. See Risk Factors.

Macrophage Therapeutics Background

In December 2014, the Company formed a new business unit, Macrophage Therapeutics, to further explore therapeutic applications for the Manocept platform. In January 2015, we incorporated the business unit as Macrophage Therapeutics, Inc., a wholly-owned subsidiary of Navidea.

Also in December 2014, Macrophage Therapeutics hosted a conference where data was presented using the Manocept platform compound, tilmanocept, that was generated by independent academic collaborators with expertise in the HIV/AIDS, cancer, TB, RA and cardiovascular disease therapeutic areas. The technical presentations highlighted tilmanocept's ability to target activated macrophages implicated in pathology.

In February 2015, we announced the appointment of leading experts to a newly formed scientific advisory board (SAB) to serve as a strategic resource to Macrophage Therapeutics as it looks to develop therapeutic applications for Navidea's Manocept platform. The inaugural SAB consortium is comprised of world-renowned scientists and clinicians in the areas of oncology, immunology, autoimmune diseases and macrophage biology. The SAB will serve as an ongoing resource to provide management with counsel and guidance pertaining to the research, development, and clinical application of Manocept technology.

In March 2015, Macrophage Therapeutics, Inc. (MT) entered into an agreement to sell up to 50 shares of its Series A Convertible Preferred Stock (MT Preferred Stock) and warrants to purchase up to 1,500 common shares of Macrophage Therapeutics (MT Common Stock) to Platinum-Montaur Life Sciences, LLC (Platinum) and Dr. Michael Goldberg for a purchase price of $50,000 per share of MT Preferred Stock. On March 13, 2015, we announced that definitive agreements with the investors had been signed for the sale of the first tranche of 10 shares of MT Preferred Stock and warrants to purchase 300 shares of MT Common Stock to these investors, with gross proceeds to Macrophage Therapeutics of $500,000. Under the agreement, 40% of the MT Preferred Stock and warrants are committed to be purchased by Dr. Goldberg, and the balance by Platinum. The full 50 shares of MT Preferred Stock and warrants to be sold under the agreement are convertible into and exercisable for MT Common Stock representing

an aggregate 1% interest on a fully converted and exercised basis.

In addition, we entered into an Exchange Agreement with the investors providing them an option to exchange their MT Preferred Stock for our common stock in the event that MT has not completed a public offering with gross proceeds to MT of at least $50 million by the second anniversary of the closing of the initial sale of MT Preferred Stock, at an exchange rate per share obtained by dividing $50,000 by the greater of (i) 80% of the twenty-day volume weighted average price per share of our common stock on the second anniversary of the initial closing or (ii) $3.00. To the extent that the investors do not timely exercise their exchange right, we have the right to redeem their MT Preferred Stock for a price equal to $58,320 per share. We also granted MT an exclusive license for certain therapeutic applications of the Manocept technology.

The Company continues to evaluate emerging data in other disease states to define areas of focus, development pathways and partnering options to capitalize on the Manocept platform, including ongoing studies in KS and RA. The immune-

inflammatory process is remarkably complex and tightly regulated with indicators that initiate, maintain and shut down the process. Macrophages are immune cells that play a critical role in the initiation, maintenance, and resolution of inflammation. They are activated and deactivated in the inflammatory process. Because macrophages may promote dysregulation that accelerates or enhances disease progression, diagnostic and therapeutic interventions that target macrophages may open new avenues for controlling inflammatory diseases. We cannot assure you that further evaluation or development will be successful, that any Manocept platform product candidate will ultimately achieve regulatory approval, or if approved, the extent to which it will achieve market acceptance. See Risk Factors.

NAV4694 (Candidate for Out-License)

NAV4694 is a Fluorine-18 labeled precision radiopharmaceutical candidate for use in the imaging and evaluation of patients with signs or symptoms of AD and potentially also MCI. NAV4694 binds to beta-amyloid deposits in the brain that can then be imaged in PET scans. Amyloid plaque pathology is a required feature of AD and the presence of amyloid pathology is a supportive feature for diagnosis of probable AD. Patients who are negative for amyloid pathology do not have AD.

NAV4694 has been studied in rigorous pre-clinical studies and clinical trials in humans. Clinical studies through Phase 3 have included subjects with MCI, suspected AD patients, and healthy volunteers. Results suggest that NAV4694 has the potential ability to image patients quickly and safely with high sensitivity and specificity.

In May 2014, the Board of Directors made the decision to refocus the Company's resources to better align the funding of our pipeline programs with the expected growth in Lymphoseek revenue. This realignment primarily involved reducing our near-term support for our neurological product candidates, including NAV4694, as we sought a development partner or partners for these programs. The Company is currently engaged in evaluating term sheets related to NAV4694.

NAV5001 (Candidate for Out-License)

NAV5001 is a patented Iodine-123 labeled small molecule radiopharmaceutical used with SPECT imaging to identify the status of specific regions in the brains of patients suspected of having PD. The agent binds to the dopamine transporter (DAT) on the cell surface of dopaminergic neurons in the striatum and substantia nigra regions of the brain. Loss of these neurons is a hallmark of PD.

Results from clinical trials to date have demonstrated that NAV5001 has high affinity for DAT and rapid kinetics which enable the generation of clean images quickly, beginning within about 20 minutes after injection, while other agents have waiting periods from 4 to 24 hours before imaging can occur. In addition to its potential use as an aid in the differential diagnosis of PD and movement disorders, NAV5001 may also be useful in the diagnosis of Dementia with Lewy Bodies, one of the most common forms of dementia after AD.

In May 2014, the Board of Directors made the decision to refocus the Company's resources to better align the funding of our pipeline programs with the expected growth in Lymphoseek revenue. This realignment primarily involves reducing our near-term support for our neurological product candidates, including NAV5001, as we seek to secure a development partner for these programs. The Company is currently engaged in evaluating term sheets related to NAV5001.

Market Overviews

Lymphoseek - Cancer Market Overview

Cancer is the second leading cause of death in the U.S. and Western Europe. The American Cancer Society (ACS) estimates that cancer will cause over 589,000 deaths in 2015 in the U.S. alone. The Agency for Healthcare Research and Quality (AHRQ) has estimated that the direct medical costs for cancer in the U.S. for 2011 were $88.7 billion. Additionally, the ACS estimates that approximately 1.7 million new cancer cases will be diagnosed in the U.S. during 2015. For the types of cancer to which our oncology agents may be applicable (breast, melanoma, head and neck, prostate, lung, colorectal, gastrointestinal and gynecologic), the ACS has estimated that nearly 1.1 million new cases will occur in the U.S. in 2015.

Currently, the application of intraoperative lymphatic mapping (ILM) is most established in breast cancer. Breast cancer is the second leading cause of death from cancer among all women in the U.S. The probability of developing breast cancer generally increases with age, rising from about 1.9% in women under age 49 to 6.7% in women age 70 or older. According to the ACS, over 231,000 new cases of invasive breast cancer are expected to be diagnosed during 2015 in the U.S. alone. The incidence rate for breast cancer appears to be stable. Thus, we believe that the aging of the population, combined with improved

education and awareness of breast cancer and diagnostic methods, will continue to lead to an increased number of breast cancer surgical diagnostic procedures.

The use of ILM is also common in melanoma. The ACS estimates that approximately 74,000 new cases of melanoma will be diagnosed in the U.S. during 2015. In addition to breast cancer and melanoma, we believe that our oncology products may have utility in other cancer types with over another 823,000 new cases expected during 2015 in the U.S.

If the potential of Lymphoseek as a radioactive tracing agent is ultimately realized, it may address not only the current breast and melanoma markets on a procedural basis, but also assist in the clinical evaluation and staging of solid tumor cancers and expanding lymph node mapping to other solid tumor cancers such as prostate, gastric, colon, head and neck, gynecologic, and non-small cell lung. Lymphoseek has now been cleared to market in the U.S. for cancers other than breast or melanoma, however, we cannot assure you that it will achieve significant revenue. See Risk Factors.

Manocept Diagnostics and Macrophage Therapeutics Market Overview

Impairment of the macrophage-driven disease mechanism is an area of increasing focus in medicine. The number of people affected by all the inflammatory diseases combined is estimated at more than 40 million in the United States and perhaps 700 million worldwide, making these macrophage-mediated diseases an area of remarkable clinical importance. There are many recognized disorders having macrophage involvement, including rheumatoid arthritis (RA), atherosclerosis/vulnerable plaque, Crohn’s disease, tuberculosis (TB), systemic lupus erythematosis, Kaposi’s sarcoma (KS), and others that span clinical areas in oncology, autoimmunity, infectious diseases, cardiology, and inflammation. Data from studies using agents from the Manocept platform in RA, KS and TB were published in a special supplement, Nature Outlook: Medical Imaging, in Nature’s October 31, 2013 issue. The supplement included a White Paper by Navidea entitled “Innovations in receptor-targeted precision imaging at Navidea: Diagnosis up close and personal,” focused on the Manocept platform. While Navidea’s development of the Manocept platform still in relatively early stage, below is a table summarizing potential target markets in which Manocept may have potential diagnostic or therapeutic applications:

Macrophage-Associated Diseases for CD206 Targeting (thousands)

	Incidence		Prevalence						
Disease	Kaposi's Sarcoma	Tuberculosis	Multiple Sclerosis	Crohn's Disease	Systemic Lupus Erythematosus	Rheumatoid Arthritis	Neuro-degenerative Diseases	Diabetes	Athero-sclerosis
Worldwide	50	8,700	1,800	3,800	27,100	60,000	33,000	122,000	480,000

NAV4694 - Alzheimer’s Disease Market Overview

The AA estimates that more than 5.2 million Americans had AD in 2014. On a global basis, Alzheimer’s Disease International estimated in 2013 that there were 44.4 million people living with dementia. AA estimates that total costs for AD care was approximately $214 billion in 2014 and is expected to rise to $1.2 trillion by 2050. AA also estimates that there are over 15 million AD and dementia caregivers providing 17.7 billion hours of unpaid care valued at over $220.2 billion. AD is the sixth-leading cause of death in the country and the only cause of death among the top 10 in the U.S. that cannot be prevented, cured or even slowed. Based on mortality data from 2000-2010, deaths from AD have risen 68 percent while deaths attributed to the number one cause of death, heart disease, decreased 16 percent during the same period. In February 2013, the American Academy of Neurology reported in the online issue of Neurology that the number of people with AD may triple by 2050.

NAV5001 - Parkinson’s Disease Market Overview

Parkinson's disease, following AD, is the second-most common neurodegenerative disorder in the United States. The Parkinson's Disease Foundation (PDF) estimates that up to 10 million people worldwide are living with PD, including 1 million people in the U.S. Approximately 60,000 new cases of PD are diagnosed in the U.S. each year. The Centers for Disease Control rated complications from PD as the 14th leading cause of death in the U.S. and as with AD, there is no cure.

The PDF estimates that the combined direct and indirect cost of PD is nearly $25 billion per year in the U.S. alone. There are approved therapies for the treatment of PD symptoms but these treatments often become ineffectual as the disease progresses and none have been approved to modify, slow or reverse the disease progression. The burden of this chronic condition is projected to grow substantially over the next few decades as the size of the elderly population grows. Such projections are

driving the need for innovative new treatments to prevent, delay onset, or alleviate symptoms of PD. Slowing Parkinson's progression by 50% would reduce health care costs for PD patients by 35%, representing a dramatic reduction in cost of care even when spread over a longer expected survival and positively impacting the patient quality of life.

Marketing and Distribution

We believe the most preferable and likely distribution partners for Lymphoseek would be entities with established radiopharmaceutical distribution channels, although it is possible that other entities with more traditional oncology or neurological pharmaceutical portfolios may also have interest.

During the fourth quarter of 2007, we executed an agreement with Cardinal Health Inc.’s (Cardinal) Nuclear Pharmacy Services division for the exclusive distribution of Lymphoseek in the U.S. The agreement is for a term of five years from the date of FDA marketing clearance, March 13, 2013. Under the terms of this agreement, Navidea receives a significant share of the revenue from each patient dose of Lymphoseek sold. In addition, Navidea will receive up to $3 million in payments upon the achievement of certain sales milestones by Cardinal Health. We cannot assure you that we will be able to maintain a successful relationship with Cardinal Health, on terms acceptable to the Company, or at all.

In May 2013 the Company announced the commercial launch of Lymphoseek in the U.S. through a distribution agreement with Cardinal. In addition to distributing Lymphoseek to hospitals, Cardinal augments product promotion to nuclear medicine professionals. The Navidea commercial team is responsible for designing and driving Lymphoseek promotional activities and conducting medical education programs tailored to the oncology treatment team, including surgeons and nuclear medicine physicians. Although it is early after the most recent FDA label expansion, we believe we are seeing positive signs in measures of success we believe are critical to the success of our new commercial strategy and deployment.

With respect to Lymphoseek commercialization in Europe, we are aiming to deploy a specialty pharmaceutical strategy to commercialization that would be supportive of premium product positioning and reinforce Lymphoseek's clinical value proposition, as opposed to a commodity or a generics positioning approach. Unlike the U.S., where institutions typically rely on radiopharmaceutical products which are compounded and delivered by specialized radiopharmacy distributors such as Cardinal, institutions in Europe predominantly purchase non-radiolabeled material and compound the radioactive product on-site. In March 2015, we announced that we had entered into an exclusive sublicense agreement for the commercialization and distribution of Lymphoseek 250 microgram kit for radiopharmaceutical preparation (tilmanocept) in the European Union with SpePharm AG (an affiliate of Norgine BV), a European specialist pharmaceutical company with an extensive pan-European presence. Under the terms of the exclusive license agreement, Navidea will supply Lymphoseek product to Norgine; however, Navidea will transfer responsibility for regulatory maintenance of the Lymphoseek Marketing Authorization to Norgine. Norgine will also be responsible for pricing, reimbursement, sales, marketing, medical affairs, and regulatory activities. In connection with entering into the agreement, Navidea is entitled to an upfront payment of $2 million, milestones totaling up to an additional $5 million, and royalties on European net sales. The initial territory covered by the agreement includes all 28 member states of the European Economic Community with the option to expand into additional geographical areas.

In November 2013, Navidea completed an agreement with Enigma Biomedical Group for the distribution of Lymphoseek in Canada, affording local access to that market as well. In January 2014, we entered into a distribution agreement for Lymphoseek in Taiwan with Global Medical Solutions Taiwan, Ltd. (GMST), a leading in-country distributor of nuclear medicine and diagnostic imaging products. The companies will work together to address all needed Taiwanese FDA regulatory requirements and expect local approval in 2015. Prior to complete regulatory approval, in appropriate situations, the product will be made available in accordance with named-patient mechanisms.

The agreement anticipates distribution of non-radioactive kits as well as unit-dose product which will be radiolabeled at the GMST commercial radiopharmacy, affording flexibility in meeting the needs of end users in the Taiwanese market.

In August 2014, Navidea entered into an exclusive agreement with a wholly-owned subsidiary of Hainan Sinotau Pharmaceutical Co., Ltd. (Sinotau), a pharmaceutical organization with a broad China focus in oncology and other therapeutic areas, who will develop and commercialize Lymphoseek in China. In exchange, Navidea will earn revenue based on unit sales to Sinotau, a royalty based on Sinotau's sales of Lymphoseek and up to $2.5 million in milestone payments from Sinotau, including a $300,000 non-refundable upfront payment. As part of the agreement, Sinotau is responsible for costs and conduct of clinical studies and regulatory applications to obtain Lymphoseek approval by the China Food and Drug Administration (CFDA). Upon approval, Sinotau will be responsible for all Lymphoseek sales, marketing, market access and medical affairs activities in China and excluding Hong Kong, Macau and Taiwan. Navidea and Sinotau will jointly support certain pre-market planning activities with a joint commitment on clinical and market development programs pending CFDA approval. In addition to the $300,000 upfront payment, Navidea is eligible for $700,000 in milestone payments up to and through product approval, and an additional $1.5 million in sales milestones.

We also commenced shipment of Lymphoseek to select medical centers in the Middle East in late 2013. In September 2014, we executed a non-exclusive distribution agreement for distribution of Lymphoseek in Puerto Rico. We believe that with international partnerships to complement our position in the U.S. and EU, we will help establish Lymphoseek as a global leader in lymphatic mapping, as we are aware of no other company which has this global geographic range. We cannot assure you that Lymphoseek will achieve regulatory approval in any market outside the U.S. or EU, or if approved, that it will achieve market acceptance in any market.

We currently have no distribution agreements for NAV4694 or NAV5001. In addition, it should be noted that the distribution model we have established with Cardinal Health in the U.S. for Lymphoseek may not necessarily be applicable to other markets or even our other potential radiopharmaceutical candidates due to differences in regional distribution infrastructure, regulation and medical practice patterns. We cannot assure you that we will be successful in securing collaborative partners for other global markets or radiopharmaceutical products, or that we will be able to negotiate acceptable terms for such arrangements. See Risk Factors.

Manufacturing

We currently use and expect to continue to be dependent upon contract manufacturers to manufacture each of our product candidates. We have established a quality control and quality assurance program, including a set of standard operating procedures and specifications with the goal that our products and product candidates are manufactured in accordance with current good manufacturing practices (cGMP) and other applicable domestic and international regulations. We will need to invest in additional manufacturing and supply chain resources, and may seek to enter into additional collaborative arrangements with other parties that have established manufacturing capabilities. It is likely that we will continue to rely on third-party manufacturers for our development and commercial products on a contract basis.

Lymphoseek Manufacturing

Reliable Biopharmaceutical Corporation (Reliable) produces the drug substance and OSO BioPharmaceuticals Manufacturing, LLC (OsoBio) performs final product manufacturing including final drug formulation, lyophilization (freeze-drying) and packaging processes. Once packaged, the vialed drug can then be shipped to a hospital or regional commercial radiopharmacy where it will be made radioactive (radiolabeled) with ^{99m}Tc to become the final form of Lymphoseek to be administered to a patient. Both organizations have assisted Navidea in the preparation of the chemistry, manufacturing and control (CMC) sections of our submissions to the FDA and the EMA. Both Reliable and OsoBio are registered manufacturers with the FDA and the EMA.

In November 2009, we completed a Manufacture and Supply Agreement with Reliable for the manufacture of the bulk drug substance with an initial term of 10 years. In September 2013, we entered into a Manufacturing Services Agreement with OsoBio for contract pharmaceutical development, manufacturing, packaging and analytical services for Lymphoseek. The agreement is through December 2016, and automatically renews for additional two-year periods. We cannot assure you that we will be successful in completing future agreements for the supply of Lymphoseek on terms acceptable to the Company, or at all.

NAV4694 Manufacturing

Supplies of NAV4694 used in clinical development through Phase 2b were manufactured by AstraZeneca through various arrangements. In May 2012, we executed an agreement with Molecular NeuroImaging, LLC (MNI) to produce and distribute NAV4694 to imaging centers within a specified geographic region. In October 2012, we completed an agreement with Spectron mrc, LLC (Spectron) to produce NAV4694 for use at certain clinical trial sites. In August

2013, we entered into a Manufacturing Services Agreement with PETNET Solutions, Inc. (PETNET) for the manufacture and distribution of NAV4694 with an initial term of 3 years. Under the terms of the agreement, PETNET will manufacture NAV4694 clinical trial material at select U.S. radiopharmacies, with the possibility of expanding into additional PETNET locations in the future. Given the uncertainty regarding our involvement in future development of NAV4694, we cannot assure you that we will be successful in executing future agreements for the supply of NAV4694 on terms acceptable to the Company, or at all.

