

NAVIDEA BIOPHARMACEUTICALS, INC.
Form S-3/A
May 23, 2014

As filed with the Securities and Exchange Commission on May 23, 2014
Registration No. 333-195806

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 1

to

Form S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

NAVIDEA BIOPHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	31-1080091
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

5600 Blazer Parkway, Suite 200

Dublin, Ohio 43017-7550

(614) 793-7500

(Address, including zip code, and telephone number, including

area code, of registrant's principal executive offices)

Brent L. Larson

Executive Vice President and Chief Financial Officer

Navidea Biopharmaceuticals, Inc.

5600 Blazer Parkway, Suite 200

Dublin, Ohio 43017-7550

(614) 793-7500

(Name, address, including zip code, and telephone number,
including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective as permitted by market conditions.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: "

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. "

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. "

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

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company
(Do not check if a smaller reporting company)

Calculation of Registration Fee

Title of each class of securities to be registered	Amount to be registered⁽¹⁾	Proposed maximum offering price per share	Proposed maximum aggregate offering price⁽²⁾	Amount of registration fee⁽⁴⁾
Common Stock, \$0.001 par value				
Preferred Stock, \$0.001 par value				
Warrants				
Subscription Rights				
Purchase Contracts				
Units				
			\$ 100,000,000	(3)
Common Stock, \$0.001 par value	3,169,015	(4) \$ 3.83	(5) \$ 12,137,328	
Total			\$ 112,137,328	\$ 14,444 (6)

Except as described in note 4, this registration statement covers an indeterminate amount of the securities of each identified class registered hereunder as may from time to time be offered and issued hereunder at indeterminate prices, along with an indeterminate number of securities that may be issued upon exercise, settlement, exchange or conversion of securities offered or sold hereunder. Separate consideration may or may not be received for securities that are issuable upon conversion, exercise, or exchange of other securities. This registration statement also covers, pursuant to Rule 416 under the Securities Act, an indeterminate number of shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends, or similar transactions.

Except as described in note 4, the proposed maximum aggregate offering price per class of security will be determined from time to time by the Registrant in connection with the issuance by the Registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act. Securities registered hereby may be sold separately, together or in units with other securities registered hereby.

Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o). Except as described in note 4, the maximum aggregate offering price of the securities to be registered will not exceed \$100,000,000.

Pursuant to Rule 415(a)(6) under the Securities Act, the securities registered pursuant to this registration statement include unsold securities previously registered by the Registrant on the Registrant's registration statement on Form S-3 (Registration No. 333-173752) filed on April 27, 2011, and declared effective on May 9, 2011 (the "Prior Registration Statement"). The Prior Registration Statement registered the offer and sale of an indeterminate number of the securities of each identified class registered thereunder as shall have an aggregate initial offering price not to exceed \$100,000,000, a portion of which remain unsold as of the date of filing of this registration statement. The Registrant has determined to include in this registration statement unsold securities under the Prior Registration

Statement with an aggregate offering price of \$60,000,000, which includes up to 3,169,015 shares of common stock issuable upon exercise of outstanding warrants issued and sold under the Prior Registration Statement for a maximum aggregate offering price of \$12,137,328, as reflected in the table above (the “Unsold Securities”). The Registrant has determined to include in this registration statement the Unsold Securities. Pursuant to Rule 415(a)(6) under the Securities Act, the filing fee of \$6,966 relating to the Unsold Securities under the Prior Registration Statement will continue to be applied to such securities registered pursuant to this Registration Statement. The Registrant is also registering new securities on this Registration Statement with an aggregate offering price of \$52,137,328 (the “New Securities”), which aggregate offering price is not specified as to each class of security (see note (2)). To the extent that, after the filing date hereof and prior to the effectiveness of this Registration Statement, the Registrant sells any Unsold Securities pursuant to the Prior Registration Statement, the Registrant will identify in a pre-effective amendment to this Registration Statement the updated amount of Unsold Securities from the Prior Registration Statement to be included in this Registration Statement pursuant to Rule 415(a)(6) and the updated amount of New Securities to be registered on this Registration Statement. Pursuant to Rule 415(a)(6) under the Securities Act, the offering of the Unsold Securities under the Prior Registration Statement will be deemed terminated as of the date of effectiveness of this Registration Statement.

- (5) Represents the exercise price of the respective warrants used to calculate the maximum aggregate offering price of the common stock issuable upon exercise of such warrants. Such warrants are also exchangeable for no additional consideration for up to 3,848,340 shares of common stock, the issuance of which is registered pursuant to this registration statement.

The filing fee of \$6,966 relating to the Unsold Securities under the Prior Registration Statement was previously (6) paid. A filing fee of \$7,478 with respect to the New Securities is being paid in connection with the filing of this registration statement. See note (4) above.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement contains two prospectuses:

a base prospectus which covers the offering, issuance and sale of such indeterminate number of any security or combination of securities described therein which together shall have an aggregate initial offering price not to exceed \$100,000,000; and

a warrant exercise or exchange prospectus for the offering, issuance and sale of up to 3,848,340 shares of the Registrant's common stock pursuant to the exercise or exchange of warrants to purchase the Registrant's common stock outstanding on May 23, 2014.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The warrant exercise or exchange prospectus immediately follows the base prospectus.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated May 23, 2014

PROSPECTUS

Navidea biopharmaceuticals, INC.