NAV5001 Manufacturing

Supplies of NAV5001 used in clinical development through Phase 3 were manufactured by Alseres Pharmaceuticals, Inc. (Alseres) under an agreement they had in place with Nordion, Inc., a Canadian corporation and well-recognized manufacturer of ^{123}I and nuclear medicine labeled imaging agents. In May 2013, we entered into an agreement with Nordion (Canada) Inc. (Nordion) to produce and supply NAV5001 for our late-phase clinical trials. Nordion will radiolabel NAV5001, manage the

manufacturing logistics, and ship it to third-party clinical trial sites on behalf of Navidea. The initial three-year term expires in May 2016. Given the uncertainty regarding our involvement in future development of NAV5001, we cannot assure you that we will be successful in executing future agreements for the supply of NAV5001 on terms acceptable to the Company, or at all.

Summary

We cannot assure you that we will be successful in securing and/or maintaining the necessary manufacturing, supply and/or radiolabeling capabilities for our product candidates in clinical development. If and when established, we also cannot assure you that we will be able to maintain agreements or other purchasing arrangements with our subcontractors on terms acceptable to us, or that our subcontractors will be able to meet our production requirements on a timely basis, at the required levels of performance and quality, including compliance with FDA cGMP requirements. In the event that any of our subcontractors are unable or unwilling to meet our production requirements, we cannot assure you that an alternate source of supply could be established without significant interruption in product supply or without significant adverse impact to product availability or cost. Any significant supply interruption or yield problems that we or our subcontractors experience would have a material adverse effect on our ability to manufacture our products and, therefore, a material adverse effect on our business, financial condition, and results of operations until a new source of supply is qualified. See Risk Factors.

Competition

Competition in the pharmaceutical and biotechnology industries is intense. We face competition from a variety of companies focused on developing oncology and neurology diagnostic drugs. We compete with large pharmaceutical and other specialized biotechnology companies. We also face competition from universities and other non-profit research organizations. Many emerging medical product companies have corporate partnership arrangements with large, established companies to support the research, development, and commercialization of products that may be competitive with our products. In addition, a number of large established companies are developing proprietary technologies or have enhanced their capabilities by entering into arrangements with or acquiring companies with technologies applicable to the detection or treatment of cancer and other diseases targeted by our product candidates. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of these competitors have products that have been approved or are in development and operate large, well-funded research and development programs. Many of our existing or potential competitors have substantially greater financial, research and development, regulatory, marketing, and production resources than we have. Other companies may develop and introduce products and processes competitive with or superior to ours.

We expect to encounter significant competition for our pharmaceutical products. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before us may achieve a significant competitive advantage if their products work through a similar mechanism as our products and if the approved indications are similar. A number of biotechnology and pharmaceutical companies are developing new products for the treatment of the same diseases being targeted by us. In some instances, such products have already entered late-stage clinical trials or received FDA approval and may be marketed for some period prior to the approval of our products.

We believe that our ability to compete successfully will be based on our ability to create and maintain scientifically advanced “best-in-class” technology, develop proprietary products, attract and retain scientific personnel, obtain patent or other protection for our products, obtain required regulatory approvals and manufacture and successfully market our products, either alone or through third parties. We expect that competition among products cleared for marketing will be based on, among other things, product efficacy, safety, reliability, availability, price, and patent position. See

Risk Factors.

Lymphoseek Competition

Surgeons who practice the lymphatic mapping procedure for which Lymphoseek is intended currently use other radiopharmaceuticals such as a sulfur colloid compound in the U.S., and other colloidal compounds in other markets. In addition, some surgeons still use vital blue dyes to assist in the visual identification of the draining lymphatic tissue around a primary tumor. In the U.S., sulfur colloid is manufactured by Pharmalucence, a subsidiary of Sun Pharmaceutical Industries Ltd. Sulfur colloid had been used “off-label” in the U.S. for ILM until July 2011, when it was approved by the FDA for use in lymphatic mapping in breast cancer patients based on a statistical meta-analysis of published literature that compared the use of sulfur colloid with that of the vital blue dyes. The product label for sulfur colloid was expanded to cover lymphatic mapping in melanoma in August 2012, again on the basis of a meta-analysis of published literature. In the EU and certain Pacific Rim markets, there are other colloidal-based compounds with various levels of approved labeling for use in lymphatic mapping, although a number of countries still employ the use of products used “off-label.”

NAV4694 Competition

Several potential competitive [18F] products have been approved for use as biomarkers to aid in detection of AD. Developed through Eli Lilly's wholly-owned Avid Radiopharmaceuticals (Avid), florbetapir, now known as Amyvid, received FDA approval to market in April 2012. Florbetapir also received marketing authorization in the EU in January 2013. In addition to fluorbetapir, there are two other beta-amyloid imaging agents available: florbetaben from Piramal Enterprises, Imaging Division, and flutemetamol from GE Healthcare. In October 2013, the FDA approved flutemetamol, under the name VizamylTM, for adults being evaluated for AD and dementia with PET brain imaging. Florbetaben, now called NeuraceqTM, received EMA approval for use in PET imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for AD and other causes of cognitive decline from the EMA in February 2014 and from the FDA in March 2014.

NAV5001 Competition

In July 2000, GE Healthcare received EMA approval to market DaTscanTM (Ioflupane 123I Injection), a radiopharmaceutical agent intended for use with SPECT imaging for the detection of dopamine transporters in the brains of adult patients with suspected Parkinsonian syndromes, in the EU. DaTscan was developed to help physicians evaluate neurodegenerative movement disorders, such as idiopathic (of unknown cause) PD. In July 2006, GE Healthcare received expanded approval in the EU for DaTscan for use in DLB. For patients with dementia, DaTscan has been successfully used in Europe to separate Alzheimer's disease from DLB. This has important implications in determining which medications can be safely used to treat the dementia. GE Healthcare received FDA approval to market DaTscan in the U.S. in January 2011.

Patents and Proprietary Rights

The patent position of biotechnology, including our company, generally is highly uncertain and may involve complex legal and factual questions. Potential competitors may have filed applications, or may have been issued patents, or may obtain additional patents and proprietary rights relating to products or processes in the same area of technology as that used by the Company. The scope and validity of these patents and applications, the extent to which we may be required to obtain licenses thereunder or under other proprietary rights, and the cost and availability of licenses are uncertain. We cannot assure you that our patent applications or those licensed to us will result in additional patents being issued or that any of our patents or those licensed to us will afford protection against competitors with similar technology; nor can we assure you that any of these patents will not be designed around by others or that others will not obtain patents that we would need to license or design around.

We also rely upon unpatented trade secrets. We cannot assure you that others will not independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets, or disclose such technology, or that we can meaningfully protect our rights to our unpatented trade secrets.

We require our employees, consultants, advisers, and suppliers to execute a confidentiality agreement upon the commencement of an employment, consulting or manufacturing relationship with us. The agreement provides that all confidential information developed by or made known to the individual during the course of the relationship will be kept confidential and not disclosed to third parties except in specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual will be the exclusive property of our company. We cannot assure you, however, that these agreements will provide meaningful protection for our trade secrets in the event of an unauthorized use or disclosure of such information. We also employ a variety of security measures to preserve the confidentiality of our trade secrets and to limit access by unauthorized persons. We cannot assure you, however, that these measures will be adequate to protect our trade secrets from unauthorized access or disclosure. See Risk Factors.

Manocept/Lymphoseek Intellectual Property

Lymphoseek , as well as certain aspects of intellectual property underlying the Manocept platform, is under exclusive worldwide license from the Regents of the University of California. The license grants Navidea the commercialization rights to Lymphoseek for diagnostic imaging and intraoperative detection applications.

Lymphoseek, including the Manocept backbone composition and methods of use, is also the subject of 3 patent families totaling 19 patents and patent applications in the United States and certain major foreign markets. The patents and patent applications held by the Regents of the University of California have been licensed exclusively to Navidea for all diagnostic and therapeutic uses worldwide. The first composition of matter patent covering Manocept was issued in the United States in June 2002. The claims of the composition of matter patent covering Manocept have been allowed in the EU and issued in the majority of major-market EU countries in 2005. The composition of matter patent has also been issued in Japan. We have filed

additional patent applications in the U.S. and certain major foreign markets related to manufacturing processes for Lymphoseek and Manocept, the first of which was issued in the U.S. in 2013. We have filed further patent applications jointly with The Ohio State Innovation Foundation related to CD206 expressing cell-related disorders. We will also rely on trademark protection for products that we expect to commercialize and have registered or are in the process of registering the marks Lymphoseek® and Manocept™ in the U.S. and other markets.

NAV4694 Intellectual Property

NAV4694 is being developed under an exclusive worldwide license from AstraZeneca. The NAV4694 license grants Navidea commercialization rights to the fluorine-18 labeled biomarker for use as an aid in the diagnosis of AD. NAV4694 is the subject of 3 issued patents and 18 patents pending in 12 foreign jurisdictions covering the [^{18}F]NAV4694 drug substance and the NAV4694 precursor.

NAV5001 Intellectual Property

NAV5001 is being developed under an exclusive sublicense from Alseres. The NAV5001 sublicense grants Navidea commercialization rights to the iodine-123 labeled biomarker for use as an aid in the diagnosis of PD and other movement disorders, with potential use as a diagnostic aid in dementia. NAV5001 is the subject of 2 issued patents, each expiring in 2030, 3 patent applications pending in the U.S., and 9 patent applications pending in 3 foreign jurisdictions.

Government Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing, among other things, of our products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, Public Health Service Act, and their implementing regulations. Failure to comply with applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications or supplemental applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution. We also may be subject to regulation under the Occupational Safety and Health Act, the Atomic Energy Act, the Toxic Substances Control Act, the Export Control Act and other present and future laws of general application as well as those specifically related to radiopharmaceuticals.

Most aspects of our business are subject to some degree of government regulation in the countries in which we conduct our operations. As a developer, manufacturer and marketer of medical products, we are subject to extensive regulation by, among other governmental entities, the FDA and the corresponding state, local and foreign regulatory bodies in jurisdictions in which our products are intended to be sold. These regulations govern the introduction of new products, the observance of certain standards with respect to the manufacture, quality, safety, efficacy and labeling of such products, the maintenance of certain records, the tracking of such products, performance surveillance and other matters.

Failure to comply with applicable federal, state, local or foreign laws or regulations could subject us to enforcement action, including product seizures, recalls, withdrawal of marketing clearances, and civil and criminal penalties, any one or more of which could have a material adverse effect on our business. We believe that we are in substantial compliance with such governmental regulations. However, federal, state, local and foreign laws and regulations regarding the manufacture and sale of radiopharmaceuticals are subject to future changes. We cannot assure you that such changes will not have a material adverse effect on our company.

For some products, and in some countries, government regulation is significant and, in general, there is a trend toward more stringent regulation. In recent years, the FDA and certain foreign regulatory bodies have pursued a more rigorous enforcement program to ensure that regulated businesses like ours comply with applicable laws and regulations. We devote significant time, effort and expense addressing the extensive governmental regulatory requirements applicable to our business. To date, we have not received a noncompliance notification or warning letter from the FDA or any other regulatory bodies of alleged deficiencies in our compliance with the relevant requirements, nor have we recalled or issued safety alerts on any of our products. However, we cannot assure you that a warning letter, recall or safety alert, if it occurred, would not have a material adverse effect on our company. See Risk Factors.

In the early- to mid-1990s, the review time by the FDA to clear medical products for commercial release lengthened and the number of marketing clearances decreased. In response to public and congressional concern, the FDA Modernization Act of 1997 (the 1997 Act) was adopted with the intent of bringing better definition to the clearance process for new medical products. While the FDA review times have improved since passage of the 1997 Act, we cannot assure you that the FDA review

processes will not delay our Company's introduction of new products in the U.S. in the future. In addition, many foreign countries have adopted more stringent regulatory requirements that also have added to the delays and uncertainties associated with the development and release of new products, as well as the clinical and regulatory costs of supporting such releases. It is possible that delays in receipt of, or failure to receive, any necessary clearance for our new product offerings could have a material adverse effect on our business, financial condition or results of operations. See Risk Factors.

The U.S. Drug Approval Process

None of our drugs may be marketed in the U.S. until such drug has received FDA approval. The steps required before a drug may be marketed in the U.S. include:

- preclinical laboratory tests, animal studies and formulation studies;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the investigational product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of FDA inspections of the manufacturing and clinical facilities at which the drug is produced, tested, and/or distributed to assess compliance with cGMPs and current good clinical practices (cGCP) standards; and
- FDA review and approval of the NDA.

Preclinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA unless, before that time, the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. The study protocol and informed consent information for study subjects in clinical trials must also be approved by an institutional review board at each institution where the trials will be conducted. Study subjects must sign an informed consent form before participating in a clinical trial. Phase 1 usually involves the initial introduction of the investigational product into people to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase 2 usually involves trials in a limited subject population to (i) evaluate dosage tolerance and appropriate dosage, (ii) identify possible adverse effects and safety risks, and (iii) evaluate preliminarily the efficacy of the product candidate for specific indications. Phase 3 trials usually further evaluate clinical efficacy and further test its safety by using the product candidate in its final form in an expanded subject population. There can be no assurance that Phase 1, Phase 2 or Phase 3 testing will be completed successfully within any specified period of time, if at all. Furthermore, we or the FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The FDA and the IND sponsor may agree in writing on the design and size of clinical studies intended to form the primary basis of an effectiveness claim in an NDA application. This process is known as a Special Protocol Assessment (SPA). These agreements may not be changed after the clinical studies begin, except in limited circumstances. The existence of a SPA, however, does not assure approval of a product candidate.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical studies, together with other detailed information, including information on the manufacturing quality and composition of the investigational product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. The testing and approval process requires substantial time, effort and financial resources. Submission of an NDA requires payment of a substantial review user fee to the FDA. Before approving a NDA, the FDA usually will inspect the facility or the facilities where the product is manufactured, tested and distributed and will not approve the product unless cGMP compliance is satisfactory. If the FDA evaluates the NDA and the manufacturing facilities as acceptable, the FDA may issue an

approval letter or a complete response letter. A complete response letter outlines conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter. The approval letter authorizes commercial marketing of the drug for specific indications. As a condition of approval, the FDA may require post-marketing testing and surveillance to monitor the product's safety or efficacy, or impose other post-approval commitment conditions.

The NDA for Lymphoseek was submitted with the intention for use in intraoperative lymphatic mapping across a broad range of cancers. As a part of their review, the FDA examined the pre-clinical, clinical and CMC data supporting our application, and, as is also typical of such reviews, conducted site audits of our facilities and those of the sites where the referenced clinical trials were performed, as well as of contract suppliers and third party vendors being used in the manufacturing and quality assessment processes for Lymphoseek. Lymphoseek was approved and indicated for use in lymphatic mapping for breast cancer and melanoma by the FDA in March 2013. In June 2014, the FDA approved a supplemental New Drug Application (sNDA) for the expanded use of Lymphoseek indicated for guiding sentinel lymph node biopsy in head and neck cancer patients with squamous cell carcinoma of the oral cavity. In October 2014, the FDA approved a second sNDA for lymphatic mapping in solid tumors and added sentinel lymph node detection for breast cancer and melanoma to the approved indications. The FDA also allowed expanded utilization of Lymphoseek with or without scintigraphic imaging, known as lymphoscintigraphy, to enable pre-operative imaging and mapping of lymph nodes to facilitate node localization during surgical procedures. Additional trials, including an ongoing trial in colorectal cancer, and others in various stages of execution, planning or consideration, are anticipated to provide additional data to potentially support expansion of the Lymphoseek opportunity. We cannot assure you that Lymphoseek will achieve regulatory approval in any market outside the U.S. or EU, or if approved, that it will achieve market acceptance in any market. See Risk Factors.

The FDA has various programs, including fast track, priority review and accelerated approval, which are intended to expedite or simplify the process of reviewing drugs and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for one or more of these programs are those for serious or life threatening conditions, those with the potential to address unmet medical needs and those that provide meaningful benefit over existing treatments. We cannot assure you that any of our drug candidates will qualify for any of these programs, or that, if a drug candidate does qualify, the review time will be reduced or the product will be approved.

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes or making certain additional labeling claims, are subject to further FDA review and approval. Obtaining approval for a new indication generally requires that additional clinical studies be conducted.

U.S. Post-Approval Requirements

Holders of an approved NDA are required to: (i) conduct pharmacovigilance and report certain adverse reactions to the FDA, (ii) comply with certain requirements concerning advertising and promotional labeling for their products, and (iii) continue to have quality control and manufacturing procedures conform to cGMP. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing and distribution facilities; this latter effort includes assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the area of production, quality control and distribution to maintain cGMP compliance. We use and will continue to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal of the product from the market.

Marketing of prescription drugs is also subject to significant regulation through federal and state agencies tasked with consumer protection and prevention of medical fraud, waste and abuse. We must comply with restrictions on off-label use promotion, anti-kickback, ongoing clinical trial registration, and limitations on gifts and payments to physicians.

Non-U.S. Regulation

Before our products can be marketed outside of the United States, they are subject to regulatory approval similar to that required in the U.S., although the requirements governing the conduct of clinical trials, including additional clinical trials that may be required, product licensing, pricing and reimbursement vary widely from country to country. No action can be taken to market any product in a country until an appropriate application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing review period often

begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices may not be approved for such product.

In Europe, marketing authorizations may be submitted at a centralized, a decentralized or national level. The centralized procedure is mandatory for the approval of biotechnology products and provides for the grant of a single marketing authorization that is valid in all EU member states. As of January 1995, a mutual recognition procedure is available at the request of the applicant for all medicinal products that are not subject to the centralized procedure.

We submitted our MAA for Lymphoseek to the EMA in December 2012. In September 2014, the CHMP adopted a positive opinion recommending marketing authorization for Lymphoseek for use in the EU in imaging and intraoperative detection of sentinel lymph nodes draining a primary tumor in adult patients with breast cancer, melanoma, or localized squamous cell carcinoma of the oral cavity. The CHMP's positive opinion was reviewed by the European Commission (EC), which has the authority to approve medicinal products for use in the 28 countries of the EU and generally follows the recommendations of the CHMP. The EC granted marketing authorization for Lymphoseek in the EU in November 2014.

While we are unable to predict the extent to which our business may be affected by future regulatory developments, we believe that our substantial experience dealing with governmental regulatory requirements and restrictions on our operations throughout the world, and our development of new and improved products, should enable us to compete effectively within this environment.

Regulation Specific to Radiopharmaceuticals

Our radiolabeled targeting agents and biologic products, if developed, would require a regulatory license to market from the FDA and from comparable agencies in foreign countries. The process of obtaining regulatory licenses and approvals is costly and time consuming, and we have encountered significant impediments and delays related to our previously proposed biologic products.

The process of completing pre-clinical and clinical testing, manufacturing validation and submission of a marketing application to the appropriate regulatory bodies usually takes a number of years and requires the expenditure of substantial resources, and we cannot assure you that any approval will be granted on a timely basis, if at all. Additionally, the length of time it takes for the various regulatory bodies to evaluate an application for marketing approval varies considerably, as does the amount of preclinical and clinical data required to demonstrate the safety and efficacy of a specific product. The regulatory bodies may require additional clinical studies that may take several years to perform. The length of the review period may vary widely depending upon the nature and indications of the proposed product and whether the regulatory body has any further questions or requests any additional data. Also, the regulatory bodies require post-marketing reporting and surveillance programs (pharmacovigilance) to monitor the side effects of the products. We cannot assure you that any of our potential drug or biologic products will be approved by the regulatory bodies or approved on a timely or accelerated basis, or that any approvals received will not subsequently be revoked or modified.

The Nuclear Regulatory Commission (NRC) oversees medical uses of nuclear material through licensing, inspection, and enforcement programs. The NRC issues medical use licenses to medical facilities and authorized physician users, develops guidance and regulations for use by licensees, and maintains a committee of medical experts to obtain advice about the use of byproduct materials in medicine. The NRC (or the responsible Agreement State) also regulates the manufacture and distribution of these products. The FDA oversees the good practices in the manufacturing of radiopharmaceuticals, medical devices, and radiation-producing x-ray machines and accelerators. The states regulate the practices of medicine and pharmacy and administer programs associated with radiation-producing x-ray machines and accelerators. We cannot assure you that we will be able to obtain all necessary licenses and permits and be able to

comply with all applicable laws. The failure to obtain such licenses and permits or to comply with applicable laws would have a materially adverse effect on our business, financial condition, and results of operations.

Corporate Information

Our executive offices are located at 5600 Blazer Parkway, Suite 200, Dublin, OH 43017. Our telephone number is (614) 793-7500. “Navidea”, the Navidea logo, “Lymphoseek” and “RIGS” are trademarks of Navidea Biopharmaceuticals, Inc. or its subsidiaries in the U.S. and/or other countries. Other trademarks or service marks appearing in this report may be trademarks or service marks of other owners.

The address for our website is http://www.navidea.com. We make available free of charge on our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings pursuant to Section 13(a) or

15(d) of the Exchange Act, and amendments to such filings, as soon as reasonably practicable after each is electronically filed with, or furnished to, the SEC.

Financial Statements

Our consolidated financial statements and the related notes, including revenues, income (loss), total assets and other financial measures are set forth at pages F-1 through F-32 of this Form 10-K.

Research and Development

We spent approximately $16.8 million, $23.7 million and $16.9 million on research and development activities in the years ended December 31, 2014, 2013 and 2012, respectively.

Employees

As of February 28, 2015, we had 46 full-time and 8 part-time employees. We consider our relations with our employees to be good.

Item 1A. Risk Factors

An investment in our common stock is highly speculative, involves a high degree of risk, and should be made only by investors who can afford a complete loss. You should carefully consider the following risk factors, together with the other information in this prospectus, including our financial statements and the related notes, before you decide to buy our common stock. Our most significant risks and uncertainties are described below; however, they are not the only risks we face. If any of the following risks actually occur, our business, financial condition, or results of operations could be materially adversely affected, the trading of our common stock could decline, and you may lose all or part of your investment therein.

If we do not achieve commercial success with our approved product or if we do not successfully develop any additional product candidates into marketable products, we may be unable to generate significant revenue or become profitable.

We divested the neoprobe GDS line of gamma detection medical devices in August 2011. Through that time, sales of gamma detection devices represented our primary source of revenue. As a result, our near-term financial success depends in large part on Lymphoseek achieving commercial success in the U.S. and, pending approval in other markets, on achievement of commercial success in those markets as well. Lymphoseek was approved and indicated for use in lymphatic mapping for breast cancer and melanoma by the FDA in March 2013. In June 2014, the FDA approved a supplemental New Drug Application (sNDA) for the expanded use of Lymphoseek indicated for guiding sentinel lymph node biopsy in head and neck cancer patients with squamous cell carcinoma of the oral cavity. In October 2014, the FDA approved a second sNDA for lymphatic mapping in solid tumors and added sentinel lymph node detection for breast cancer and melanoma to the approved indications. The FDA also allowed expanded utilization of Lymphoseek with or without scintigraphic imaging, known as lymphoscintigraphy, to enable pre-operative imaging and mapping of lymph nodes to facilitate node localization during surgical procedures. Additional trials, including an ongoing trial in colorectal cancer, and others in various stages of execution, planning or consideration, are anticipated to provide additional data to potentially support expansion of the Lymphoseek opportunity. We began generating revenues from product sales of Lymphoseek in the second quarter of 2013. As we continue to realize revenues from Lymphoseek, it is possible we will ultimately receive payments related to the achievement of certain sales milestones by our marketing partner in the U.S. However, we cannot assure you that Lymphoseek will achieve commercial success in the U.S. or any other global market, that we will realize sales at

levels necessary for us to achieve sales milestone payments, or that revenue from Lymphoseek will lead to us becoming profitable.

Additional product candidates based on the Manocept platform are in various stages of pre-clinical and clinical development. Regulatory approval for additional Manocept-based product candidates may not be successful, or if successful, may not result in increased sales. Additional clinical testing for products based on our Manocept platform, NAV4694, NAV5001, or other product candidates, may not be successful and, even if they are, we may not be successful in developing any of them into a commercial product which will provide sufficient revenue to make us profitable.

Many companies in the pharmaceutical industry suffer significant setbacks in advanced clinical trials even after reporting promising results in earlier trials. Even if our trials are viewed as successful, we may not get regulatory approval. Our product candidates will be successful only if:

- they are developed to a stage that will enable us to commercialize them or sell related marketing rights to pharmaceutical companies;
- we are able to commercialize them in clinical development or sell the marketing rights to third parties; and
- upon being developed, they are approved by the regulatory authorities.

We are dependent on the achievement of a number of these goals in order to generate future revenues. The failure to generate such revenues may preclude us from continuing our research and development of these and other product candidates.

We cannot guarantee that we will obtain regulatory approval to manufacture or market our unapproved drug candidates and our approval to market our products or anticipated commercial launch may be delayed as a result of the regulatory review process.

Obtaining regulatory approval to market drugs to diagnose or treat cancer and other diseases is expensive, difficult and risky. Preclinical and clinical data as well as information related to the CMC processes of drug production can be interpreted in different ways which could delay, limit or preclude regulatory approval. Negative or inconclusive results, adverse medical events during a clinical trial, or issues related to CMC processes could also delay, limit or prevent regulatory approval. Even if we receive regulatory clearance to market a particular product candidate, the approval could be conditioned on us conducting additional costly post-approval studies or could limit the indicated uses included in our labeling.

Our radiopharmaceutical products will remain subject to ongoing regulatory review following the receipt of marketing approval. If we fail to comply with continuing regulations, we could lose these approvals and the sale of our products could be suspended.

Approved products may later cause adverse effects that limit or prevent their widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, any contract manufacturer we use in the process of producing a product and its facilities will continue to be subject to FDA review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing clearance, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping related to the product will remain subject to extensive regulatory requirements. We may be slow to adapt, or we may never adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements.

If we fail to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities or previously unknown problems with our products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;

- product seizures or detentions;
- import bans;
- voluntary or mandatory product recalls and publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications.

Even if our drug candidates are successful in clinical trials, we may not be able to successfully commercialize them.

With the historical exception of our discontinued medical device businesses, we have dedicated and will continue to dedicate substantially all of our resources to the research and development of our radiopharmaceutical technologies and related compounds. Lymphoseek is now approved for use in lymphatic mapping in solid tumors and in sentinel lymph node detection for breast cancer and melanoma in the U.S. Lymphoseek has also been approved for use in imaging and intraoperative detection of sentinel lymph nodes draining a primary tumor in adult patients with breast cancer, melanoma, or localized squamous cell carcinoma of the oral cavity in the EU. However, our other compounds currently are in research or development and have not received marketing approval.

Prior to commercialization, each product candidate requires significant research, development and preclinical testing and extensive clinical investigation before submission of any regulatory application for marketing approval. The development of radiopharmaceutical technologies and compounds, including those we are currently developing, is unpredictable and subject to numerous risks. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons including that they may:

- be found ineffective or cause harmful side effects during preclinical testing or clinical trials;
- fail to receive necessary regulatory approvals;
- be difficult to manufacture on a scale necessary for commercialization;
- be uneconomical to produce;
- fail to achieve market acceptance; or
- be precluded from commercialization by proprietary rights of third parties.

The occurrence of any of these events could adversely affect the commercialization of our product candidates. Products, if introduced, may not be successfully marketed and/or may not achieve customer acceptance. If we fail to commercialize products or if our future products do not achieve significant market acceptance, we will not likely generate significant revenues or become profitable.

Clinical trials for our product candidates will be lengthy and expensive and their outcome is uncertain.

Before obtaining regulatory approval for the commercial sale of any product candidates, we must demonstrate through preclinical testing and clinical trials that our product candidates are safe and effective for use in humans. Conducting clinical trials is a time consuming, expensive and uncertain process and may take years to complete.

With respect to Lymphoseek, we expect to support a number of efforts in various indications, whether internally sponsored or under investigator-sponsored studies, to provide additional data to support expansion of the Lymphoseek opportunity. We also expect to sponsor efforts to explore the Manocept platform, whether in potential diagnostic uses or investigation of uses related to Macrophage Therapeutics.

With respect to NAV4694, AstraZeneca completed clinical development through a Phase 2a level. We currently have active trials in subjects with MCI initiated in March 2013 and a Phase 3 autopsy-based trial initiated in June 2013 to support registration in the U.S. and the EU; however, enrollment in both of these trials has been temporarily suspended while we determine the future of the program in connection with evaluation of a term sheet.

With respect to NAV5001, Alseres completed five clinical trials in over 600 subjects. Alseres received a Phase 3 SPA from the FDA for NAV5001 in 2009. We are currently supporting Phase 3 trials in subjects with PD; however, enrollment in both of these trials has been temporarily suspended while we evaluate the future of the program within Navidea in connection with evaluation of a term sheet. Each Phase 3 trial is the subject of a SPA agreement with the FDA.

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We continually assess our clinical trial plans and may, from time to time, initiate additional clinical trials to support our overall strategic development objectives. Historically, the results from preclinical testing and early clinical trials often do not predict the results obtained in later clinical trials. Frequently, drugs that have shown promising results in preclinical or early clinical trials subsequently fail to establish sufficient safety and efficacy data necessary to obtain regulatory approval. At any time during the clinical trials, we, the participating institutions, the FDA or the EMA might delay or halt any clinical trials for our product candidates for various reasons, including:

- ineffectiveness of the product candidate;
- discovery of unacceptable toxicities or side effects;
- development of disease resistance or other physiological factors;
- delays in patient enrollment; or
- other reasons that are internal to the businesses of our potential collaborative partners, which reasons they may not share with us.

While we have achieved some level of success in our clinical trials for Lymphoseek as indicated by the FDA and EMA approvals, and our licensing partners have also achieved successful outcomes from earlier trials of NAV4694 and NAV5001, the results of some of these clinical trials that have not been yet reviewed by the FDA or other regulatory bodies, as well as pending and future trials for these and other product candidates that we may develop or acquire, are subject to review and interpretation by various regulatory bodies during the regulatory review process and may ultimately fail to demonstrate the safety or effectiveness of our product candidates to the extent necessary to obtain regulatory approval, or that commercialization of our product candidates is worthwhile. Any failure or substantial delay in successfully completing clinical trials and obtaining regulatory approval for our product candidates could materially harm our business.

We extensively outsource our clinical trial activities and usually perform only a small portion of the start-up activities in-house. We rely on independent third-party contract research organizations (CROs) to perform most of our clinical studies, including document preparation, site identification, screening and preparation, pre-study visits, training, post-study audits and statistical analysis. Many important aspects of the services performed for us by the CROs are out of our direct control. If there is any dispute or disruption in our relationship with our CROs, our clinical trials may be delayed. Moreover, in our regulatory submissions, we rely on the quality and validity of the clinical work performed by third-party CROs. If any of our CROs' processes, methodologies or results were determined to be invalid or inadequate, our own clinical data and results and related regulatory approvals could be adversely impacted.

If we fail to establish and maintain collaborations or if our partners do not perform, we may be unable to develop and commercialize our product candidates.

We expect to enter into collaborative arrangements with third-parties to develop and/or commercialize product candidates and are currently seeking additional collaborations. Such collaborations might be necessary in order for us to fund our research and development activities and third-party manufacturing arrangements, seek and obtain regulatory approvals and successfully commercialize our existing and future product candidates. If we fail to enter into collaborative arrangements or fail to maintain our existing collaborative arrangements, the number of product candidates from which we could receive future revenues would decline.

Our dependence on collaborative arrangements with third parties will subject us to a number of risks that could harm our ability to develop and commercialize products including that:

- collaborative arrangements may not be on terms favorable to us;
- disagreements with partners or regulatory compliance issues may result in delays in the development and marketing of products, termination of our collaboration agreements or time consuming and expensive legal action;

- we cannot control the amount and timing of resources partners devote to product candidates or their prioritization of product candidates and partners may not allocate sufficient funds or resources to the development, promotion or marketing of our products, or may not perform their obligations as expected;
- partners may choose to develop, independently or with other companies, alternative products or treatments. including products or treatments which compete with ours;
- agreements with partners may expire or be terminated without renewal, or partners may breach collaboration agreements with us;
- business combinations or significant changes in a partner's business strategy might adversely affect that partner's willingness or ability to complete its obligations to us; and
- the terms and conditions of the relevant agreements may no longer be suitable.

The occurrence of any of these events could adversely affect the development or commercialization of our products.

If users of our products are unable to obtain adequate reimbursement from third-party payers, or if new restrictive legislation is adopted, market acceptance of our products may be limited and we may not achieve anticipated revenues.

Our ability to commercialize our products will depend in part on the extent to which appropriate reimbursement levels for the cost of our products and related treatment are obtained by governmental authorities, private health insurers and other organizations such as health maintenance organizations (HMOs). Third-party payers are increasingly challenging the prices charged for medical care. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to further reform health care or reduce government insurance programs, may all result in lower prices for our products if approved for commercialization. The cost containment measures that health care payers and providers are instituting and the effect of any health care reform could materially harm our ability to sell our products at a profit.

In August 2013, we announced that the CMS issued a HCPCS “C Code” for Lymphoseek. We anticipate that the reimbursement code, which became effective on October 1, 2013, will streamline the billing and reimbursement process for hospital providers who use Lymphoseek and support its fair and equitable reimbursement. The pass-through provisions supporting this C Code are expected to extend through December 31, 2015. Lymphoseek has also been granted a permanent “A Code” effective January 1, 2014. We believe these developments may assist in advancing utilization of Lymphoseek. However, we cannot assure you that, following the expiration of the pass-through provisions, we will be successful in establishing or obtaining a separately reimbursable status for Lymphoseek and therefore the cost of Lymphoseek may need to be absorbed by the institution as a part of the bundled procedural code for the surgical procedure in which Lymphoseek is used. If this is the case, our expectations of the pricing we expect to achieve for Lymphoseek and the related potential revenue may be significantly diminished.

We may be unable to establish or contract for the pharmaceutical manufacturing capabilities necessary to develop and commercialize our potential products.

We are in the process of establishing third-party clinical manufacturing capabilities for our compounds under development. We intend to rely on third-party contract manufacturers to produce sufficiently large quantities of drug materials that are and will be needed for clinical trials and commercialization of our potential products. Third-party manufacturers may not be able to meet our needs with respect to timing, quantity or quality of materials.

We have a supply agreement with Reliable to manufacture the drug substance for our Lymphoseek product and a manufacturing agreement with OsoBio for the finishing and vialing of our Lymphoseek product. However, if we are unable to contract for a sufficient supply of needed materials on acceptable terms, or if we should encounter delays or difficulties in our relationships with manufacturers, revenues from Lymphoseek may be adversely impacted. In addition, clinical trials for our other product candidates may be delayed, thereby delaying the submission of product candidates for regulatory approval and the market introduction and subsequent commercialization of our potential products, and for approved products, any such delays, interruptions or other difficulties may render us unable to supply sufficient quantities to meet demand. Any such delays or interruptions may lower our revenues and potential profitability.

We and any third-party manufacturers that we may use must continually adhere to cGMPs and regulations enforced by the FDA through its facilities inspection program and/or foreign regulatory authorities where our products will be tested and/or marketed. If our facilities or the facilities of third-party manufacturers cannot pass a pre-approval plant

inspection, the FDA and/or foreign regulatory authorities will not grant approval to market our product candidates. In complying with these regulations and foreign regulatory requirements, we and any of our third-party manufacturers will be obligated to expend time, money and effort on production, record-keeping and quality control to assure that our potential products meet applicable specifications and other requirements. The FDA and other regulatory authorities may take action against a contract manufacturer who violates cGMPs.

We may lose out to larger or better-established competitors.

The biotechnology industry is intensely competitive. Some of our competitors have significantly greater financial, technical, manufacturing, marketing and distribution resources as well as greater experience in the pharmaceutical industry than we have. The particular medical conditions our product lines address can also be addressed by other medical procedures or drugs. Many of these alternatives are widely accepted by physicians and have a long history of use.

Physicians may use our competitors' products and/or our products may not be competitive with other technologies. Lymphoseek is expected to compete against sulfur colloid in the U.S. and other colloidal agents in other global markets.

NAV4694 is expected to compete against florbetapir, also known as Amyvid, a first-generation beta-amyloid imaging agent for which Eli Lilly received FDA approval in 2012. Florbetapir also received marketing authorization in the EU in January 2013. There are two additional first-generation beta-amyloid imaging agents available: florbetaben from Piramal Enterprises, Imaging Division, and flutemetamol from GE Healthcare. In October 2013, the FDA approved flutemetamol, under the name Vizamyl, for adults being evaluated for AD and dementia with PET brain imaging. Florbetaben, now called Neuraceq, received EMA approval for use in PET imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for AD and other causes of cognitive decline from the EMA in February 2014 and from the FDA in March 2014.

NAV5001's primary competitor is expected to be ioflupane, marketed as DaTscan by GE Healthcare. DaTscan was developed to help physicians evaluate neurodegenerative movement disorders, such as idiopathic (of unknown cause) PD. GE Healthcare received EMA approval to market DaTscan in the EU in July 2000. In July 2006, GE Healthcare received expanded approval in the EU for DaTscan for use in DLB. GE Healthcare received FDA approval to market DaTscan in the U.S. in January 2011.

If our competitors are successful in establishing and maintaining market share for their products, our sales and revenues may not occur at the rate we anticipate. In addition, our current and potential competitors may establish cooperative relationships with larger companies to gain access to greater research and development or marketing resources. Competition may result in price reductions, reduced gross margins and loss of market share.

We may be exposed to product liability claims for our product candidates and products that we are able to commercialize.