\$100,000,000

Common Stock

Preferred Stock

Warrants

Subscription Rights

Purchase Contracts

Units

We may offer and sell, from time to time in one or more offerings, any security or combination of securities described in this prospectus having an aggregate initial offering price not exceeding \$100,000,000 on terms to be determined at the time of the offering.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

We will sell these securities directly to purchasers, or through agents on our behalf, or through underwriters or dealers as designated from time to time. If any agents or underwriters are involved in the sale of any of these securities, the applicable prospectus supplement will provide the names of the agents or underwriters and any applicable fees, commissions or discounts.

The last reported sale price of our common stock on May 22, 2014 was \$1.37 per share.

Our common stock is currently listed on the NYSE MKT under the symbol “NAVB.”

Investing in our securities involves a high degree of risk. Before investing in our securities, we recommend that you carefully read this entire prospectus, including the “Risk Factors” section beginning on page 3, any applicable supplements to this prospectus and the documents we file with the Securities and Exchange Commission from time to time.

Neither the Securities and Exchange Commission nor any state securities commission has approved of anyone’s investment in these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Navidea Biopharmaceuticals, Inc.

5600 Blazer Parkway, Suite 200

Dublin, OH 43017-7550

(614) 793-7500

The date of this prospectus is _____, 2014.

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the Commission, utilizing a “shelf” registration process. Under this shelf registration process, we may offer to sell the securities described in this prospectus, alone or in combination, in one or more offerings up to a total dollar amount of \$100,000,000. This prospectus provides you with a general description of the securities we may offer. We may add to or modify in a prospectus supplement any of the information contained in this prospectus or in the documents that we have incorporated into this prospectus by reference. To the extent that any statement made in a prospectus supplement conflicts with statements made in this prospectus, the statements made in the prospectus supplement will be deemed to modify or supersede those made in this prospectus. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering. You should read both this prospectus and any prospectus supplement, including all documents incorporated herein or therein by reference, together with additional information described under “Where You Can Find More Information and Incorporation by Reference.”

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and the accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or the accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

In this prospectus, “we,” “us,” “our” and “Navidea” refer to Navidea Biopharmaceuticals, Inc. and its subsidiaries.

ABOUT NAVIDEA BIOPHARMACEUTICALS, INC.

Navidea Biopharmaceuticals, Inc., a Delaware corporation, is a biopharmaceutical company focused on the development and commercialization of precision diagnostics. Toward that end, we are currently developing five pharmaceutical platforms:

Lymphoseek® (technetium Tc 99m tilmanocept) Injection is a novel, receptor-targeted, small-molecule radiopharmaceutical used in lymphatic mapping procedures that are performed to help evaluate patients with breast cancer and melanoma. Lymphoseek is designed to identify the lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. It was approved by the U.S. Food and Drug Administration (FDA) in March 2013, and launched commercially in the United States in May 2013.

Navidea's Manocept™ platform is predicated on the ability to specifically target the CD206 mannose receptor expressed on macrophages. This flexible and versatile 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 SPECT, PET, intra-operative and/or optical-fluorescence detection in a variety of disease states.

NAV4694 is a Fluorine-18 (F-18) radiolabeled positron emission tomography (PET) imaging agent being developed as an aid in the diagnosis of patients with signs or symptoms of cognitive impairment such as Alzheimer's disease (AD).

NAV5001 is an Iodine-123 (I-123) radiolabeled single photon emission computed tomography (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.

NAV 1800 (formerly RIGScan™) is a radiolabeled monoclonal antibody being developed as a diagnostic aid for use during surgery to help surgeons locate occult or metastatic cancer, with a primary focus on colorectal cancer.

The last four drug product platforms are still in development and must be cleared for marketing by the appropriate regulatory authorities before they can be sold in any markets.

We plan to evaluate opportunities to expand our product pipeline by acquiring at attractive valuations or engaging in license arrangements involving other drug development programs with substantial potential. Initially, we intend to focus on identifying later stage product opportunities within the radiopharmaceutical sector; however, we may evaluate opportunities in other sectors to the extent we become aware of them during our pipeline expansion evaluation process.

We were originally incorporated in Ohio in 1983 and reincorporated in Delaware in 1988. Our executive offices are located at 5600 Blazer Parkway, Suite 200, Dublin, Ohio 43017. Our telephone number is (614) 793-7500. Our corporate website is www.navidea.com. This reference to our website is a textual reference only. We do not incorporate the information on our website into this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

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.

Risks Relating to the Company

If we do not achieve commercial success with our approved product or if we do not successfully develop our 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 in the U.S. by the FDA in March 2013. Additional trials, one in head and neck cancer (NEO3-06) which is the focus of a supplemental New Drug Application (sNDA) that now has a Prescription Drug User Fee Act (PDUFA) target date of June 16, 2014, an ongoing trial in colorectal cancer and other planned investigator-sponsored trials, are anticipated to provide additional support for the potential expansion of Lymphoseek utilization into multiple other cancer types. A second sNDA aimed at expanding the Lymphoseek label to support more flexible utilization practices for Lymphoseek in lymphatic mapping and lymphoscintigraphy imaging has a PDUFA target date of October 16, 2014. We began generating revenues from product sales of Lymphoseek in the U.S. in the second quarter of 2013. A Marketing Authorization Application (MAA) for the registration of Lymphoseek in the European Union was submitted to the European Medicines Agency (EMA) in December 2012. Most recently, the EMA confirmed in March 2014 that the EMA is continuing its review of the MAA although the review is currently under a 'clock stop' as we prepare responses to questions from the EMA. As we continue to generate 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.