The testing, manufacturing, marketing and use of our commercial products, as well as product candidates in development, involve substantial risk of product liability claims. These claims may be made directly by consumers, healthcare providers, pharmaceutical companies or others. In recent years, coverage and availability of cost-effective product liability insurance has decreased, so we may be unable to maintain sufficient coverage for product liabilities that may arise. In addition, the cost to defend lawsuits or pay damages for product liability claims may exceed our coverage. If we are unable to maintain adequate coverage or if claims exceed our coverage, our financial condition and our ability to clinically test our product candidates and market our products will be adversely impacted. In addition, negative publicity associated with any claims, regardless of their merit, may decrease the future demand for our products and impair our financial condition.

The administration of drugs in humans, whether in clinical studies or commercially, carries the inherent risk of product liability claims whether or not the drugs are actually the cause of an injury. Our products or product candidates may cause, or may appear to have caused, injury or dangerous drug interactions, and we may not learn about or understand those effects until the product or product candidate has been administered to patients for a prolonged period of time. We may be subject from time to time to lawsuits based on product liability and related claims, and we cannot predict the eventual outcome of any future litigation. We may not be successful in defending ourselves in the litigation and, as a result, our business could be materially harmed. These lawsuits may result in large judgments or settlements against us, any of which could have a negative effect on our financial condition and business if in excess of our insurance coverage. Additionally, lawsuits can be expensive to defend, whether or not they have merit, and the defense of these actions may divert the attention of our management and other resources that would otherwise be engaged in managing our business.

As a result of a number of factors, product liability insurance has become less available while the cost has increased significantly. We currently carry product liability insurance that our management believes is appropriate given the risks that we face. We will continually assess the cost and availability of insurance; however, there can be no guarantee that insurance coverage will be obtained or, if obtained, will be sufficient to fully cover product liabilities that may arise.

If any of our license agreements for intellectual property underlying Lymphoseek, our Manocept platform, or any other products or potential products are terminated, we may lose the right to develop or market that product.

We have licensed intellectual property, including patents and patent applications relating to the underlying intellectual property for Lymphoseek and our Manocept platform. We may also enter into other license agreements or acquire other product candidates. The potential success of our product development programs depend on our ability to maintain rights under these licenses, including our ability to achieve development or commercialization milestones contained in the licenses. Under certain circumstances, the licensors have the power to terminate their agreements with us if we fail to

meet our obligations under these licenses. We may not be able to meet our obligations under these licenses. If we default under any license agreement, we may lose our right to market and sell any products based on the licensed technology.

We may not have sufficient legal protection against infringement or loss of our intellectual property, and we may lose rights or protection related to our intellectual property if diligence requirements are not met, or at the expiry of underlying patents.

Our success depends, in part, on our ability to secure and maintain patent protection for our products and product candidates, to preserve our trade secrets, and to operate without infringing on the proprietary rights of third parties. While we seek to protect our proprietary positions by filing United States and foreign patent applications for our important inventions and improvements, domestic and foreign patent offices may not issue these patents. Third parties may challenge, invalidate, or circumvent our patents or patent applications in the future. Competitors, many of which have significantly more resources than we have and have made substantial investments in competing technologies, may apply for and obtain patents that will prevent, limit, or interfere with our ability to make, use, or sell our products either in the United States or abroad.

Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are or may be developing products. As the biotechnology and pharmaceutical industry expands and more patents are issued, the risk increases that we will be subject to claims that our products or product candidates, or their use, infringe the rights of others. In the United States, most patent applications are secret for a period of 18 months after filing, and in foreign countries, patent applications are secret for varying periods of time after filing. Publications of discoveries tend to significantly lag the actual discoveries and the filing of related patent applications. Third parties may have already filed applications for patents for products or processes that will make our products obsolete, limit our patents, invalidate our patent applications or create a risk of infringement claims.

Under recent changes to U.S. patent law, the U.S. has moved to a “first to file” system of patent approval, as opposed to the former “first to invent” system. As a consequence, delays in filing patent applications for new product candidates or discoveries could result in the loss of patentability if there is an intervening patent application with similar claims filed by a third party, even if we or our collaborators were the first to invent.

We or our suppliers may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our products, product candidates and/or technologies infringe their intellectual property rights or that the process of manufacturing our products or any of their respective component materials, or the component materials themselves, or the use of our products, product candidates or technologies, infringe their intellectual property rights. If one of these patents was found to cover our products, product candidates, technologies or their uses, or any of the underlying manufacturing processes or components, we could be required to pay damages and could be unable to commercialize our products or use our technologies or methods unless we are able to obtain a license to the patent or intellectual property right. A license may not be available to us in a timely manner or on acceptable terms, if at all. In addition, during litigation, a patent holder could obtain a preliminary injunction or other equitable remedy that could prohibit us from making, using or selling our products, technologies or methods.

Our currently held and licensed patents expire over the next one to sixteen years. Expiration of the patents underlying our technology, in the absence of extensions or other trade secret or intellectual property protection, may have a material and adverse effect on us.

In addition, it may be necessary for us to enforce patents under which we have rights, or to determine the scope, validity and unenforceability of other parties’ proprietary rights, which may affect our rights. There can be no assurance that our patents would be held valid by a court or administrative body or that an alleged infringer would be

found to be infringing. The uncertainty resulting from the mere institution and continuation of any patent related litigation or interference proceeding could have a material and adverse effect on us.

We typically require our employees, consultants, advisers and suppliers to execute confidentiality and assignment of invention agreements in connection with their employment, consulting, advisory, or supply relationships with us. They may breach these agreements and we may not obtain an adequate remedy for breach. Further, third parties may gain unauthorized access to our trade secrets or independently develop or acquire the same or equivalent information.

Agencies of the United States government conducted some of the research activities that led to the development of antibody technology that some of our proposed antibody-based surgical cancer detection products use. When the United States government participates in research activities, it retains rights that include the right to use the technology for governmental purposes under a royalty-free license, as well as rights to use and disclose technical data that could preclude us from asserting trade secret rights in that data and software.

We and our collaborators, including AstraZeneca, Alseres, and the University of California Board of Regents, may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our product candidates and products, when and if we have any, in every jurisdiction would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we or our licensors have not obtained patent protection to develop their own products. These products may compete with our products, when and if we have any, and may not be covered by any of our or our licensors' patent claims or other intellectual property rights.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biotechnology and/or pharmaceuticals, which could make it difficult for us to stop the infringement of our patents. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

The intellectual property protection for our product candidates depends on third parties.

With respect to Lymphoseek and Manocept, NAV4694 and NAV5001, we have exclusively licensed certain issued patents and pending patent applications covering the respective technologies underlying these product candidates and their commercialization and use and we have licensed certain issued patents and pending patent applications directed to product compositions and chemical modifications used in product candidates for commercialization, and the use and the manufacturing thereof.

The patents and pending patent applications underlying our licenses do not cover all potential product candidates, modifications and uses. In the case of patents and patent applications licensed from UCSD, we did not have any control over the filing of the patents and patent applications before the effective date of the Lymphoseek license, and have had limited control over the filing and prosecution of these patents and patent applications after the effective date of the Lymphoseek license. In the case of patents and patent applications licensed from AstraZeneca, we have limited control over the filing, prosecution or enforcement of these patents or patent applications. We also have limited rights to enforce patents and patent applications licensed from AstraZeneca and Alseres. We cannot be certain that such prosecution efforts have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents. We also cannot be assured that our licensors or their respective licensing partners will agree to enforce any such patent rights at our request or devote sufficient efforts to attain a desirable result. Any failure by our licensors or any of their respective licensing partners to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operation.

We may become involved in disputes with UCSD, AstraZeneca, Alseres or potential future collaborators over intellectual property ownership, and publications by our research collaborators and scientific advisors could impair our ability to obtain patent protection or protect our proprietary information, which, in either case, could have a significant effect on our business.

Inventions discovered under research, material transfer or other such collaborative agreements may become jointly owned by us and the other party to such agreements in some cases and the exclusive property of either party in other cases. Under some circumstances, it may be difficult to determine who owns a particular invention, or whether it is jointly owned, and disputes could arise regarding ownership of those inventions. These disputes could be costly and

time consuming and an unfavorable outcome could have a significant adverse effect on our business if we were not able to protect our license rights to these inventions. In addition, our research collaborators and scientific advisors generally have contractual rights to publish our data and other proprietary information, subject to our prior review. Publications by our research collaborators and scientific advisors containing such information, either with our permission or in contravention of the terms of their agreements with us, may impair our ability to obtain patent protection or protect our proprietary information, which could significantly harm our business.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and business partners, and personally identifiable information of employees and clinical trial subjects, in our data centers and on our networks. The secure maintenance and transmission of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure

may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, and regulatory penalties, disrupt our operations, and damage our reputation, which could adversely affect our business, revenues and competitive position.

Failure to comply with domestic and international privacy and security laws can result in the imposition of significant civil and criminal penalties. The costs of compliance with these laws, including protecting electronically stored information from cyber-attacks, and potential liability associated with failure to do so could adversely affect our business, financial condition and results of operations. We are subject to various domestic and international privacy and security regulations, including but not limited to The Health Insurance Portability and Accountability Act of 1996 (HIPAA). HIPAA mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. In addition, many states have enacted comparable laws addressing the privacy and security of health information, some of which are more stringent than HIPAA.

We do not currently carry cyber risk insurance.

We are subject to domestic and foreign anticorruption laws, the violation of which could expose us to liability, and cause our business and reputation to suffer.

We are subject to the U.S. Foreign Corrupt Practices Act and similar anti-corruption laws in other jurisdictions. These laws generally prohibit companies and their intermediaries from engaging in bribery or making other prohibited payments to government officials for the purpose of obtaining or retaining business, and some have record keeping requirements. The failure to comply with these laws could result in substantial criminal and/or monetary penalties. We operate in jurisdictions that have experienced corruption, bribery, pay-offs and other similar practices from time-to-time and, in certain circumstances, such practices may be local custom. We have implemented internal control policies and procedures that mandate compliance with these anti-corruption laws. However, we cannot be certain that these policies and procedures will protect us against liability. There can be no assurance that our employees or other agents will not engage in such conduct for which we might be held responsible. If our employees or agents are found to have engaged in such practices, we could suffer severe criminal or civil penalties and other consequences that could have a material adverse effect on our business, financial position, results of operations and/or cash flow, and the market value of our common stock could decline.

Our international operations expose us to economic, legal, regulatory and currency risks.

Our operations extend to countries outside the United States, and are subject to the risks inherent in conducting business globally and under the laws, regulations, and customs of various jurisdictions. These risks include, but are not limited to: (i) compliance with a variety of national and local laws of countries in which we do business, including but not limited to restrictions on the import and export of certain intermediates, drugs, and technologies, (ii) compliance with a variety of US laws including, but not limited to, the Iran Threat Reduction and Syria Human Rights Act of 2012; and rules relating to the use of certain “conflict minerals” under Section 1502 of the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) changes in laws, regulations, and practices affecting the pharmaceutical industry and the health care system, including but not limited to imports, exports, manufacturing, quality, cost, pricing, reimbursement, approval, inspection, and delivery of health care, (iv) fluctuations in exchange rates for transactions conducted in currencies other than the functional currency, (v) adverse changes in the economies in which we or our partners and suppliers operate as a result of a slowdown in overall growth, a change in government or economic policies, or financial, political, or social change or instability in such countries that affects the markets in

which we operate, particularly emerging markets, (vi) differing local product preferences and product requirements, (vii) changes in employment laws, wage increases, or rising inflation in the countries in which we or our partners and suppliers operate, (viii) supply disruptions, and increases in energy and transportation costs, (ix) natural disasters, including droughts, floods, and earthquakes in the countries in which we operate, (x) local disturbances, terrorist attacks, riots, social disruption, or regional hostilities in the countries in which we or our partners and suppliers operate and (xi) government uncertainty, including as a result of new or changed laws and regulations. We also face the risk that some of our competitors have more experience with operations in such countries or with international operations generally and may be able to manage unexpected crises more easily. Furthermore, whether due to language, cultural or other differences, public and other statements that we make may be misinterpreted, misconstrued, or taken out of context in different jurisdictions. Moreover, the internal political stability of, or the relationship between, any country or countries where we conduct business operations may deteriorate. Changes in a country’s political stability or the state of relations between any such countries are difficult to predict and could adversely affect our operations, profitability and/or adversely impact our ability to do business there. The occurrence

of any of the above risks could have a material adverse effect on our business, financial position, results of operations and/or cash flow, and could cause the market value of our common stock to decline.

We may have difficulty raising additional capital, which could deprive us of necessary resources to pursue our business plans.

We expect to devote significant capital resources to fund research and development, to maintain existing and secure new manufacturing resources, and to acquire new product candidates. In order to support the initiatives envisioned in our business plan, we will need to raise additional funds through the sale of assets, public or private debt or equity financing, collaborative relationships or other arrangements. Our ability to raise additional financing depends on many factors beyond our control, including the state of capital markets, the market price of our common stock and the development or prospects for development of competitive technology by others. Sufficient additional financing may not be available to us or may be available only on terms that would result in further dilution to the current owners of our common stock.

Our future expenditures on our programs are subject to many uncertainties, including whether our product candidates will be developed or commercialized with a partner or independently. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the costs of seeking regulatory approval for our product candidates, including any nonclinical testing or bioequivalence or clinical studies, process development, scale-up and other manufacturing and stability activities, or other work required to achieve such approval, as well as the timing of such activities and approval;
- the extent to which we invest in or acquire new technologies, product candidates, products or businesses and the development requirements with respect to any acquired programs;
- the scope, prioritization and number of development and/or commercialization programs we pursue and the rate of progress and costs with respect to such programs;
- the costs related to developing, acquiring and/or contracting for sales, marketing and distribution capabilities and regulatory compliance capabilities, if we commercialize any of our product candidates for which we obtain regulatory approval without a partner;
- the timing and terms of any collaborative, licensing and other strategic arrangements that we may establish;
- the extent to which we will need to expand our workforce to pursue our business plan, and the costs involved in recruiting, training and incentivizing new employees;
- the effect of competing technological and market developments; and
- the cost involved in establishing, enforcing or defending patent claims and other intellectual property rights.

We believe that we have access to sufficient financial resources with which to fund our operations and those of our subsidiaries for the foreseeable future. However, certain events or actions may shorten the period through which our current operating funds will sustain us, including, without limitation, if we decide to grow our organization in pursuit of development or commercialization activities for our current or newly acquired or developed product candidates, if we incur unexpected expenses, or if Lymphoseek does not generate our expected levels of sales and cash flow. We may also acquire new technologies, product candidates and/or products and the cost to acquire, develop and/or commercialize such new technologies, product candidates and/or products may shorten the period through which our current operating funds will sustain us. If our current funds become inadequate, we may not be able to obtain sufficient additional funding for such activities, on satisfactory terms, if at all. If we are unsuccessful in raising additional capital, or the terms of raising such capital are unacceptable, we may have to modify our business plan and/or significantly curtail our planned development activities, acquisition of new product candidates and other operations.

There may be future sales or other dilution of our equity, which may adversely affect the market price of shares of our common stock.

Our existing and future preferred stock, warrants or other securities convertible into or exchangeable for our common stock may contain adjustment provisions that could increase the number of shares issuable upon exercise, conversion or exchange, as the case may be, and decrease the exercise, conversion or exchange price. The market price of our shares of common stock or preferred stock could decline as a result of sales of a large number of shares of our common stock or preferred stock or similar securities in the market, the triggering of any such adjustment provisions or the perception that such sales could occur in the future.

Our indebtedness imposes significant restrictions on us, and a default could materially adversely affect our operations and financial condition.

All of our material assets, except our intellectual property, have been pledged as collateral for our borrowings under the Loan and Security Agreement (the Oxford Loan Agreement) with Oxford Finance, LLC (Oxford).

In addition to the security interest in our assets, the Oxford Loan Agreement carries covenants that impose significant requirements on us, including, among others, requirements that:

- we pay all principal, interest and other charges on the outstanding balance of the borrowed funds when due;
- we keep reserved out of our authorized shares of common stock sufficient shares to satisfy our obligation to issue shares upon the exercise of the warrants issued in connection with the Oxford Loan Agreement;
- we provide certain financial information and reports to Oxford in a timely manner; and
- we indemnify Oxford against certain liabilities.

Additionally, with certain exceptions, the Oxford Loan Agreement prohibits us from:

- making any material dispositions of our assets, except for permitted dispositions;
- making any changes in our business, management, ownership, or business locations;
- entering into any merger or consolidation without Oxford's consent;
- acquiring or making investments in any other person other than permitted investments;
- incurring any indebtedness, other than permitted indebtedness;
- granting or permitting liens against our assets, other than permitted liens; declaring or paying any dividends or making any other distributions; or
- entering into any material transaction with any affiliate, other than in the ordinary course of business;.

Our ability to comply with these provisions may be affected by changes in our business condition or results of our operations, or other events beyond our control. The breach of any of these covenants would result in a default under the Loan Agreement, permitting Oxford to increase the interest rate on the outstanding principal amount, accelerate the maturity of the debt and to sell the assets securing it. Such actions by Oxford could materially adversely affect our operations, results of operations and financial condition, including causing us to substantially curtail our product development activities.

In addition, our Loan Agreement with Platinum (the Platinum Loan Agreement) carries covenants typical for commercial loan agreements, and similar to those contained in the Oxford Loan Agreement, that impose significant requirements on us. Our ability to comply with these provisions may be affected by changes in our business condition or results of our operations, or other events beyond our control. The breach of any of these covenants would result in a default under the Platinum Loan Agreement, permitting Platinum to terminate our ability to obtain additional draws under the Platinum Loan Agreement and accelerate the maturity of the debt. Such actions by Platinum could materially adversely affect our operations, results of operations and financial condition, including causing us to substantially curtail our product development activities.

Platinum may exercise its conversion right, and that could dilute your ownership and the net tangible book value per share of our common stock.

Platinum may exercise the right to convert all or any portion of the unpaid principal or unpaid interest (the Conversion Amount) accrued on any draw advanced by Platinum under the Platinum Loan Agreement on or after June 25, 2013, beginning on a date that is two years from the date on which such draw was advanced, and thereafter at any time while any portion of such draw is outstanding, into shares of Navidea's common stock. Platinum may also exercise a

conversion right on the amount of any mandatory repayment due following the Company achieving $2,000,000 in cumulative revenues from sales or licensing of Lymphoseek. The conversion option applies to the Conversion Amount if the Company is prohibited from making such repayment under the terms of the Subordination Agreement between Platinum, Oxford and the Company. If Platinum exercises any or all of its conversion rights, the percentage ownership of our current stockholders will be reduced. The issuance of additional common stock may also result in dilution in the net tangible book value per share of our common stock. The $3.2 million outstanding under the Platinum credit facility as of December 31, 2014 is not subject to the conversion option, however the $3.0 million advanced to date in 2015 is subject to the conversion option.

Shares of common stock are equity securities and are subordinate to our existing and future indebtedness and preferred stock.

Shares of our common stock are common equity interests. This means that our common stock ranks junior to our outstanding shares of Series B Preferred Stock and any preferred stock that we may issue in the future, to our indebtedness and to all

creditor claims and other non-equity claims against us and our assets available to satisfy claims on us, including claims in a bankruptcy or similar proceeding. Our existing indebtedness and preferred stock restrict payment of dividends on our common stock, and future indebtedness and preferred stock may restrict payments of dividends on our common stock.

Additionally, unlike indebtedness, where principal and interest customarily are payable on specified due dates, in the case of our common stock, (i) dividends are payable only when and if declared by our Board of Directors or a duly authorized committee of our Board of Directors, and (ii) as a corporation, we are restricted to making dividend payments and redemption payments out of legally available assets. We have never paid a dividend on our common stock and have no current intention to pay dividends in the future. Furthermore, our common stock places no restrictions on our business or operations or on our ability to incur indebtedness or engage in any transactions, subject only to the voting rights available to shareholders generally.

The continuing contentious federal budget negotiations may have an impact on our business and financial condition in ways that we currently cannot predict, and may further limit our ability to raise additional funds.

The continuing federal budget disputes not only may adversely affect financial markets, but could also delay or reduce research grant funding and adversely affect operations of government agencies that regulate us, including the FDA, potentially causing delays in obtaining key regulatory approvals.

Our failure to maintain continued compliance with the listing requirements of the NYSE MKT exchange could result in the delisting of our common stock.

Our common stock has been listed on the NYSE MKT since February 2011. The rules of NYSE MKT provide that shares be delisted from trading in the event the financial condition and/or operating results of the Company appear to be unsatisfactory, the extent of public distribution or the aggregate market value of the common stock has become so reduced as to make further dealings on the NYSE MKT inadvisable, the Company has sold or otherwise disposed of its principal operating assets, or has ceased to be an operating company, or the Company has failed to comply with its listing agreements with the Exchange. For example, the NYSE MKT may consider suspending trading in, or removing the listing of, securities of an issuer that has stockholders’ equity of less than $6.0 million if such issuer has sustained losses from continuing operations and/or net losses in its five most recent fiscal years. As of December 31, 2014, the Company had a stockholders’ deficit of approximately $29.8 million. Even if an issuer has a stockholders’ deficit, the NYSE MKT will not normally consider removing from the list securities of an issuer that fails to meet these requirements if the issuer has (1) total value of market capitalization of at least $50,000,000; or total assets and revenue of $50,000,000 each in its last fiscal year, or in two of its last three fiscal years; and (2) the issuer has at least 1,100,000 shares publicly held, a market value of publicly held shares of at least $15,000,000 and 400 round lot shareholders. Based on the number of outstanding shares of our common stock, recent trading price of that stock, and number of round lot holders, we believe that we meet these exception criteria and that our common stock will not be delisted as a result of our failure to meet the minimum stockholders' equity requirement for continued listing. We cannot assure you that the Company will continue to meet these and other requirements necessary to maintain the listing of our common stock on the NYSE MKT. For example, we may determine to grow our organization or product pipeline or pursue development or other activities at levels or on timelines that reduces our stockholders’ equity below the level required to maintain compliance with NYSE MKT continued listing standards.

The delisting of our common stock from the NYSE MKT likely would reduce the trading volume and liquidity in our common stock and may lead to decreases in the trading price of our common stock. The delisting of our common stock may also materially impair our stockholders’ ability to buy and sell shares of our common stock. In addition, the delisting of our common stock could significantly impair our ability to raise capital, which is critical to the execution of our current business strategy.

The price of our common stock has been highly volatile due to several factors that will continue to affect the price of our stock.

Our common stock traded as low as $0.97 per share and as high as $2.12 per share during the 12-month period ended February 28, 2015. The market price of our common stock has been and is expected to continue to be highly volatile. Factors, including announcements of technological innovations by us or other companies, regulatory matters, new or existing products or procedures, concerns about our financial position, operating results, litigation, government regulation, developments or disputes relating to agreements, patents or proprietary rights, may have a significant impact on the market price of our stock. In addition, potential dilutive effects of future sales of shares of common stock by the Company and by stockholders, and subsequent sale of common stock by the holders of warrants and options could have an adverse effect on the market price of our shares.

Some additional factors which could lead to the volatility of our common stock include:

- price and volume fluctuations in the stock market at large or of companies in our industry which do not relate to our operating performance;
- changes in securities analysts' estimates of our financial performance or deviations in our business and the trading price of our common stock from the estimates of securities analysts;
- FDA or international regulatory actions and regulatory developments in the U.S. and foreign countries;
- financing arrangements we may enter that require the issuance of a significant number of shares in relation to the number of shares currently outstanding;
- public concern as to the safety of products that we or others develop;
- activities of short sellers in our stock; and
- fluctuations in market demand for and supply of our products.

The realization of any of the foregoing could have a dramatic and adverse impact on the market price of our common stock. In addition, class action litigation has often been instituted against companies whose securities have experienced substantial decline in market price. Moreover, regulatory entities often undertake investigations of investor transactions in securities that experience volatility following an announcement of a significant event or condition. Any such litigation brought against us or any such investigation involving our investors could result in substantial costs and a diversion of management's attention and resources, which could hurt our business, operating results and financial condition.

An investor's ability to trade our common stock may be limited by trading volume.

During the 12-month period beginning on March 1, 2014 and ending on February 28, 2015, the average daily trading volume for our common stock on the NYSE MKT was approximately 920,000 shares. We cannot assure you that this trading volume will be consistently maintained in the future.

The market price of our common stock may be adversely affected by market conditions affecting the stock markets in general, including price and trading fluctuations on the NYSE MKT exchange.

The market price of our common stock may be adversely affected by market conditions affecting the stock markets in general, including price and trading fluctuations on the NYSE MKT. These conditions may result in (i) volatility in the level of, and fluctuations in, the market prices of stocks generally and, in turn, our shares of common stock, and (ii) sales of substantial amounts of our common stock in the market, in each case that could be unrelated or disproportionate to changes in our operating performance.

Because we do not expect to pay dividends on our common stock in the foreseeable future, stockholders will only benefit from owning common stock if it appreciates.

We have paid no cash dividends on any of our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, with respect to our common stock, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our Board of Directors. Furthermore, we are subject to various laws and regulations that may restrict our ability to pay dividends and we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Due to our intent to retain any future earnings rather than pay cash dividends on our common stock and applicable laws, regulations and contractual obligations that may restrict our ability to pay dividends on our common stock, the success of your investment in our common stock will likely depend entirely upon

any future appreciation and there is no guarantee that our common stock will appreciate in value.

We may have difficulty attracting and retaining qualified personnel and our business may suffer if we do not.

Our business has experienced a number of successes and faced several challenges in recent years that have resulted in several significant changes in our strategy and business plan, including the shifting of resources to support our current development initiatives. Our management will need to remain flexible to support our business model over the next few years. However, losing members of the Navidea management team could have an adverse effect on our operations. Our success depends on our ability to attract and retain technical and management personnel with expertise and experience in the pharmaceutical industry, and the acquisition of additional product candidates may require us to acquire additional highly qualified personnel. The competition for qualified personnel in the biotechnology industry is intense and we may not be successful in hiring or retaining

the requisite personnel. If we are unable to attract and retain qualified technical and management personnel, we will suffer diminished chances of future success.

We may be adversely affected if our controls over external financial reporting fail or are circumvented.

We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes Oxley Act of 2002 to report annually on our internal control over financial reporting. If it were to be determined that our internal control over financial reporting is not effective, such shortcoming could have an adverse effect on our business and financial results and the price of our common stock could be negatively affected. This reporting requirement could also make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. Any system of internal controls, however well designed and operated, is based in part on certain assumptions and can provide only reasonable, not absolute, assurances that the objectives of the system are met. Any failure or circumvention of the controls and procedures or failure to comply with regulation concerning control and procedures could have a material effect on our business, results of operation and financial condition. Any of these events could result in an adverse reaction in the financial marketplace due to a loss of investor confidence in the reliability of our financial statements, which ultimately could negatively affect the market price of our shares, increase the volatility of our stock price and adversely affect our ability to raise additional funding. The effect of these events could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors and our Board committees and as executive officers.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently lease approximately 25,000 square feet of office space at 5600 Blazer Parkway, Dublin, Ohio, as our principal offices. The current lease term expires in October 2022, at a monthly base rent of approximately $24,000 during 2015. We must also pay a pro-rata portion of the operating expenses and real estate taxes of the building. We also lease approximately 6,000 square feet of office space at 10 New England Business Center Drive, Andover, Massachusetts, primarily for our business development and commercialization departments. The current lease term expires in March 2015, at a monthly base rent of approximately $10,000 during 2015. We must also pay a pro-rata portion of the electricity cost of the building. We do not intend to renew the lease for the Andover facility. We believe both facilities are in good condition.

Item 3. Legal Proceedings

None.

Item 4. Mine Safety Disclosure

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock trades on the NYSE MKT exchange under the trading symbol NAVB. Prior to our name change from Neoprobe Corporation to Navidea Biopharmaceuticals, Inc. on January 5, 2012, our common stock was traded on the NYSE MKT under the trading symbol NEOP. The prices set forth below reflect the quarterly high and low sales prices for shares of our common stock during the last two fiscal years.

	High	Low
Fiscal Year 2014:		
First Quarter	$2.12	$1.62
Second Quarter	1.99	1.29
Third Quarter	1.53	1.20
Fourth Quarter	2.02	0.97
Fiscal Year 2013:		
First Quarter	$3.59	$2.42
Second Quarter	2.80	2.26
Third Quarter	3.31	2.57
Fourth Quarter	2.71	1.11

As of March 2, 2015, we had 679 holders of common stock of record.

We have not paid any dividends on our common stock and do not anticipate paying cash dividends on our common stock in the foreseeable future. We intend to retain any earnings to finance the growth of our business. We cannot assure you that we will ever pay cash dividends. Whether we pay cash dividends in the future will be at the discretion of our Board of Directors and will depend upon our financial condition, results of operations, capital requirements and any other factors that the Board of Directors decides are relevant. See Management's Discussion and Analysis of Financial Condition and Results of Operations.

During the three-month period ended December 31, 2014, we issued 67,710 shares of our common stock to our Board of Directors as payment of their third quarter 2014 retainers. The issuance of these securities was exempt from registration under Section 4(2) of the Securities Act and Regulation D promulgated thereunder.

Also during the three-month period ended December 31, 2014, Crede CG III, Ltd. (Crede) exchanged their Series JJ warrant for 3,843,223 shares of our common stock in accordance with the terms of the Series JJ warrant. The issuance of these securities was exempt from registration under Section 4(2) of the Securities Act and Regulation D promulgated thereunder.

There were no repurchases of our common stock during the three-month period ended December 31, 2014.

Stock Performance Graph

The following graph compares the cumulative total return on a $100 investment in each of the common stock of the Company, the Russell 3000, and the NASDAQ Biotechnology Index for the period from December 31, 2009 through December 31, 2014. This graph assumes an investment in the Company's common stock and the indices of $100 on December 31, 2009 and that all dividends were reinvested.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Navidea Biopharmaceuticals, the Russell 3000 Index, and the NASDAQ Biotechnology Index
*$100 invested on 12/31/2009 in stock or index, including reinvestment of dividends.

	Cumulative Total Return as of December 31,					
	2009	2010	2011	2012	2013	2014
Navidea Biopharmaceuticals	100.00	168.85	214.75	231.97	169.67	154.92
Russell 3000	100.00	114.75	113.70	129.59	169.69	187.42
NASDAQ Biotechnology	100.00	115.01	128.59	169.61	280.89	376.68

Item 6. Selected Financial Data

The following summary financial data are derived from our consolidated financial statements that have been audited by our independent registered public accounting firm. These data are qualified in their entirety by, and should be read in conjunction with, our Consolidated Financial Statements and Notes thereto included elsewhere in this Form 10-K as well as Management's Discussion and Analysis of Financial Condition and Results of Operations. Summary financial data for 2012 and prior periods reflect the disposition of our gamma detection device business in August 2011 and the reclassification of certain related items to discontinued operations.

(Amounts in thousands, except per share data)	Years Ended December 31,				
	2014	2013	2012	2011	2010
Statement of Operations Data:					
Revenue	$6,275	$1,131	$79	$598	$617
Cost of goods sold	1,586	333	—	—	—
Research and development expenses	16,780	23,710	16,890	15,154	8,941
Selling, general and administrative expenses	15,542	15,526	11,178	9,548	4,353
Loss from operations	(27,633)	(38,438)	(27,989)	(24,104)	(12,677)
Other expenses, net	(8,094)	(4,261)	(1,168)	(943)	(43,567)
Benefit from income taxes	—	—	—	7,880	2,135
Loss from continuing operations	(35,727)	(42,699)	(29,157)	(17,167)	(54,109)
Discontinued operations, net of tax effect	—	—	—	22,780	4,144
Net (loss) income	(35,727)	(42,699)	(29,157)	5,613	(49,965)
Preferred stock dividends	—	—	(43)	(100)	(8,207)
(Loss) income attributable to common stockholders	$(35,727)	$(42,699)	$(29,200)	$5,513	$(58,172)
(Loss) income per common share (basic and diluted):					
Continuing operations	$(0.24)	$(0.35)	$(0.29)	$(0.17)	$(0.77)
Discontinued operations	$—	$—	$—	$0.23	$0.05
(Loss) income attributable to common stockholders	$(0.24)	$(0.35)	$(0.29)	$0.06	$(0.72)
Shares used in computing (loss) income per common share: (1)					
Basic and diluted	148,748	121,809	99,060	90,509	80,726

	As of December 31,				
	2014	2013	2012	2011	2010
Balance Sheet Data:					
Total assets	$11,920	$40,317	$11,972	$31,194	$10,863
Long-term obligations	32,629	33,035	7,187	6,714	2,787
Accumulated deficit	(352,984)	(317,257)	(274,558)	(245,357)	(250,870)

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(1) Basic earnings (loss) per share is calculated by dividing net income (loss) attributable to common stockholders by the weighted-average number of common shares and, except for periods with a loss from operations, participating securities outstanding during the period. Diluted earnings (loss) per share reflects additional common shares that would have been outstanding if dilutive potential common shares had been issued. Potential common shares that may be issued by the Company include convertible securities, options and warrants.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion should be read together with our Consolidated Financial Statements and the Notes related to those statements, as well as the other financial information included in this Form 10-K. Some of our discussion is forward-looking and involves risks and uncertainties. For information regarding risk factors that could have a material adverse effect on our business, refer to Item 1A of this Form 10-K, Risk Factors.

The Company

Navidea Biopharmaceuticals, Inc., a Delaware corporation, is a precision medicine company focused on the development and commercialization of precision diagnostics, therapeutics and radiopharmaceutical agents. Navidea is developing multiple precision-targeted products based on the Manocept™ platform to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making, targeted treatment and, ultimately, patient care.

Navidea's Manocept platform is predicated on the ability of the chemical backbone of the tilmanocept molecule to specifically target the CD206 mannose receptor expressed on macrophages. The Manocept platform serves as the molecular backbone of Lymphoseek® (technetium Tc 99m tilmanocept) injection, the first product developed by Navidea based on the platform. Lymphoseek 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 the U.S. Food and Drug Administration (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 has also received European approval in imaging and intraoperative detection of sentinel lymph nodes in patients with melanoma, breast cancer or localized squamous cell carcinoma of the oral cavity.

Building on the success of Lymphoseek, the flexible and versatile 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, including single photon emission computed tomography (SPECT), positron emission tomography (PET), intra-operative and/or optical-fluorescence detection in a variety of disease states.

Recent preclinical data being developed by the Company using tilmanocept linked to various therapeutic agents also suggest 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, cardiovascular, and central nervous system diseases. Thus, in January 2015, the Company formed a new subsidiary, Macrophage Therapeutics, Inc., to further explore therapeutic applications for the Manocept platform.

In addition, over the last year, the company's Board of Directors made the decision to reduce our support while seeking to partner or out-license two of our development programs:

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NAV4694 is a fluorine-18 (F-18) radiolabeled PET imaging agent being developed as an aid in the diagnosis of patients with signs or symptoms of Alzheimer's disease (AD) and mild cognitive impairment (MCI). NAV4694 is in Phase 3 clinical development.

- NAV5001 is an iodine-123 (I-123) radiolabeled SPECT imaging agent being developed as an aid in the diagnosis of Parkinson's disease (PD) and other movement disorders, with potential use as a diagnostic aid in dementia. NAV5001 is in Phase 3 clinical development.

The company is in discussions with potential parties interested in sublicensing and/or assuming financial responsibility for the ongoing development of these two neuro tracer compounds and is currently evaluating term sheets.

Other than Lymphoseek, none of the Company's drug product candidates have been approved for sale in any market.

Executive Summary

Our primary development efforts over the last few years have been focused on our now-approved Lymphoseek product, as well as more recently on our other pipeline programs, including NAV4694, NAV5001, and our Manocept platform. In May 2014, the Board of Directors made the decision to refocus the Company's resources to better align the funding of our pipeline programs with the expected growth in Lymphoseek revenue. This realignment primarily involves reducing our near-term support for our two neurological product candidates, NAV4694 and NAV5001, as we seek to partner or divest these two programs. In addition, we are looking for ways to move Macrophage Therapeutics forward with a combination of grant funding and seed financing obtained from outside investors while retaining the vast majority of ownership benefits for existing Navidea shareholders. The level of future expenditures on our development programs will depend on the scope, requirements and timing of our strategic development initiatives in different territories around the world.

Our efforts in 2014 and to date in 2015 have resulted in the following milestone achievements:

Corporate

- Appointed Rick Gonzalez as CEO, bringing more than 20 years of experience in the pharmaceutical industry with notable global commercial expertise with oncology and radiotherapy products.
- Added Tom Klima as Chief Commercial Officer to lead commercial strategy design and execution and Michael Tomblyn, M.D. as Executive Medical Director to develop, in collaboration with the medical community and potentially other corporate partners, the application of Lymphoseek across multiple tumor types.

Lymphoseek

- Experienced encouraging sales metrics as measured by increasing number of procedures, account growth and re-order rates.
- Expanded indications in the U.S. for sentinel lymph node biopsy (SLNB) in melanoma, head and neck, and breast cancers as well as for lymphatic mapping in all solid tumors.
- Attained European approval of a Lymphoseek Marketing Authorization Application for SLNB in melanoma, breast and certain head and neck cancers.
- Executed a sublicense agreement with SpePharm AG, an affiliate of Norgine BV, covering distribution of Lymphoseek in the European Union. In connection with the agreement, the Company is entitled to receive an upfront payment of $2 million, additional commercial milestone payments up to $5 million, and royalties on European net sales.
- Received orphan drug designation for head and neck cancers, resulting in a $1.1 million refund of PDUFA fees associated with the head and neck cancer sNDA.
- Signed development and commercialization agreements in China, Taiwan and Hong Kong.
- Published the Lymphoseek Phase 3 head and neck cancer clinical trial results and results of a Lymphoseek comparative study in breast cancer in peer-reviewed journals.
- Supported Lymphoseek lifecycle management efforts with Fast Track NIH Small Business Innovation Research grants and investigator-initiated studies in several cancer types.