In addition, NAV4694, NAV5001, the Manocept platform, and NAV1800 are in various stages of clinical development. Regulatory approval for additional indications for Lymphoseek may not be successful, or if successful,

may not result in increased sales. Additional clinical trials for NAV4694, NAV5001, NAV1800, products based on our Manocept platform, 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, Alzheimer's disease, Parkinson's 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;

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.

If we are not successful in licensing or acquiring additional drug candidates or technologies to expand our product pipeline, our future product portfolio and potential profitability could be harmed.

One component of our business strategy is to in-license drug compounds developed by other pharmaceutical and biotechnology companies or academic research laboratories. All of our product candidates in clinical development are sourced or in-licensed from third parties, consisting of Lymphoseek, NAV4694, NAV5001, the Manocept platform, and NAV1800. We may not successfully acquire additional drug candidates or technologies to expand our product pipeline. The number of such candidates and technologies is limited. Competition among large pharmaceutical companies and biopharmaceutical companies for promising drug candidates and technologies is intense because such companies generally desire to expand their product pipelines through purchase or in-licensing. If we fail to expand our product pipeline, our potential future revenues may be adversely affected.

Clinical trials for our radiopharmaceutical 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.

During 2011, we successfully completed a second Phase 3 clinical trial in subjects with breast cancer or melanoma for our most advanced radiopharmaceutical product candidate, Lymphoseek. The Phase 3 clinical trials served as the basis for the approval of Lymphoseek in March 2013. We successfully completed a third Phase 3 clinical trial for Lymphoseek in subjects with head and neck cancer in 2013, the results of which are anticipated to provide support for the potential expansion of the product labeling for Lymphoseek to address other cancer types or potentially the enhanced indication for sentinel lymph node biopsy in certain cancers.

With respect to NAV4694, AstraZeneca completed clinical development through a Phase 2a level. We are currently supporting a Phase 2 trial that we initiated in September 2012, primarily to expand the safety database for the compound, and a Phase 2b trial in subjects with MCI initiated in March 2013. In June 2013, we initiated a Phase 3 autopsy-based trial to support registration in the U.S. and the EU.

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 initiated a Phase 2b program in DLB in April 2013, commencing an investigator-initiated study. We also initiated a Phase 3 trial in subjects with PD in December 2013. Each Phase 3 trial is the subject of a SPA agreement with the FDA.

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 March 2013 FDA approval, 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, there can be no assurance 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 be 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 radiopharmaceutical 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, a first-generation beta-amyloid imaging agent for which Eli Lilly received FDA approval in 2012 and marketing authorization in the EU in January 2013, florbetaben, from Piramal Enterprises, Imaging Division which received FDA approval in March 2014 and marketing authorization in the EU in February 2014, and flutemetamol from GE Healthcare which received FDA approval in October 2013. In addition, NAV5001, if approved, is expected to compete against a product marketed by GE Healthcare. 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, NAV4694, NAV5001 or NAV1800, 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, NAV4694, NAV5001 and NAV1800. 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, NAV4694, NAV5001 and NAV1800, 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, the NIH 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 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.

Holders of our Series B Preferred Stock may exercise their conversion right, and that could dilute your ownership and the net tangible book value per share of our common stock.

Each share of our Series B Preferred Stock is convertible at any time into 3,270 common shares. If holders of our Series B Preferred Stock exercise any or all of their 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.

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 (the Platinum Loan Agreement) with Platinum-Montaur Life Sciences, LLC (Platinum) 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 related to future drawdowns of debt under the Platinum Loan Agreement which 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, 2013, is not 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 and partisan 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, 2013, the Company had a stockholders' deficit of approximately \$4.0 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 \$1.11 per share and as high as \$3.31 per share during the 12-month period ended April 30, 2014. 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 May 1, 2013, and ending on April 30, 2014, the average daily trading volume for our common stock on the NYSE MKT was approximately 1.0 million 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.

If we make any acquisitions, we will incur a variety of costs and may never realize the anticipated benefits.

If appropriate opportunities become available, we may attempt to acquire businesses and assets that we believe are a strategic fit with our business. While we periodically are engaged in discussions regarding potential business or product acquisitions, we currently have no binding agreements to consummate any material acquisitions. If we pursue any such transaction, the process of negotiating the acquisition and integrating an acquired business and assets may result in operating difficulties and expenditures and may require significant management attention that would otherwise be available for ongoing development of our business whether or not any such transaction is ever consummated. Moreover, we may never realize the anticipated benefits of any acquisition. Future acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or amortization expenses related to goodwill and other intangible assets which could harm our business, financial condition, operating results and prospects and the trading price of our securities.

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.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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. This prospectus and the information incorporated by reference in this prospectus contain forward-looking statements. We sometimes use words such as “anticipate,” “believe,” “continue,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will” and similar expressions, as the

our management and our industry, to identify forward-looking statements. Forward-looking statements relate to our expectations, beliefs, plans, strategies, prospects, future performance, anticipated trends and other future events. Specifically, this prospectus and the information incorporated by reference in this prospectus contain forward-looking statements relating to, among other things:

our revenue;

our primary operating costs and expenses;

capital expenditures;

evaluation of possible acquisitions of, or investments in business, products and technologies; and

sufficiency of existing cash to meet operating requirements.

These statements involve known and unknown risks, uncertainties, and other factors that may cause our or our industry's past results, levels of activity, performance, or achievements to be materially different from any future results, levels of activity, performance, or achievements expressed or implied by such forward-looking statements. Actual results may differ materially. Some of the risks, uncertainties and assumptions that may cause actual results to differ from these forward-looking statements are described in "Risk Factors" and elsewhere in this prospectus, and may also be found in an accompanying prospectus supplement and in information incorporated by reference.

You should read this prospectus, the documents that we filed as exhibits to the registration statement of which this prospectus is a part and the documents that we incorporate by reference in this prospectus completely and with the understanding that our future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements, and we assume no obligation to update these forward-looking statements publicly for any reason.

WHERE YOU CAN FIND MORE INFORMATION

AND INCORPORATION BY REFERENCE

We have filed a registration statement on Form S-3 with the Securities and Exchange Commission. This prospectus does not contain all of the information in the registration statement. In addition, we file annual, quarterly and special reports, proxy statements and other information with the Commission. Our Commission filings are available to the public over the Internet at the Commission's web site at <http://www.sec.gov>. You may also read and copy any document we file with the Commission at its public reference facilities at 100 F Street, N.E., Washington, DC 20549. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the Commission at 100 F Street, N.E., Washington, DC 20549. Please call the Commission at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

We "incorporate by reference" into this prospectus the information we file with the Commission (Commission file number 001-35076), which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. Information that we file with the Commission after the date of this prospectus will automatically update this prospectus. We incorporate by reference the documents listed below, and any filings we make with the Commission under Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934 after the initial filing of the registration statement that contains this prospectus (except for information furnished and not filed with the Commission in a Current Report on Form 8-K):

our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the Commission on March 14, 2014;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, filed with the Commission on May 9, 2014;

our Current Reports on Form 8-K, dated January 1, 2014 (filed January 2, 2014), dated January 28, 2014 (filed February 3, 2014), dated February 17, 2014 (filed February 19, 2014), dated March 4, 2014 (filed March 7, 2014), dated March 10, 2014 (filed March 11, 2014), dated April 21, 2014 (filed April 24, 2014), and dated May 15, 2014 (filed May 19, 2014); and

the description of our common stock which is contained in our Form 8-A filed with the Commission pursuant to Section 12 of the Securities Exchange Act of 1934, as amended, as updated in any amendment or report filed for the purpose of updating such description.

Information furnished by us in Current Reports on Form 8-K under Items 2.02 and 7.01 (and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) is expressly not incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge, upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You may request a copy of these filings at no cost, by writing to or telephoning us at:

Navidea Biopharmaceuticals, Inc.

Attn: Brent L. Larson

5600 Blazer Parkway, Suite 200

Dublin, Ohio 43017-7550

(614) 793-7500

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we intend to use the net proceeds from the sale of securities under this prospectus for general corporate purposes, which may include additions to working capital, repayment of indebtedness and financing capital expenditures and licenses or acquisitions. The prospectus supplement relating to a particular offering of securities by us will identify the use of proceeds for that offering.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is only a summary and is subject to the provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which are included as exhibits to the registration statement of which this prospectus forms a part, and provisions of applicable law.

Our certificate of incorporation authorizes our board of directors to issue 200,000,000 shares of common stock, \$0.001 par value per share, and 5,000,000 shares of undesignated preferred stock, \$0.001 par value per share. As of April 30, 2014, 150,724,574 shares of common stock were issued and outstanding, and 3,143 shares of preferred stock were issued and outstanding.

Common Stock

Dividends

Each share of common stock is entitled to receive an equal dividend, if one is declared, which is unlikely. We have never paid dividends on our common stock and do not intend to do so in the foreseeable future. We intend to retain any future earnings to finance our growth. See Risk Factors.

Liquidation

If our company is liquidated, any assets that remain after the creditors are paid, and the owners of preferred stock receive any liquidation preferences, will be distributed to the owners of our common stock pro-rata.

Voting Rights

Each share of our common stock entitles the owner to one vote. There is no cumulative voting. A simple majority can elect directors at a given meeting and the minority would not be able to elect any directors at that meeting.

Preemptive Rights

Owners of our common stock have no preemptive rights. We may sell shares of our common stock to third parties without first offering it to current stockholders.

Redemption Rights

We do not have the right to buy back shares of our common stock except in extraordinary transactions such as mergers and court approved bankruptcy reorganizations. Owners of our common stock do not ordinarily have the right to require us to buy their common stock. We do not have a sinking fund to provide assets for any buy back.

Conversion Rights

Shares of our common stock cannot be converted into any other kind of stock except in extraordinary transactions, such as mergers and court approved bankruptcy reorganizations.