Manocept Platform

- Formed Macrophage Therapeutics, Inc. as a subsidiary to explore therapeutic applications of Manocept platform compounds.
- Completed agreement for up to $2.5 million of funding for Macrophage Therapeutics, Inc. in exchange for convertible preferred stock and warrants representing a 1% interest in the subsidiary on a fully converted and exercised basis.
- Assembled an expert Scientific Advisory Board to serve as a strategic resource to develop therapeutic applications for the Manocept platform.
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Completed the initial cohort of a physician-initiated study in Kaposi's Sarcoma patients at the University of California, San Francisco.

- Formed R-NAV joint venture with Essex Woodlands' Rheumco to explore diagnostic and therapeutic applications in rheumatoid arthritis and canine osteoarthritis.

Neurodegenerative Products

- Evaluating out-licensing/divestiture proposals for the Phase 3 NAV4694 and NAV5001 assets.

Our Outlook

Following the U.S. approval of Lymphoseek in March 2013, the Company undertook the initial stages of product launch in the U.S. with our commercialization partner, Cardinal Health, in May 2013. We began reporting revenue from Lymphoseek beginning in the second quarter of 2013, though revenue for that quarter consisted primarily of inventory stocking of Cardinal Health's nuclear pharmacies. We plan to retain additional direct sales personnel as part of our effort to accelerate Lymphoseek revenue growth in 2015 and beyond. Our strategy for increasing Lymphoseek revenue also includes focusing on areas where the concentration of diagnosis occurs, increasing the number of doses per account, and continuing to evolve the brand. Based on Lymphoseek revenue to date and anticipated growth, Navidea expects Lymphoseek revenue for 2015 to be between $10 million and $12 million, representing total brand revenue to end customers of our distributor in excess of $20 million.

Our operating expenses in recent years have been focused primarily on support of Lymphoseek, our Manocept platform, and NAV4694 and NAV5001 product development. We incurred approximately $16.8 million, $23.7 million and $16.9 million in total on research and development activities during the years ended December 31, 2014, 2013 and 2012, respectively. Of the total amounts we have spent on research and development during those periods, excluding costs related to our internal research and development headcount and our general and administrative staff which we do not currently allocate among the various development programs that we have underway, we incurred out-of-pocket charges by program as follows:

Development Program	2014	2013	2012
Lymphoseek	$995,511	$4,702,829	$5,632,183
Manocept platform	503,587	503,338	—
NAV4694	6,788,286	7,812,602	3,339,592
NAV5001	1,441,442	2,602,461	2,159,483

We expect to continue the advancement of our efforts with Lymphoseek and our Manocept platform during 2015, however, we expect the cost of these advances to be more than offset by reductions in development costs of NAV4694 and NAV5001, and as a result, we expect our total research and development expenses for 2015 to decrease significantly from 2014.

Lymphoseek was approved and indicated for use in lymphatic mapping in patients with breast cancer and melanoma by the FDA in March 2013, with expanded use of Lymphoseek indicated for guiding sentinel lymph node biopsy in head and neck cancer patients with squamous cell carcinoma of the oral cavity approval in June 2014, and for lymphatic mapping in solid tumors and sentinel lymph node detection for breast cancer and melanoma as well as with or without scintigraphic imaging, known as lymphoscintigraphy, in October 2014. Lymphoseek was also approved by the EMA for use in imaging and intraoperative detection of sentinel lymph nodes draining a primary tumor in adult patients with breast cancer, melanoma, or localized squamous cell carcinoma of the oral cavity in the EU in November 2014.

Although our marketing partners will bear much of the direct marketing, sales and distribution costs related to the sale of Lymphoseek, we expect to incur ongoing costs to support product marketing efforts, to target surgical oncologists at the core of the oncology treatment team, as well as medical education-related and market outreach activities associated with Lymphoseek commercialization. Additionally, we anticipate that we will incur costs related to supporting the other product, regulatory, manufacturing and commercial activities related to the potential marketing registration and sale of Lymphoseek in other markets. We also expect to incur costs related to ongoing clinical development efforts to support the use of Lymphoseek in additional cancer types. We cannot assure you that Lymphoseek will achieve regulatory approval in any other market outside the U.S. or EU, or if approved in those markets, that it will achieve market acceptance in the U.S., EU or any other market.

We are currently evaluating existing and emerging data on the potential use of Manocept-related agents in the diagnosis and disease-staging of disorders in which macrophages are involved, such as KS, RA, vulnerable plaque/atherosclerosis, TB and other disease states, to define areas of focus, development pathways and partnering options to capitalize on the Manocept platform. In the near-term, our more active development efforts with respect to the Manocept platform will likely be limited to such evaluations. We will also be evaluating potential funding and other resources required for continued development, regulatory approval and commercialization of any Manocept platform product candidates that we identify for further development, and potential options for advancing development. We cannot assure you that further evaluation or development will be successful, that any Manocept platform product candidate will ultimately achieve regulatory approval, or if approved, the extent to which it will achieve market acceptance.

On March 12, 2015, the Company initiated a reduction in force that will include seven staff members and three executives. The three executives will continue as employees during transition periods of varying lengths, depending upon the nature and extent of responsibilities to be transitioned or wound down. As of the filing date of this document, the specific terms of the executive

transition and separation were still being determined, and therefore the impact to our first quarter 2015 financial statements is not yet known. We expect the financial impact to be material, but anticipate that the initial cost will be offset with savings in compensation expense in the longer term.

Results of Operations

Years Ended December 31, 2014 and 2013

Net Sales and Margins. Net sales of Lymphoseek were $4.2 million during 2014, compared to $614,000 during 2013. The increase was primarily due to sales starting in late April of 2013, coupled with an increase in the initial transfer price to Cardinal beginning in the second quarter of 2014. Gross margins on net sales were 63% in 2014 and 46% in 2013. Cost of goods sold in 2014 included a reserve for inventory obsolescence of $539,000 related to a specific lot that was originally produced for commercial validation purposes and that is nearing its product expiry and therefore is no longer expected to be sold. Excluding the one-time inventory obsolescence charge, gross margin on net sales for 2014 would have been 83%. Cost of goods sold in both periods included post-production testing activities required by regulatory authorities, which are charged as one-time period costs, and a royalty on net sales payable under our license agreement with UCSD.

Lymphoseek Milestone Revenue. During 2014, we recognized $300,000 of Lymphoseek milestone revenue from a non-refundable upfront milestone payment received by the Company related to the Lymphoseek distribution agreement for China for which the Company has no future obligations. No Lymphoseek milestone revenue was recognized during 2013.

Grant and Other Revenue. During 2014, we recognized $1.7 million of grant revenue as compared to $516,000 during 2013, primarily related to SBIR grants from the NIH supporting NAV4694 and Manocept platform development. The net increase was primarily due to higher NAV4694 grants offset by lower Manocept platform and Lymphoseek grants. Grant and other revenue for 2014 also included $90,000 of revenue related to services provided to R-NAV for Manocept development.

Research and Development Expenses. Research and development expenses decreased $6.9 million, or 29%, to $16.8 million during 2014 from $23.7 million in 2013. The decrease was primarily due to net decreases in drug project expenses related to (i) decreased Lymphoseek development costs of $3.7 million including decreased regulatory filing fees and consulting costs coupled with decreased manufacturing-related activities, offset by increased license fees related to EMA approval; (ii) decreased NAV5001 development costs of $1.2 million including decreased manufacturing-related activities and license fees, offset by increased clinical trial costs; and (iii) a net decrease in NAV4694 development costs of $1.0 million including decreased manufacturing-related activities and program management expenses, offset by increased clinical trial costs. The net decrease in research and development expenses also included decreased compensation including incentive-based awards and other expenses related to net decreased headcount resulting from the second quarter 2014 reduction in force of $567,000.

Selling, General and Administrative Expenses. Selling, general and administrative expenses remained steady at $15.5 million for both 2014 and 2013. Decreased investor relations of $880,000, compensation including incentive-based awards and other expenses related to net decreased headcount resulting from the second quarter 2014 reduction in force of $458,000, and out-of-pocket Lymphoseek marketing costs of $138,000 were offset by increased support costs including depreciation, facilities, Board compensation and travel of $808,000, medical education costs to support Lymphoseek of $484,000, and legal and professional services costs of $274,000.

Other Income (Expense). Other expense, net, was $8.1 million during 2014 as compared to $4.3 million during 2013. Interest expense increased $927,000 to $3.7 million during 2014 from $2.8 million in 2013, primarily due to increased

interest related to the Oxford Note, offset by decreased interest related to the GECC/MidCap Notes, Hercules Note and Platinum credit facility. Of this interest expense, $844,000 and $765,000 in 2014 and 2013, respectively, was non-cash in nature related to the amortization of debt issuance costs and debt discounts related to the Oxford Note, GECC/MidCap Notes, and Hercules Note. During 2014, we recorded a loss on extinguishment of debt of $2.6 million related to paying off the balance of the GECC/MidCap Notes. During 2013, we recorded losses on extinguishment of debt of $943,000 related to the modification of the Platinum credit facility and $429,000 upon paying off the balance of the Hercules Note. For the years ended December 31, 2014 and 2013, we recorded non-cash expenses of $1.3 million and $112,000, respectively, related to changes in the estimated fair value of financial instruments. During 2014, we recorded non-cash expense from our equity in the loss of R-NAV of $524,000.

Years Ended December 31, 2013 and 2012

Net Sales and Margins. Net sales of Lymphoseek were $614,000 during 2013. We did not record any sales revenue during the same period in 2012. Gross margins on net sales of Lymphoseek were 46% for the year ended 2013. Cost of goods sold included a royalty on net sales payable under our license agreement with UCSD. During the year ended December 31, 2013, margins on Lymphoseek sales were negatively impacted due to the proportion of sales made up of lower margin inventory-stocking units, coupled with post-production testing activities at launch, required by regulatory authorities, which are charged as one-time period costs, including certain post-manufacture testing costs related to normal ongoing processes required by the FDA.

Grant and Other Revenue. During 2013, we recognized $440,000 of grant revenue related to SBIR grants from the NIH to support NAV4694 and NAV1800 development. Grant revenue of $76,000 was received from Ohio Third Frontier and included $50,000 toward the development of alternative uses of Lymphoseek. During the year ended December 31, 2012, we recognized $60,000 of revenue related to reimbursement of certain Lymphoseek commercialization activities by our distribution partner, Cardinal Health.

Research and Development Expenses. Research and development expenses increased $6.8 million, or 40%, to $23.7 million during 2013 from $16.9 million during the same period in 2012. The increase was primarily due to net increases in drug project expenses related to (i) increased NAV4694 development costs of $4.5 million including increased clinical trial costs coupled with increased manufacturing-related activities, (ii) increased Manocept platform development costs of $503,000, and (iii) a net increase in NAV5001 development costs of $443,000 including increased clinical trial costs and manufacturing-related activities of $1.9 million, offset by a decrease in licensing fees of $1.4 million; offset by (iv) a net decrease in Lymphoseek development costs of $929,000 resulting from decreased manufacturing-related costs, decreased EMA filing fees and regulatory consulting costs primarily related to filing a MAA in 2012, and decreased clinical trial costs, offset by increased costs of $2.2 million related to sNDA submissions for two additional Lymphoseek indications in 2013 and (v) decreased consulting costs related to potential pipeline products of $407,000. The net increase in research and development expenses also included increased compensation including incentive-based awards and other related expenses of $2.6 million related to increased headcount required for expanded development efforts, as well as increased travel and other support costs.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased $4.3 million, or 39%, to $15.5 million during 2013 from $11.2 million during the same period in 2012. The net increase was primarily due to increased medical education costs to support Lymphoseek of $2.6 million, increased compensation including incentive-based awards and other expenses of $1.3 million related to increased headcount, and increased investor relations, legal and professional services costs, offset by decreased out-of-pocket marketing costs related to the commercial launch of Lymphoseek of $1.3 million.

Other Income (Expense). Other expense, net, was $4.3 million during 2013 as compared to $1.2 million during the same period in 2012. Interest expense increased $1.6 million to $2.8 million during 2013 from $1.2 million for the same period in 2012, primarily due to the interest related to the GECC/MidCap Notes as well as the draws on the Platinum credit facility, offset by the decreased balance of the Hercules Note. Of this interest expense, $765,000 and $545,000 in 2013 and 2012, respectively, was non-cash in nature related to the amortization of debt issuance costs and debt discounts related to the GECC/MidCap Notes and Hercules Note. During 2013, we recorded losses on extinguishment of debt of $943,000 related to the modification of the Platinum credit facility and $429,000 upon paying off the balance of the Hercules Note. For the years ended December 31, 2013 and 2012, we recorded non-cash expense of $112,000 and income of $32,000, respectively, related to changes in the estimated fair value of financial instruments.

Liquidity and Capital Resources

Cash balances decreased to $5.5 million at December 31, 2014 from $32.9 million at December 31, 2013. The net decrease was primarily due to cash used to fund our operations, mainly for research and development activities, of $29.1 million, purchases of equipment of $1.1 million, and an investment in R-NAV of $333,000, offset by a net increase of $3.2 million related to borrowings under the Oxford Note and the extinguishment of the GECC/Midcap Notes. The current ratio decreased to 0.9:1 as of December 31, 2014 from 3.3:1 December 31, 2013.

As of December 31, 2014, $31.8 million was still immediately available under the Platinum credit facility. We believe that our current cash balance, our credit facility with Platinum, our projected revenue derived from sales of Lymphoseek, our ability to control expenses, the potential for partnership funding, the potential to access debt or royalty instruments, and the potential to access capital markets through our shelf registration (though we have no current intention to raise additional equity capital using the shelf registration), provide us with adequate financial resources to continue to fund our business plan for the foreseeable future and enable us to reach break-even cash flow from operations in the first quarter of 2016.

Operating Activities. Cash used in operations decreased $6.5 million to $29.1 million during 2014 compared to $35.6 million during 2013. Cash used in operations increased $11.7 million to $35.6 million during the year ended December 31, 2013, compared to $23.9 million during the same period in 2012.

Accounts receivable decreased to $817,000 at December 31, 2014 from $1.2 million at December 31, 2013, primarily due to decreased amounts due from the landlord of our Dublin office space for tenant improvements, offset by increased receivables due from Cardinal Health resulting from the increase in sales of Lymphoseek. Accounts receivable increased to $1.2 million at December 31, 2013 from $18,000 at December 31, 2012, primarily due to receivables due from the landlord of our Dublin office space for tenant improvements, from Cardinal Health for sales of Lymphoseek and from the NIH for SBIR grants.

Inventory levels decreased to $932,000 at December 31, 2014 from $2.2 million at December 31, 2013, primarily due to finished goods inventory sold, a non-cash reserve for inventory obsolescence related to a specific lot that was originally produced for commercial validation purposes and that is nearing its product expiry and therefore is no longer expected to be sold, and materials inventory consumed for product testing and development purposes, offset by in-process and completed new lots of Lymphoseek finished drug product. Inventory levels increased to $2.2 million at December 31, 2013, from $298,000 at December 31, 2012. Increases in work-in-process and finished goods were related to in-process and completed new lots of Lymphoseek finished drug product. Increases in materials were related to purchases of Lymphoseek drug substance. We expect inventory levels to increase during 2015 as we produce additional Lymphoseek inventory to meet increasing demand.

Prepaid expenses and other current assets increased to $1.4 million at December 31, 2014 from $1.0 million at December 31, 2013, primarily due to prepayments to our third party manufacturers of Lymphoseek inventory. Prepaid expenses and other current assets decreased to $1.0 million at December 31, 2013 from $1.2 million at December 31, 2012, primarily due to the utilization of prepayments to our third party manufacturers of Lymphoseek inventory.

Accounts payable decreased to $1.5 million at December 31, 2014 from $2.4 million at December 31, 2013, primarily due to decreased NAV5001 development activities, coupled with normal fluctuations in timing of receipt and payment of invoices. Accrued liabilities and other current liabilities decreased to $3.2 million at December 31, 2014 from $4.8 million at December 31, 2013, primarily due to decreases in accrued NAV4694 development costs. Accounts payable increased to $2.4 million at December 31, 2013 from $1.4 million at December 31, 2012, primarily due to increases in Lymphoseek and NAV5001 development activities, coupled with normal fluctuations in timing of receipt and payment of invoices. Accrued liabilities and other current liabilities increased to $4.8 million at December 31, 2013 from $2.0 million at December 31, 2012, primarily due to increases in accrued NAV4694 development costs and net increases in compensation-related accruals. Our payable and accrual balances will continue to fluctuate but will likely decrease overall as we decrease our level of development activity related to NAV4694 and NAV5001 while we seek to secure a development partner or partners for these programs, offset by planned increases in commercial activity related to Lymphoseek and development activity related to the Manocept platform.

Investing Activities. Investing activities used $1.5 million during 2014 compared to $1.3 million used during 2013 and $672,000 used during 2012. Capital expenditures of $1.1 million during 2014 were primarily for leasehold improvements, office furniture and NAV4694 production equipment. Capital expenditures of $1.2 million during 2013 were primarily for equipment to be used in the production of NAV4694 and Lymphoseek, leasehold improvements, computers, and software. Capital expenditures of $663,000 during 2012 were primarily for production and laboratory equipment, software, computers, and office furniture. Investing activities also included an investment in R-NAV of $333,000 during 2014.

Financing Activities. Financing activities provided $3.2 million during 2014 compared to $60.7 million during 2013 and $5.1 million during 2012. The $3.2 million provided by financing activities in 2014 consisted primarily of proceeds from the Oxford Note of $30.0 million, offset by payment of the principal and fees related to the extinguishment of the GECC/Midcap Notes of $26.7 million. The $60.7 million provided by financing activities in 2013 consisted primarily of proceeds from the issuance of common stock of $41.3 million and proceeds from notes payable of $29.0 million, offset by principal payments on our notes payable of $6.0 million, payment of common stock issuance costs of $1.8 million, payment of debt issuance costs of $1.2 million, and payment of minimum tax withholdings related to stock-based compensation of $659,000. The $5.1 million provided by financing activities during 2012 consisted primarily of $4.0 million of proceeds from notes payable and $2.7 million of proceeds from the exercise of warrants and stock options, offset by $1.3 million of principal payments on our convertible debt.

Investment in R-NAV, LLC

In July 2014, Navidea announced that it formed a joint enterprise with Essex Woodlands-backed Rheumco, LLC, to develop and commercialize radiolabeled diagnostic and therapeutic products for rheumatologic and arthritic diseases. The joint

enterprise, called R-NAV, will combine Navidea's proprietary Manocept CD206 macrophage targeting platform and Rheumco's proprietary Tin-117m radioisotope technology to focus on leveraging the platforms across several indications with high unmet medical need:

R-NAV Subsidiary 1A: Detection of RA initially using Tc-99m tilmanocept, commercially known as Lymphoseek,
R-NAV Subsidiary 1B: Combination of the Manocept platform with Tin-117m for detection and treatment of RA,
R-NAV Subsidiary 2: Detection and treatment of human and veterinary osteoarthritis (OA) using the Tin-117m technology, and
R-NAV Subsidiary 3: Treatment of pediatric hemophilic arthropathy (PHA), a rare rheumatologic condition.

Both Rheumco and Navidea have contributed licenses for intellectual property and technology to R-NAV in exchange for common units in R-NAV. Each of the licenses has grant-back provisions with respect to inventions and other intellectual property developed in these programs outside of the exclusive fields of use specified in the license.

R-NAV was initially capitalized through a $4.0 million investment from Infinity Capital III, of Houston-based McRay Money Management, and other third-party private investors, and the technology contributions from Rheumco and Navidea. Navidea has committed an additional $1.0 million investment to be paid over three years, with $333,334 in cash contributed at inception and a promissory note in the principal amount of $666,666, payable in two equal installments on the first and second anniversaries of the transaction. The note will bear interest at the applicable federal rate, currently 0.31% per annum. In exchange for its capital and in-kind investment, the Company received 1,000,000 Series A preferred units of R-NAV (Series A Units). The Company will receive an additional 500,000 Series A Units for management and technical services associated with the programs described above to be performed by the Company for R-NAV pursuant to a services agreement. The Series A Units are convertible into common units at the option of the holder for a conversion price of $1 per unit, subject to broad-based weighted average anti-dilution rights.

Navidea initially owned approximately 33.7% of the combined entity. In December 2014, the third-party private investors contributed an additional $570,000 in exchange for 570,000 Series A Units. Following the additional investment by the private investors, Navidea owns approximately 32.5% of R-NAV. Joint oversight over certain aspects of R-NAV is shared between Navidea, Rheumco, Infinity Capital, and the other investors; Navidea does not control the operations of R-NAV. Navidea has three-year call options to acquire, at its sole discretion, all of the equity of Subsidiary 1A for $10.5 million prior to the launch of a Phase 3 clinical trial for its development program, and all of the equity of Subsidiary 1B at fair value upon completion of radiochemistry and biodistribution studies for its development program.

Warrant Exercises

During 2012, the holder of 20,000 Series V warrants exercised them in exchange for issuance of 20,000 shares of our common stock, resulting in gross proceeds of $6,200. Also during 2012, Platinum exercised 6,000,000 Series W warrants in exchange for issuance of 6,000,000 shares of our common stock, resulting in gross proceeds of $1,920,000. In March 2013, Platinum exercised 3,000,000 Series X warrants in exchange for issuance of 3,000,000 shares of our common stock, resulting in gross proceeds of $1,380,000.

Platinum Credit Facility

In July 2012, we entered into an agreement with Platinum to provide us with a credit facility of up to $50 million (the Platinum Loan Agreement). Following the approval of Lymphoseek, Platinum was committed under the terms of the agreement to extend up to $35 million in debt financing to the Company at an interest rate equal to the greater of (a) the U.S. Prime Rate as reported in the Wall Street Journal plus 6.75%; (b) 10.0%; or (c) the highest rate of interest

then payable pursuant to the Hercules Loan Agreement (discussed below) plus 0.125%. Through June 25, 2013, we drew a total of $8.0 million under the original facility. The agreement also provided for Platinum to extend an additional $15 million on terms to be negotiated. Principal amounts were due the earlier of two years from the date of draw or June 30, 2016.

In June 2013, in connection with entering into the GECC/MidCap Loan Agreement (discussed below), the Company and Platinum entered into an Amendment to the Platinum Loan Agreement (the First Platinum Amendment). Navidea, Platinum, and GECC/MidCap also entered into a Subordination Agreement, providing for subordination of the Company’s indebtedness under the Platinum Loan Agreement to the Company’s indebtedness under the GECC/MidCap Loan Agreement, among other customary terms and conditions.

Concurrent with the execution of the First Platinum Amendment, the Company delivered an Amended and Restated Promissory Note (the First Amended Platinum Note) to Platinum, which amended and restated the original promissory note issued to

Platinum, in the principal amount of up to $35 million. The First Amended Platinum Note also adjusted the interest rate to the greater of (a) the U.S. Prime Rate as reported in the Wall Street Journal plus 6.75%; (b) 10.0%; or (c) the highest rate of interest then payable pursuant to the GECC/MidCap Loan Agreement plus 0.125%. In addition, the First Platinum Amendment granted Platinum the right, at Platinum's option subject to certain conditions, to convert all or any portion of the unpaid principal or unpaid interest accrued on any future draw (the Conversion Amount), beginning on a date two years from the date the draw is advanced, into the number of shares of Navidea's common stock computed by dividing the Conversion Amount by a conversion price equal to the lesser of (i) 90% of the lowest VWAP for the 10 trading days preceding the date of such conversion request, or (ii) the average VWAP for the 10 trading days preceding the date of such conversion request. The First Platinum Amendment also provided a conversion right on the same terms with respect to the amount of any mandatory repayment due following the Company achieving $2,000,000 in cumulative revenues from sales or licensing of Lymphoseek. The conversion option applies to the Conversion Amount if the Company is prohibited from making such prepayment under the terms of the Subordination Agreement.

Also in connection with the First Platinum Amendment, the Company and Platinum entered into a Warrant Exercise Agreement (Exercise Agreement), pursuant to which Platinum exercised its Series X Warrant and Series AA Warrant. The warrants were exercised on a cashless basis by canceling a portion of the indebtedness outstanding under the Platinum Loan Agreement equal to $4,781,333, the aggregate exercise price of the warrants. Pursuant to the Exercise Agreement, in lieu of common stock, Platinum received on exercise of the warrants 2,364.9 shares of the Company's Series B, convertible into 7,733,223 shares of our common stock in the aggregate (3,270 shares of common stock per preferred share).

In March 2014, in connection with entering into the Oxford Loan Agreement (discussed below), we repaid all amounts outstanding under the GECC/MidCap Loan Agreement and entered into a second amendment to the Platinum Loan Agreement (the Second Platinum Amendment). Concurrent with the execution of the Second Platinum Amendment, the Company delivered an Amended and Restated Promissory Note (the Second Amended Platinum Note) to Platinum, which amended and restated the First Amended Platinum Note. The Second Amended Platinum Note adjusted the interest rate to the greater of (i) the United States prime rate as reported in The Wall Street Journal plus 6.75%, (ii) 10.0%, and (iii) the highest rate of interest then payable by the Company pursuant to the Oxford Loan Agreement plus 0.125% (effective interest rate as of December 31, 2014 was 10.0%). Navidea, Platinum, and Oxford also entered into a Subordination Agreement, providing for subordination of the Company's indebtedness under the Platinum Loan Agreement to the Company's indebtedness under the Oxford Loan Agreement, among other customary terms and conditions.

We drew a total of $4.0 million under the credit facility in each of the years ended December 31, 2013 and 2012. We did not make any draws under the credit facility during the year ended December 31, 2014. As of December 31, 2014, the remaining outstanding principal balance was $3.2 million, with $31.8 million still immediately available under the credit facility. Based on the balance as of December 31, 2014, annual principal and interest payments on the Platinum credit facility are expected to be $326,000, $327,000, $326,000, $326,000 and $3.3 million in 2015, 2016, 2017, 2018 and 2019, respectively.

Hercules Debt

In December 2011, we executed a Loan and Security Agreement (the Hercules Loan Agreement) with Hercules Technology II, L.P. (Hercules), pursuant to which we issued Hercules: (1) a Secured Term Promissory Note in the principal amount of $7,000,000 (the Hercules Note), and (2) a Series GG warrant to purchase 333,333 shares of our common stock at an exercise price of $2.10 per share, expiring in December 2016 (the Series GG warrants). In June 2013, the Company used a portion of the proceeds from the GECC/MidCap Notes (discussed below) to pay the remaining $4.4 million of principal outstanding on the Hercules Note, as well as a $250,000 end-of-term fee and a

$66,000 early payment penalty in accordance with the terms of the Hercules Loan Agreement. The Series GG warrants remained outstanding as of December 31, 2014.

GECC/MidCap Debt

In June 2013, we executed a Loan and Security Agreement (the GECC/MidCap Loan Agreement) with General Electric Capital Corporation (GECC) and MidCap Financial SBIC, LP (MidCap), pursuant to which we issued GECC and MidCap: (1) Term Notes in the aggregate principal amount of $25,000,000 (the GECC/MidCap Notes), and (2) Series HH warrants to purchase an aggregate of 301,205 shares of our common stock at an exercise price of $2.49 per share, expiring in June 2023 (the Series HH warrants). In March 2014, in connection with the consummation of the Oxford Loan Agreement (discussed below, we repaid all amounts outstanding under the GECC/MidCap Loan Agreement upon the receipt by GECC/MidCap of a payoff amount of $26.7 million, including $500,000 as a pre-payment fee and $1,000,000 as an end-of-term final payment fee. The Series HH warrants remained outstanding as of December 31, 2014.

Oxford Debt

In March 2014, we executed a Loan and Security Agreement the (Oxford Loan Agreement) with Oxford Finance, LLC (Oxford), providing for a loan to the Company of $30 million. Pursuant to the Oxford Loan Agreement, we issued Oxford: (1) Term Notes in the aggregate principal amount of $30,000,000, bearing interest at 8.5% (the Oxford Notes), and (2) Series KK warrants to purchase an aggregate of 391,032 shares of our common stock at an exercise price of $1.918 per share, expiring in March 2021 (the Series KK warrants). We made monthly payments of interest only commencing on April 1, 2014, and continuing on the first calendar day of each successive month thereafter through and including the first calendar day of the month immediately preceding April 1, 2015 (the Amortization Date). Commencing on the Amortization Date, and continuing on the first calendar day of each month thereafter, the Company will make 48 consecutive equal monthly payments of principal and interest, in arrears, to the lenders then party to the Oxford Loan Agreement. All unpaid principal, and accrued and unpaid interest, with respect to the Oxford Notes is due and payable in full on March 1, 2019. We will also make a final payment to the lenders in an aggregate amount equal to the original principal amount of loan multiplied by 7.95%. The Oxford Notes are collateralized by a security interest in substantially all of the Company's assets except for intellectual property, as to which the security interest is in rights to income or proceeds from the sale or licensing thereof. The Oxford Loan Agreement requires that the Company adhere to certain affirmative and negative covenants, including, without limitation, financial reporting requirements and a prohibition against the incurrence of indebtedness, or creation of additional liens, other than as specifically permitted by the terms of the Oxford Loan Agreement. As of December 31, 2014, we were in compliance with all covenants of the Oxford Loan Agreement.

In July 2014, in connection with the formation of R-NAV, we entered into an amendment to the Oxford Loan Agreement that amended certain covenants to permit our investment in R-NAV, and R-NAV entered into a Subordination Agreement with Oxford to subordinate our indebtedness to R-NAV to our obligations under the Oxford Loan Agreement.

During 2014, we recorded interest expense of $2.8 million on the Oxford Notes, which included amortization of the debt discount and issuance costs. As of December 31, 2014, the remaining outstanding principal balance of the debt was $30.0 million, and the Series KK warrants remained outstanding. Annual principal and interest payments on the Oxford Notes are expected to be $7.3 million, $8.9 million, $8.9 million, $8.9 million and $2.2 million in 2015, 2016, 2017, 2018 and 2019, respectively.

In March 2015, in connection with the organization and initial financing of Macrophage Therapeutics, Inc., we entered into an amendment to the Oxford Loan Agreement that amended certain covenants to permit these actions and to consent to the grant of a license to Macrophage Therapeutics, Inc. for certain therapeutic applications of the Manocept technology, and Macrophage Therapeutics, Inc. became a co-obligor on the Oxford Notes.

2013 Public Offerings

During 2013, we completed two public offerings resulting in issuance of 3,642,389 shares of the Company's common stock. The net proceeds to the Company were approximately $9.3 million after deducting expenses associated with the offerings. The 2013 public offerings were made pursuant to the Company's existing effective shelf registration statement on Form S-3.

Additionally, in September 2013, we entered into a Securities Purchase Agreement with Crede for a registered direct public offering of 10,563,381 shares of our common stock at a price of $2.84 per share for total gross proceeds of $30.0 million. The net proceeds to the Company upon issuance in 2013 were approximately $28.8 million after deducting expenses associated with the Securities Purchase Agreement, including placement agent fees of $999,000 (3.3% of the gross proceeds). In addition to the common stock, we issued Series JJ warrants to purchase 3,169,015

shares of our common stock at an exercise price of $3.83 per share, expiring in September 2016. In November 2014, Crede exchanged their Series JJ warrants for 3,843,223 shares of our common stock in accordance with the terms of the Series JJ warrant agreement.

Summary

Our future liquidity and capital requirements will depend on a number of factors, including our ability to achieve market acceptance of our products, our ability to complete the development and commercialization of new products, our ability to monetize our investment in non-core technologies, our ability to obtain milestone or development funds from potential development and distribution partners, regulatory actions by the FDA and international regulatory bodies, the ability to procure required financial resources, and intellectual property protection.

In May 2014, the Board of Directors made the decision to refocus the Company's resources to better align the funding of our pipeline programs with the expected growth in Lymphoseek revenue. This realignment primarily involves reducing our near-

term support for our two neurological product candidates, NAV4694 and NAV5001, as we seek to secure a development partner or partners for these programs. The Company is also working to establish new sources of non-dilutive funding, including collaborations and grant funding that can augment the balance sheet as the Company works to reduce spending to levels that can be increasingly offset by growing Lymphoseek revenue. In particular, substantial progress on the Manocept platform has resulted in several promising opportunities, including our R-NAV venture, which we believe may further expand the Company's pipeline but requires less near-term funding from Navidea than the two temporarily suspended Phase 3 neurological development programs. We plan to focus our resources in 2015 primarily on increasing sales of Lymphoseek and development of products based on the Manocept platform. Although management believes that it will be able to achieve these objectives, they are subject to a number of variables beyond our control, including the nature and timing of any partnering opportunities, the ability to modify contractual commitments made in connection with these programs, and the timing and expense associated with suspension or alteration of clinical trials, and consequently we cannot assure you that we will be able to achieve our objective of bringing our expenses in line with our revenues, and we may need to seek additional debt or equity financing if we cannot achieve that objective in a timely manner.

As stated above, we believe that our current cash balance, our credit facility with Platinum, our projected revenue derived from sales of Lymphoseek, our ability to control expenses, the potential for partnership funding, the potential to access debt or royalty instruments, and the potential to access capital markets through our shelf registration (though we have no current intention to raise additional equity capital using the shelf registration), provide us with adequate financial resources to continue to fund our business plan for the foreseeable future and enable us to reach break-even cash flow from operations in the first quarter of 2016. However, we cannot assure you that Lymphoseek will generate our expected levels of sales and cash flow. We will continue to evaluate our time lines, strategic needs, and balance sheet requirements. We cannot assure you that if we attempt to raise additional capital through debt, royalty, equity or otherwise, we will be successful in doing so on terms acceptable to the Company, or at all. We also cannot assure you that we will be able to gain access and/or be able to execute on securing new development opportunities, successfully obtain regulatory approval for and commercialize new products, achieve significant product revenues from our products, or achieve or sustain profitability in the future.

Recent Accounting Developments

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers, which supersedes nearly all existing revenue recognition guidance under U.S. GAAP. The core principle of ASU 2014-09 is built on the contract between a vendor and a customer for the provision of goods and services. It attempts to depict the exchange of rights and obligations between the parties in the pattern of revenue recognition based on the consideration to which the vendor is entitled. To accomplish this objective, ASU 2014-09 requires five basic steps: (i) identify the contract with the customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, (v) recognize revenue when (or as) the entity satisfies a performance obligation. Entities will generally be required to make more estimates and use more judgment than under current guidance, which will be highlighted for users through increased disclosure requirements. ASU 2014-09 is effective for public entities for annual periods beginning after December 15, 2016, including interim periods therein. Three basic transition methods are available - full retrospective, retrospective with certain practical expedients, and a cumulative effect approach. Early adoption is prohibited. We are currently evaluating the impact of our pending adoption of ASU 2014-09 on our consolidated financial statements and have not yet determined the method by which we will adopt the standard in 2017.

In June 2014, the FASB issued ASU No. 2014-12, Compensation-Stock Compensation. ASU 2014-12 requires that a performance target included in a share-based payment award that affects vesting and that could be achieved after the requisite service period be treated as a performance condition. Therefore, under the existing stock compensation

guidance in Topic 718, the performance target should not be reflected in estimating the grant-date fair value of the award. Compensation cost should be recognized in the period in which it becomes probable that the performance target will be achieved and should represent the compensation cost attributable to the period(s) for which the requisite service has already been rendered. If the performance target becomes probable of being achieved before the end of the requisite service period, the remaining unrecognized compensation cost should be recognized prospectively over the remaining requisite service period. The total amount of compensation cost recognized during and after the requisite service period should reflect the number of awards that are expected to vest and should be adjusted to reflect those awards that ultimately vest. The requisite service period ends when the employee can cease rendering service and still be eligible to vest in the award if the performance target is achieved. ASU 2014-12 is effective for annual periods beginning after December 15, 2015, including interim periods therein. Earlier adoption is permitted. Entities may apply the amendments in ASU 2014-12 either (a) prospectively to all awards granted or modified after the effective date or (b) retrospectively to all awards with performance targets that are outstanding as of the beginning of the earliest annual period presented in the financial statements and to all new or modified awards thereafter. If retrospective transition is adopted, the cumulative effect of applying ASU 2014-12 as of the beginning of the earliest annual period presented

in the financial statements should be recognized as an adjustment to the opening retained earnings balance at that date. Additionally, if retrospective transition is adopted, an entity may use hindsight in measuring and recognizing the compensation cost. We do not expect the adoption of ASU 2014-12 to have a material effect on our consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements-Going Concern. ASU 2014-15 defines when and how companies are required to disclose going concern uncertainties, which must be evaluated each interim and annual period. ASU 2014-15 requires management to determine whether substantial doubt exists regarding the entity's going concern presumption. Substantial doubt about an entity's ability to continue as a going concern exists when relevant conditions and events, considered in the aggregate, indicate that it is probable that the entity will be unable to meet its obligations as they become due within one year after the date that the financial statements are issued (or available to be issued). If substantial doubt exists, certain disclosures are required; the extent of those disclosures depends on an evaluation of management's plans (if any) to mitigate the going concern uncertainty. ASU 2014-15 is effective prospectively for annual periods ending after December 15, 2016, and to annual and interim periods thereafter. Early adoption is permitted. We do not expect the adoption of ASU 2014-15 to have a material effect on our consolidated financial statements, however it may affect our disclosures.

In November 2014, the FASB issued ASU No. 2014-16, Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share Is More Akin to Debt or to Equity. ASU 2014-16 does not change the current criteria in GAAP for determining when separation of certain embedded derivative features in a hybrid financial instrument is required. Rather, ASU 2014-16 clarifies how current GAAP should be interpreted in evaluating the economic characteristics and risks of a host contract in a hybrid financial instrument that is issued in the form of a share. Specifically, ASU 2014-16 clarifies that an entity should consider all relevant terms and features - including the embedded derivative feature being evaluated for bifurcation - in evaluating the nature of the host contract. Further, ASU 2014-16 clarifies that no single term or feature would necessarily determine the host economic characteristics and risks of the host contract. Rather, the nature of the host contract depends upon the economic characteristics and risks of the entire hybrid financial instrument. In addition, ASU 2014-16 clarifies that, in evaluating the nature of a host contract, an entity should assess the substance of the relevant terms and features (that is, the relative strength of the debt-like or equity-like terms and features given the facts and circumstances) when considering how to weight those terms and features. Specifically, the assessment of the substance of the relevant terms and features should incorporate a consideration of (1) the characteristics of the terms and features themselves, (2) the circumstances under which the hybrid financial instrument was issued or acquired, and (3) the potential outcomes of the hybrid financial instrument, as well as the likelihood of those potential outcomes. ASU 2014-16 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2015. Early adoption is permitted. Initial adoption should be applied on a modified retrospective bases to existing hybrid financial instruments issued in the form of a share as of the beginning of the fiscal year for which the amendments are effective. We are evaluating the potential impact of ASU 2014-16, however we do not expect the adoption of ASU 2014-16 to have a material effect on our consolidated financial statements.