Preferred Stock

Our certificate of incorporation authorizes our board of directors to issue “blank check” preferred stock. The board of directors may divide this stock into series and set their rights. On December 26, 2007, the board of directors designated 3,000 shares of preferred stock as Series A 8% Cumulative Convertible Preferred Stock. On December 5, 2008, we issued 3,000 shares of Series A 8% Cumulative Convertible Preferred Stock (Series A Preferred Stock) to Platinum-Montaur Life Sciences, LLC (Platinum). On June 22, 2010, the board of directors designated 10,000 shares of preferred stock as Series B Convertible Preferred Stock, \$0.001 par value (Series B Preferred Stock), and 1,000 shares of preferred stock as Series C Convertible Preferred Stock, \$0.001 par value (Series C Preferred Stock). On June 22, 2010, Platinum surrendered all 3,000 shares of Series A Preferred Stock issued to it on December 5, 2008. On June 22, 2010, we issued 10,000 shares of Series B Preferred Stock to Platinum, and 1,000 shares of Series C Preferred Stock to David C. Bupp, our former president and chief executive officer, and Cynthia B. Gochoco, both individually and as co-executors of the Estate of Walter H. Bupp, referred to as the Bupp Investors. During 2011 and 2012, Platinum converted 917 and 3,063 shares, respectively, of Series B Preferred Stock into 2,998,590 and 10,016,010 shares, respectively, of the Company’s common stock. On November 27, 2012, pursuant to a Securities Exchange Agreement with the Company, Platinum Partners Value Arbitrage Fund, L.P. (PPVA), an affiliate of Platinum, exchanged 3,001,860 shares of our common stock for 918 shares of Series B Preferred Stock. On December 31, 2012, all issued and outstanding shares of Series C Preferred Stock automatically converted into 3,226,000 shares of common stock pursuant to the terms of the Company’s Series C certificate of designations. On June 25, 2013, the Company and Platinum entered into a Warrant Exercise Agreement, pursuant to which Platinum exercised its Series X Warrant and Series AA Warrant for 2,364.9 shares of our Series B Preferred Stock, which are convertible into 7,733,223 shares of our common stock in the aggregate (3,270 shares of common stock per preferred share). During 2013 and in 2014 through April 30, 2014, Platinum converted 1,737.9 and 4,422 shares, respectively, of Series B Preferred Stock into 5,682,933 and 14,459,940 shares, respectively, of the Company’s common stock.

The Series B Preferred Stock ranks senior to our common stock.

Shares of our Series B Preferred Stock have class voting rights which limit our ability to carry out certain corporate actions. If 25% or more of our Series B Preferred Stock is outstanding, we must obtain the affirmative vote of a majority of the shares of such series to repurchase, redeem or pay dividends on our common stock, or effect any distribution with respect to common stock. In addition, if 25% of our Series B Preferred Stock is outstanding, subject to certain exceptions described in the Series B certificate of designations, we may not issue common stock or a common stock equivalent for a per share effective price less than \$1.35. Except as otherwise provided in the Series B

certificate of designations, we may not amend, alter or repeal the provisions of such series so as to adversely affect any right, preference or voting power of the Series B Preferred Stock without obtaining the affirmative vote or consent of the holders of a majority of such series.

Platinum and PPVA currently hold an aggregate of 3,143 shares of Series B Preferred Stock, which they may convert at any time into an aggregate of 10,277,610 shares of our common stock. Each share of Series B Preferred Stock converts into 3,270 common shares. The applicable certificate of designations provides for adjustments to the conversion rate upon certain corporate events, including stock splits, combinations, substitutions and certain other distributions. The Series B Preferred Stock is automatically convertible upon the occurrence of certain automatic conversion events described in the Series B certificate of designations.

Pursuant to the Series B certificate of designations, a conversion of shares of Series B Preferred Stock cannot result in the number of shares of common stock when aggregated with all other shares of common stock owned by such holder, to exceed 9.99% of all of our common stock outstanding at such time, unless such holder provides us with 61 days' notice that such holder would like to waive this restriction with respect to any or all of the shares of common stock issuable upon conversion of Series B Preferred Stock.

The board of directors may, without prior stockholder approval, issue any of the remaining 4,996,857 shares of authorized preferred stock with dividend, liquidation, conversion, voting or other rights which could adversely affect the relative voting power or other rights of the common stock. Preferred stock could be used as a method of discouraging, delaying, or preventing a take-over of our company. If we do issue preferred stock in the future, it could have a dilutive effect upon the common stock. See "Risk Factors."

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock in one or more series. We may issue warrants independently or together with common stock, and the warrants may be traded separate and apart from our common stock. Each series of warrants will be issued under a warrant agreement, as described in the applicable prospectus supplement. We urge you to read any applicable warrant agreements, because those documents, and not these descriptions, define your rights as a holder of warrants. A copy of the form of warrant agreement reflecting the provisions of the warrants in a particular offering will be filed as an exhibit to a current report on form 8-K, to be incorporated into the registration statement of which this prospectus constitutes a part prior to the issuance of any warrants.

The applicable prospectus supplement will describe the terms of the warrants offered thereby and the warrant agreement relating to such warrants, including but not limited to the following:

- the offering price or prices;
- the aggregate amount of common stock that may be purchased upon exercise of such warrants and minimum number of warrants that are exercisable;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the number of securities, if any, with which such warrants are being offered and the number of such warrants being offered with each security;
- the date on and after which such warrants and the related securities, if any, will be transferrable separately;
- the amount of securities purchasable upon exercise of each warrant and the price at which the securities may be purchased upon such exercise, and events or conditions under which the amount of securities may be subject to adjustment;
- the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;
- the circumstances, if any, which will cause the warrants to be deemed to be automatically exercised;
- any material risk factors, if any, relating to such warrants;
- the identity of any warrant agent; and
- any other terms of such warrants (which shall not be inconsistent with the provisions of the warrant agreement).

The terms of the warrants that we offer may or may not have the same material terms as our currently outstanding warrants.

Prior to the exercise of any warrants, holders of such warrants will not have any rights of holders of the securities purchasable upon such exercise, including the right to receive payments of dividends, if any, on the securities purchasable upon such exercise, statutory appraisal rights or the right to vote such underlying securities. Prospective purchasers of warrants should be aware that material U.S. federal income tax, accounting and other considerations may be applicable to instruments such as warrants.

DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase common stock, preferred stock, or other securities. We may issue subscription rights independently or together with any other offered security, which may or may not be transferable by the securityholder. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we may offer will contain the specific terms of the subscription rights. These terms may include the following:

- the price, if any, for the subscription rights;
- the exercise price payable for each common stock, preferred stock, or other securities upon the exercise of the subscription rights;
- the number of subscription rights issued to each securityholder;
- the number and terms of each common stock, preferred stock, or other securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any provisions for adjustment of the number or amount of securities receivable upon exercise of the subscription rights or the exercise price of the subscription rights;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities; and
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate or subscription rights agreement, which will be filed with the Commission if we offer subscription rights. For more information on how you can obtain copies of any subscription rights certificate or subscription rights agreement if we offer subscription rights, see the section entitled "Where You Can Find More Information." We urge you to read the applicable subscription rights certificate, the applicable subscription rights agreement and any applicable prospectus supplement in their entirety.

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts for the purchase or sale of common stock, preferred stock or other securities issued by us or by third parties as specified in the applicable prospectus supplement. Each purchase contract will entitle the holder thereof to purchase or sell, and obligate us to sell or purchase on specified dates, such securities at a specified purchase price, which may be based on a formula, all as set forth in the applicable prospectus supplement. We may, however, satisfy our obligations, if any, with respect to any purchase contract by delivering the cash value of such purchase contract or the cash value of the securities otherwise deliverable, as set forth in the applicable prospectus supplement. The applicable prospectus supplement will also specify the methods by which the holders may purchase or sell such securities, and any acceleration, cancellation or termination provisions or other provisions relating to the settlement of a purchase contract. The price per security and the number of securities may be fixed at the time the purchase contracts are entered into or may be determined by reference to a specific formula set forth in the applicable purchase contracts.

The purchase contracts may be issued separately or as part of units consisting of a purchase contract and debt securities or debt obligations of third parties, including U.S. treasury securities, or any other securities described in the applicable prospectus supplement or any combination of the foregoing, securing the holders' obligations to purchase the securities under the purchase contracts, which we refer to herein as "purchase units."

The purchase contracts may require holders to secure their obligations under the purchase contracts in a specified manner. The purchase contracts also may require us to make periodic payments to the holders of the purchase contracts or the purchase units, as the case may be, or vice versa, and those payments may be unsecured or pre-funded on some basis.

The prospectus supplement relating to any purchase contracts or purchase units we may offer will contain the specific terms of the purchase contracts or purchase units. These terms may include the following:

- whether the purchase contracts obligate the holder to purchase or sell, or both, our common stock, preferred stock, or debt securities, and the nature and amount of each of those securities, or method of determining those amounts;
- whether the purchase contracts are to be prepaid or not;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of our common stock or preferred stock;
- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts; and
- whether the purchase contracts will be issued in fully registered global form.

The description in the applicable prospectus supplement of any purchase contract or purchase unit we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable purchase contract or purchase unit, which will be filed with the Commission if we offer purchase contracts or purchase units. For more information on how you can obtain copies of any purchase contract or purchase unit we may offer, see the section entitled “Where You Can Find More Information.” We urge you to read the applicable purchase contract or applicable purchase unit and any applicable prospectus supplement in their entirety.

DESCRIPTION OF UNITS

We may issue units comprised of one or more of the other securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. A unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and

any additional terms of the governing unit agreement.

The applicable prospectus supplement will describe the terms of any units. The preceding description and any description of units in the applicable prospectus supplement does not purport to be complete and is subject to and is qualified in its entirety by reference to the unit agreement and, if applicable, collateral arrangements and depositary arrangements relating to such units.

Anti-Takeover Charter Provisions and Laws

Some features of our certificate of incorporation and bylaws and the Delaware General Corporation Law (DGCL), which are further described below, may have the effect of deterring third parties from making takeover bids for control of our company or may be used to hinder or delay a takeover bid. This would decrease the chance that our stockholders would realize a premium over market price for their shares of common stock as a result of a takeover bid. See Risk Factors.

Limitations on Stockholder Actions

Our certificate of incorporation provides that stockholder action may only be taken at a meeting of the stockholders. Thus, an owner of a majority of the voting power could not take action to replace the board of directors, or any class of directors, without a meeting of the stockholders, nor could he amend the bylaws without presenting the amendment to a meeting of the stockholders. Furthermore, under the provisions of the certificate of incorporation and bylaws, only the board of directors has the power to call a special meeting of stockholders. Therefore, a stockholder, even one who owns a majority of the voting power, may neither replace sitting board of directors members nor amend the bylaws before the next annual meeting of stockholders.

Advance Notice Provisions

Our bylaws establish advance notice procedures for the nomination of candidates for election as directors by stockholders, as well as for other stockholder proposals to be considered at annual meetings. Generally, we must receive a notice of intent to nominate a director or raise any other matter at a stockholder meeting not less than 120 days before the first anniversary of the mailing of our proxy statement for the previous year's annual meeting. The notice must contain required information concerning the person to be nominated or the matters to be brought before the meeting and concerning the stockholder submitting the proposal.

Delaware Law

We are incorporated in Delaware, and as such are subject to Section 203 of the DGCL, which provides that a corporation may not engage in any business combination with an interested stockholder during the three years after the stockholder becomes an interested stockholder unless:

- the corporation's board of directors approved in advance either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- the interested stockholder owned at least 85 percent of the corporation's voting stock at the time the transaction commenced; or
- the business combination is approved by the corporation's board of directors and the affirmative vote of at least two-thirds of the voting stock which is not owned by the interested stockholder.

An interested stockholder is anyone who owns 15 percent or more of a corporation's voting stock, or who is an affiliate or associate of the corporation and was the owner of 15 percent or more of the corporation's voting stock at any time within the previous three years; and the affiliates and associates of any those persons. Section 203 of the DGCL makes

it more difficult for an interested stockholder to implement various business combinations with our Company for a three-year period, although our stockholders may vote to exclude it from the law's restrictions.

Classified Board

Our certificate of incorporation and bylaws divide our board of directors into three classes with staggered three year terms. There are currently seven directors. Two classes are comprised of two directors each and a third class is comprised of three directors. At each annual meeting of stockholders, the terms of one class of directors will expire and the newly nominated directors of that class will be elected for a term of three years. The board of directors will be able to determine the total number of directors constituting the full board of directors and the number of directors in each class, but the total number of directors may not exceed nine nor may the number of directors in any class exceed six. No reduction in the total number of directors or in the number of directors in a given class will have the effect of removing a director from office or reducing the term of any then sitting director. Stockholders may only remove directors for cause. If the board of directors increases the number of directors in a class, it will be able to fill the vacancies created for the full remaining term of a director in that class even though the term may extend beyond the next annual meeting. The directors will also be able to fill any other vacancies for the full remaining term of the director whose death, resignation or removal caused the vacancy.

A person who has a majority of the voting power at a given meeting will not in any one year be able to replace a majority of the directors since only one class of the directors will stand for election in any one year. As a result, at least two annual meeting elections will be required to change the majority of the directors by the requisite vote of stockholders. The purpose of classifying the board of directors is to provide for a continuing body, even in the face of a person who accumulates a sufficient amount of voting power, whether by ownership or proxy or a combination, to have a majority of the voting power at a given meeting and who may seek to take control of our Company without paying a fair premium for control to all of the owners of our common stock. This will allow the board of directors time to negotiate with such a person and to protect the interests of the other stockholders who may constitute a majority of the shares not actually owned by that person. However, it may also have the effect of deterring third parties from making takeover bids for control of our Company or may be used to hinder or delay a takeover bid.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company, located in New York, New York.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, “at-the-market” offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities separately or together:

- through one or more underwriters or dealers in a public offering and sale by them;
- through a market maker or into an existing trading market, on an exchange or otherwise;
- through agents; and/or
- directly to one or more purchasers.

The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may solicit directly offers to purchase the securities being offered by this prospectus, and may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale and we will provide the name of any underwriter in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8.0% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

We will provide in the applicable prospectus supplement any compensation we will pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act or to contribute to payments they may be required to make in respect thereof.

The securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involves the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with any derivative transaction, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be identified in the applicable prospectus supplement or a post-effective amendment to the registration statement of which this prospectus is a part. In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. The underwriters, dealers and agents may engage in transactions with us, or perform services for us,

in the ordinary course of business.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, has been passed upon for us by Porter, Wright, Morris & Arthur LLP, 41 South High Street, Columbus, Ohio 43215.

EXPERTS

The financial statements as of December 31, 2013 and 2012 and for each of the three years in the period ended December 31, 2013 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2013 incorporated by reference in this Prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated May 23, 2014

PROSPECTUS

Navidea biopharmaceuticals, Inc.

3,848,340 Shares of Common Stock

Issuable Upon Exercise or Exchange of Warrants

This prospectus relates to our offer and sale of up to 3,848,340 shares of our common stock issuable upon the exercise or exchange of warrants. The warrants have an exercise price of \$3.83 per share of our common stock. The warrants are exercisable on or after the date of issuance and will terminate on the third anniversary of the date of issuance. For a more detailed description of the warrants, see the section entitled "Description of Warrants" beginning on page 22.

The last reported sale price of our common stock on May 22, 2014 was \$1.37 per share.

Our common stock is currently listed on the NYSE MKT under the symbol "NAVB."

Investing in our securities involves a high degree of risk. Before investing in our securities, we recommend that you carefully read this entire prospectus, including the "Risk Factors" section beginning on page 3, any applicable supplements to this prospectus and the documents we file with the Securities and Exchange Commission from time to time.

Neither the Securities and Exchange Commission nor any state securities commission has approved of anyone's investment in these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Navidea Biopharmaceuticals, Inc.

5600 Blazer Parkway, Suite 200

Dublin, OH 43017-7550

(614) 793-7500

The date of this prospectus is , 2014.

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ABOUT THIS PROSPECTUS

This prospectus relates to the offer and sale of up to 3,848,340 shares of our common stock (“Warrant Shares”) issuable upon the exercise or exchange of outstanding warrants (“September 24, 2013 Warrants”).

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and the accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or the accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

In this prospectus, “we,” “us,” “our” and “Navidea” refer to Navidea Biopharmaceuticals, Inc. and its subsidiaries.

ABOUT NAVIDEA BIOPHARMACEUTICALS, INC.

Navidea Biopharmaceuticals, Inc., a Delaware corporation, is a biopharmaceutical company focused on the development and commercialization of precision diagnostics. Toward that end, we are currently developing five pharmaceutical platforms:

Lymphoseek® (technetium Tc 99m tilmanocept) Injection is a novel, receptor-targeted, small-molecule radiopharmaceutical used in lymphatic mapping procedures that are performed to help evaluate patients with breast cancer and melanoma. Lymphoseek is designed to identify the lymph nodes that drain from a primary tumor, which have the highest probability of harboring cancer. It was approved by the U.S. Food and Drug Administration (FDA) in March 2013, and launched commercially in the United States in May 2013.