Critical Accounting Policies

Revenue Recognition. We currently generate revenue primarily from sales of Lymphoseek. Our standard shipping terms are FOB shipping point, and title and risk of loss passes to the customer upon delivery to a carrier for shipment from Cardinal Health’s national distribution center to another point of destination. We generally recognize sales revenue related to sales of our products when the products are shipped. Our customers have no right to return products purchased in the ordinary course of business.

We earn additional revenues based on a percentage of the actual net revenues achieved by Cardinal Health on sales to end customers made during each fiscal year. The amount we charge Cardinal Health related to end customer sales of

Lymphoseek are subject to a retroactive annual adjustment. To the extent that we can reasonably estimate the end-customer prices received by Cardinal Health, we record sales based upon these estimates at the time of sale. If we are unable to reasonably estimate end customer sales prices related to products sold, we record revenue related to these product sales at the minimum (i.e., floor) price provided for under our distribution agreement with Cardinal Health.

We also earn revenue related to milestones as defined in our distribution agreements. Such revenue is recognized when the milestones are achieved with no future obligations and payments under the agreements become contractually due.

We generate additional revenue from grants to support various product development initiatives. We generally recognize grant revenue when expenses reimbursable under the grants have been paid and payments under the grants become contractually due.

Research and Development. Research and development (R&D) expenses include both internal R&D activities and external contracted services. Internal R&D activity expenses include salaries, benefits, and stock-based compensation, as well as travel,

supplies, and other costs to support our R&D staff. External contracted services include clinical trial activities, chemistry, manufacturing and control-related activities, and regulatory costs. R&D expenses are charged to operations as incurred. We review and accrue R&D expenses based on services performed and rely upon estimates of those costs applicable to the stage of completion of each project.

Use of Estimates. The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. We base these estimates and assumptions upon historical experience and existing, known circumstances. Actual results could differ from those estimates. Specifically, management may make significant estimates in the following areas:

- Stock-Based Compensation. Stock-based payments to employees and directors, including grants of stock options and restricted stock, are recognized in the statements of operations based on their estimated fair values on the date of grant. The fair value of each option award is estimated on the date of grant using the Black-Scholes option pricing model to value share-based payments and the portion that is ultimately expected to vest is recognized as compensation expense over either (1) the requisite service period or (2) the estimated performance period. The determination of fair value using the Black-Scholes option pricing model is affected by our stock price as well as assumptions regarding a number of complex and subjective variables, including expected stock price volatility, risk-free interest rate, expected dividends and projected employee stock option behaviors. We estimate the expected term based on the contractual term of the awards and employees' exercise and expected post-vesting termination behavior. The restricted stock awards are valued based on the closing stock price on the date of grant and amortized ratably over the estimated life of the award.

Since stock-based compensation is recognized only for those awards that are ultimately expected to vest, we have applied an estimated forfeiture rate to unvested awards for the purpose of calculating compensation cost. These estimates will be revised, if necessary, in future periods if actual forfeitures differ from estimates. Changes in forfeiture estimates impact compensation cost in the period in which the change in estimate occurs.

- Inventory Valuation. We record our inventory at the lower of cost (first-in, first-out method) or market. Our valuation reflects our estimates of excess and obsolete inventory as well as inventory with a carrying value in excess of its net realizable value. Write-offs are recorded when product is removed from saleable inventory. We review inventory on hand at least quarterly and record provisions for excess and obsolete inventory based on several factors, including current assessment of future product demand, anticipated release of new products into the market and product expiration. Our industry is characterized by rapid product development and frequent new product introductions. Regulations regarding use and shelf life, product recalls and variation in product utilization all impact the estimates related to excess and obsolete inventory.

- Fair Value of Derivative Instruments. Derivative instruments embedded in contracts, to the extent not already a free-standing contract, are bifurcated and accounted for separately. All derivatives are recorded on the consolidated balance sheets at fair value in accordance with current accounting guidelines for such complex financial instruments. Unrealized gains and losses on the derivatives are classified in other expenses as a change in derivative liabilities in the statements of operations. We do not use derivative instruments for hedging of market risks or for trading or speculative purposes.

Contractual Obligations and Commercial Commitments

The following table presents our contractual obligations and commercial commitments as of December 31, 2014.

	Payments Due By Period						
Contractual Cash Obligations	Total	2015	2016	2017	2018	2019	Thereafter
Purchase obligations	$912,411	$912,411	$—	$—	$—	$—	$—
Capital lease obligation	5,317	3,039	2,278	—	—	—	—
Operating lease obligations	2,275,398	295,695	271,831	277,946	284,247	290,734	854,945
Principal and interest on long-term debt	41,379,377	7,954,279	9,534,987	9,199,726	9,199,726	5,490,659	—
Total contractual cash obligations	$44,572,503	$9,165,424	$9,809,096	$9,477,672	$9,483,973	$5,781,393	$854,945

* This table does not include obligations such as license agreements, contracted services, or employment agreements as such obligations are dependent upon performance conditions.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk. As of December 31, 2014, our $5.5 million in cash was primarily invested in interest-bearing money market accounts. Due to the low interest rates being realized on these accounts, we believe that a hypothetical 10% increase or decrease in market interest rates would not have a material impact on our consolidated financial position, results of operations or cash flows.

We also have exposure to changes in interest rates on our variable-rate debt obligations. As of December 31, 2014, the interest rate on certain of our debt obligations was based on the U.S. prime rate. Based on the amount of our variable-rate borrowings at December 31, 2014, which totaled approximately $3.2 million, an immediate one percentage point increase in the U.S. prime rate would increase our annual interest expense by approximately $32,000. This estimate assumes that the amount of variable rate borrowings remains constant for an annual period and that the interest rate change occurs at the beginning of the period. Because our debt obligations are currently subject to the minimum interest rates defined in the loan agreements, a decrease in the U.S. prime rate would not affect our annual interest expense.

Foreign Currency Exchange Rate Risk. We do not currently have material foreign currency exposure related to our assets as the majority are denominated in U.S. currency and our foreign-currency based transaction exchange risk is not material. For the years ended December 31, 2014, 2013 and 2012, we recorded foreign currency transaction gains (losses) of approximately $87,000, $(8,000) and $(15,000), respectively.

Equity Price Risk. We do not use derivative instruments for hedging of market risks or for trading or speculative purposes. Derivative instruments embedded in contracts, to the extent not already a free-standing contract, are bifurcated and accounted for separately. All derivatives are recorded on the consolidated balance sheet at fair value in accordance with current accounting guidelines for such complex financial instruments. As of December 31, 2014, we did not have any derivative liabilities on our consolidated balance sheet.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, and the related notes, together with the report of BDO USA, LLP dated March 16, 2015 are set forth at pages F-1 through F-32 attached hereto and incorporated herein by reference.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

We maintain disclosure controls and procedures designed to ensure that information required to be disclosed in reports filed under the Exchange Act is recorded, processed, summarized, and reported within the specified time periods. As a part of these controls, our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of December 31, 2014. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Based on our evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this report, our disclosure controls and procedures are adequately designed and are effective.

Our management, including our Chief Executive Officer and Chief Financial Officer, understands that our disclosure controls and procedures do not guarantee that all errors and all improper conduct will be prevented. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, a design of a control system must reflect the fact that there are resource constraints, and the benefit of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of improper conduct, if any, have been detected. These inherent limitations include the realities that judgments and decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more persons, or by management override of the control. Further, the design of any system of controls is also based in part upon assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations of a cost-effective control system, misstatements due to error or fraud may occur and may not be detected.

Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control system was designed to provide reasonable assurance to management and the Board of Directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company;
-

provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles and that receipts and expenditures of the company are being made only in accordance with authorization of management and directors of the company; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2014. In making this assessment, it used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control – Integrated Framework (2013). Based on our assessment we concluded that, as of December 31, 2014, our internal control over financial reporting was effective based on those criteria. BDO USA, LLP, our independent registered public accounting firm, has issued an attestation report covering our internal control over financial reporting, which begins on page 57.

Changes in Internal Control Over Financial Reporting

During the year ended December 31, 2014, there were no changes in our internal control over financial reporting that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders
Navidea Biopharmaceuticals, Inc.
Dublin, Ohio

We have audited Navidea Biopharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Navidea Biopharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Management's Report on Internal Control Over Financial Reporting" included in Item 9A. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Navidea Biopharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Navidea Biopharmaceuticals, Inc. as of December 31, 2014 and 2013, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2014 and our report dated March 16, 2015 expressed an unqualified opinion thereon.

/s/ BDO USA, LLP

Chicago, Illinois
March 16, 2015

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Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors

Set forth below are the names and committee assignments of the persons who constitute our Board of Directors.

Name	Age	Committee(s)
Peter F. Drake, Ph.D.	61	Compensation, Nominating and Governance (Chairman)
Brendan A. Ford	56	Audit (Chairman)
Michael M. Goldberg, M.D.	56	—
Ricardo J. Gonzalez	44	—
Perry A. Karsen	59	Audit; Compensation, Nominating and Governance
Eric K. Rowinsky, M.D.	58	—
Gordon A. Troup	61	Audit; Compensation, Nominating and Governance

Director Qualifications

The Board of Directors believes that individuals who serve on the Board should have demonstrated notable or significant achievements in their respective field; should possess the requisite intelligence, education and experience to make a significant contribution to the Board and bring a range of skills, diverse perspectives and backgrounds to its deliberations; and should have the highest ethical standards, a strong sense of professionalism and intense dedication to serving the interests of our stockholders. The following are qualifications, experience and skills for Board members which are important to our business and its future:

- General Management. Directors who have served in senior leadership positions are important to us as they bring experience and perspective in analyzing, shaping, and overseeing the execution of important operational and policy issues at a senior level. These directors' insights and guidance, and their ability to assess and respond to situations encountered in serving on our Board of Directors, are enhanced by their leadership experience developed at businesses or organizations that operated on a global scale, faced significant competition, or involved other evolving business models.
- Industry Knowledge. Because we are a pharmaceutical development company, education or experience in our industry, including medicine, pharmaceutical development, marketing, distribution, or the regulatory environment, is important because such experience assists our Directors in understanding and advising our Company.
- Business Development/Strategic Planning. Directors who have a background in strategic planning, business development, strategic alliances, mergers and acquisitions, and teamwork and process improvement provide insight into developing and implementing strategies for growing our business.
- Finance/Accounting/Control. Knowledge of capital markets, capital structure, financial control, audit, reporting, financial planning, and forecasting are important qualities of our directors because such qualities assist in understanding, advising, and overseeing our Company's capital structure, financing and investing activities, financial reporting, and internal control of such activities.
- Board Experience/Governance. Directors who have served on other public company boards can offer advice and insights with regard to the dynamics and operation of a board of directors, the relations of a board to the chief executive officer and other management personnel, the importance of particular agenda and oversight matters, and oversight of a changing mix of strategic, operational, and compliance-related matters.

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Biographical Information

Set forth below is current biographical information about our directors, including the qualifications, experience and skills that make them suitable for service as a director. Each listed director's respective experience and qualifications described below led the Compensation, Nominating and Governance Committee (CNG Committee) of our Board of Directors to conclude that such director is qualified to serve as a member of our Board of Directors.

Directors whose terms continue until the 2015 Annual Meeting:

Peter F. Drake, Ph.D. has served as a director of Navidea since April 2011. Dr. Drake began his career as a biotechnology analyst at Kidder, Peabody and Co. where he was a partner and head of the Healthcare Research Group. In 1988, Dr. Drake co-founded Vector Securities International, an investment banking firm specializing in the life sciences industry, where he was Executive Vice President and Director of Research. In 1993, Dr. Drake co-founded Vector Fund Management, a life sciences venture fund, and Deerfield Management, a healthcare hedge fund. In 1999, Vector Securities International was purchased by Prudential Securities, where he was a Managing Director and Head of Healthcare Research. Dr. Drake is a board member of Trustmark Insurance, a mutual insurance company, and Sequoia Sciences, Inc., a private biotechnology company. Dr. Drake received his undergraduate degree from Bowdoin College, and his Ph.D. in neurobiology and biochemistry from Bryn Mawr College.

Perry A. Karsen has served as a director of Navidea since February 2014. Mr. Karsen is currently Chief Executive Officer of Celgene Cellular Therapeutics (CCT), Celgene Corporation's placental stem cell research and development division. Previously, he was Executive Vice President and Chief Operations Officer at Celgene. Mr. Karsen served as President and Chief Executive Officer at Pearl Therapeutics, a privately-held biotechnology company that was subsequently acquired by Astra-Zeneca, from February 2009 until July 2010. From 2004 to 2009, Mr. Karsen was Senior Vice President and Head of Worldwide Business Development at Celgene and was also responsible for emerging businesses as President, Asia/Pacific Region. Mr. Karsen also held executive roles at Human Genome Sciences, Bristol-Myers Squibb, Genentech and Abbott Laboratories. In addition, Mr. Karsen was a General Partner at Pequot Ventures. Mr. Karsen is a member of the Board of Directors of the Biotechnology Industry Organization (BIO) and a member of the Executive Committee; he is a member of the Board of Directors for the Life Sciences Foundation; a member of the Board of Directors of Agios Pharmaceuticals; and a member of the Board of Directors of Aquilla, Inc. Mr. Karsen has a Masters of Management degree from Northwestern University's Kellogg Graduate School of Management, a Masters in Teaching of Biology from Duke University, and a B.S. in Biological Sciences from the University of Illinois, Urbana.

Gordon A. Troup has served as a director of Navidea since July 2008. Mr. Troup served as President of the Nuclear Pharmacy Services business at Cardinal Health, Inc. (Cardinal), a multinational medical products and services company, from January 2003 until his retirement in December 2007. Mr. Troup joined Cardinal Health in 1990 and was appointed Group President of Pharmaceutical Distribution and Specialty Distribution Services in 1999. Prior to joining Cardinal Health, Mr. Troup was employed for 10 years by American Hospital Supply Corporation and for 3 years by Zellerbach Paper, a Mead Company. Mr. Troup is currently a partner and Chairman of the Board of Scioto Properties, LLC, a provider of group homes to the developmentally disabled nationwide, and Chairman of the Advisory Board of Guild Associates, Inc., a chemical engineering and research and development company serving the energy and military community. Mr. Troup is also a member of several national healthcare trade organizations and is active in a number of not-for-profit organizations. Mr. Troup has a B.S. degree in Business Management from San Diego State University.

Directors whose terms continue until the 2016 Annual Meeting:

Brendan A. Ford has served as a director of Navidea since July 2010. Since 2007, Mr. Ford has been a partner in Talisman Capital Partners, a private investment partnership focusing on middle-market companies. From 1991 through 2007, Mr. Ford served in various executive positions including Executive Vice President, Business Development and Corporate Strategy with Cardinal Health, Inc., primarily in capacities related to mergers, acquisitions and related strategic activities, and was involved in over $19 billion in acquisition and disposition transactions for Cardinal. Prior to his service with Cardinal Health, Mr. Ford practiced law with Baker and Hostetler from 1986 to 1991. From 1980 to 1983, Mr. Ford was employed by Touche Ross LLP as a certified public accountant. Mr. Ford has a B.S. in Business from Miami University, and a J.D. from The Ohio State University. Mr. Ford serves as a director and board committee member for several privately held companies.

Eric K. Rowinsky, M.D. has served as a director of Navidea since July 2010. Dr. Rowinsky has served as the Head of Research and Development and Chief Medical Officer of Stemline Therapeutics, Inc. since January 2012. From 2005 to 2009, he served as the Chief Medical Officer and Executive Vice President of Clinical Development, Medical Affairs and Regulatory Affairs of ImClone Systems Incorporated, a life sciences company. Prior to that, Dr. Rowinsky held several positions at the

Cancer Therapy & Research Center's Institute of Drug Development, including Director of the Institute, Director of Clinical Research and SBC Endowed Chair for Early Drug Development, and concurrently served as Clinical Professor of Medicine in the Division of Medical Oncology at the University of Texas Health Science Center at San Antonio. Dr. Rowinsky was an Associate Professor of Oncology at the Johns Hopkins University School of Medicine and on active staff at the Johns Hopkins School of Medicine from 1987 to 1996. Dr. Rowinsky is a member of the boards of directors of Biogen Idec, Inc., BIND Therapeutics, Inc., and Coronado Biosciences, Inc., publicly-held life sciences companies. Dr. Rowinsky has extensive research and drug development experience, oncology expertise and broad scientific and medical knowledge.

Directors whose terms continue until the 2017 Annual Meeting:

Michael M. Goldberg, M.D. has served as a director of Navidea since November 2013. Dr. Goldberg has served as a Managing Partner of Montaur Capital Partners since January 2007. Dr. Goldberg served as the Chief Executive Officer of Emisphere Technologies, Inc., from August 1990 to January 2007 and as its President from August 1990 to October 1995. He served as Vice President of The First Boston Corp., where he was a founding member of the Healthcare Banking Group. Dr. Goldberg is or has been a director of Alliqua, Inc., Echo Therapeutics, Inc., AngioLight, Inc., Urigen Pharmaceuticals, Inc., and Adventrx Pharmaceuticals, Inc. Dr. Goldberg received a B.S. degree from Rensselaer Polytechnic Institute, an M.D. from Albany Medical College of Union University in 1982, and an M.B.A. from Columbia University Graduate School of Business in 1985.

Ricardo J. Gonzalez has served as President and Chief Executive Officer of Navidea since January 2015, and as Chief Executive Officer from October 2014 to December 2014. Prior to joining Navidea, Mr. Gonzalez held positions of increasing responsibility at Spectrum Pharmaceuticals, Inc. (Spectrum) from March 2008 to October 2014. While at Spectrum, Mr. Gonzalez led teams in the U.S. and abroad and played an active role in the evolution of the organization from a product development company to a global commercial enterprise. Most recently he was responsible for designing and leading the globalization and commercialization strategy for international markets including Europe, Asia, Middle East and Latin America. Of Mr. Gonzalez's over 20 years of experience in the pharmaceutical industry, 14 years have been focused in specialty markets, including HIV/AIDS, Hematology and Oncology. Mr. Gonzalez's prior experience includes roles in all aspects of product commercialization including sales, marketing, operations, distribution, managed markets, contracting, reimbursement, pricing and government affairs with several companies including Abraxis Oncology, Genzyme, Ligand Pharmaceuticals, Roche Laboratories and GlaxoSmithKline. Mr. Gonzalez earned his B.S. in Business Logistics from Penn State University.