Navidea’s Manocept™ platform is predicated on the ability to specifically target the CD206 mannose receptor expressed on macrophages. This flexible and versatile 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 SPECT, PET, intra-operative and/or optical-fluorescence detection in a variety of disease states.

NAV4694 is a Fluorine-18 (F-18) radiolabeled positron emission tomography (PET) imaging agent being developed as an aid in the diagnosis of patients with signs or symptoms of cognitive impairment such as Alzheimer's disease (AD).

NAV5001 is an Iodine-123 (I-123) radiolabeled single photon emission computed tomography (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.

NAV 1800 (formerly RIGScan™) is a radiolabeled monoclonal antibody being developed as a diagnostic aid for use during surgery to help surgeons locate occult or metastatic cancer, with a primary focus on colorectal cancer.

The last four drug product platforms are still in development and must be cleared for marketing by the appropriate regulatory authorities before they can be sold in any markets.

We plan to evaluate opportunities to expand our product pipeline by acquiring at attractive valuations or engaging in license arrangements involving other drug development programs with substantial potential. Initially, we intend to focus on identifying later stage product opportunities within the radiopharmaceutical sector; however, we may evaluate opportunities in other sectors to the extent we become aware of them during our pipeline expansion evaluation process.

We were originally incorporated in Ohio in 1983 and reincorporated in Delaware in 1988. Our executive offices are located at 5600 Blazer Parkway, Suite 200, Dublin, Ohio 43017. Our telephone number is (614) 793-7500. Our corporate website is www.navidea.com. This reference to our website is a textual reference only. We do not incorporate the information on our website into this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

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.

Risks Relating to the Company

If we do not achieve commercial success with our approved product or if we do not successfully develop our 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 in the U.S. by the FDA in March 2013. Additional trials, one in head and neck cancer (NEO3-06) which is the focus of a supplemental New Drug Application (sNDA) that now has a Prescription Drug User Fee Act (PDUFA) target date of June 16, 2014, an ongoing trial in colorectal cancer and other planned investigator-sponsored trials, are anticipated to provide additional support for the potential expansion of Lymphoseek utilization into multiple other cancer types. A second sNDA aimed at expanding the Lymphoseek label to support more flexible utilization practices for Lymphoseek in lymphatic mapping and lymphoscintigraphy imaging has a PDUFA target date of October 16, 2014. We began generating revenues from product sales of Lymphoseek in the U.S. in the second quarter of 2013. A Marketing Authorization Application (MAA) for the registration of Lymphoseek in the European Union was submitted to the European Medicines Agency (EMA) in December 2012. Most recently, the EMA confirmed in March 2014 that the EMA is continuing its review of the MAA although the review is currently under a 'clock stop' as we prepare responses to questions from the EMA. As we continue to generate 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.

In addition, NAV4694, NAV5001, the Manocept platform, and NAV1800 are in various stages of clinical development. Regulatory approval for additional indications for Lymphoseek may not be successful, or if successful,

may not result in increased sales. Additional clinical trials for NAV4694, NAV5001, NAV1800, products based on our Manocept platform, 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, Alzheimer's disease, Parkinson's 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;

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.

If we are not successful in licensing or acquiring additional drug candidates or technologies to expand our product pipeline, our future product portfolio and potential profitability could be harmed.

One component of our business strategy is to in-license drug compounds developed by other pharmaceutical and biotechnology companies or academic research laboratories. All of our product candidates in clinical development are sourced or in-licensed from third parties, consisting of Lymphoseek, NAV4694, NAV5001, the Manocept platform, and NAV1800. We may not successfully acquire additional drug candidates or technologies to expand our product pipeline. The number of such candidates and technologies is limited. Competition among large pharmaceutical companies and biopharmaceutical companies for promising drug candidates and technologies is intense because such companies generally desire to expand their product pipelines through purchase or in-licensing. If we fail to expand our product pipeline, our potential future revenues may be adversely affected.

Clinical trials for our radiopharmaceutical 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.

During 2011, we successfully completed a second Phase 3 clinical trial in subjects with breast cancer or melanoma for our most advanced radiopharmaceutical product candidate, Lymphoseek. The Phase 3 clinical trials served as the basis for the approval of Lymphoseek in March 2013. We successfully completed a third Phase 3 clinical trial for Lymphoseek in subjects with head and neck cancer in 2013, the results of which are anticipated to provide support for the potential expansion of the product labeling for Lymphoseek to address other cancer types or potentially the enhanced indication for sentinel lymph node biopsy in certain cancers.

With respect to NAV4694, AstraZeneca completed clinical development through a Phase 2a level. We are currently supporting a Phase 2 trial that we initiated in September 2012, primarily to expand the safety database for the compound, and a Phase 2b trial in subjects with MCI initiated in March 2013. In June 2013, we initiated a Phase 3 autopsy-based trial to support registration in the U.S. and the EU.

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 initiated a Phase 2b program in DLB in April 2013, commencing an investigator-initiated study. We also initiated a Phase 3 trial in subjects with PD in December 2013. Each Phase 3 trial is the subject of a SPA agreement with the FDA.

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 March 2013 FDA approval, 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, there can be no assurance 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 be 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 radiopharmaceutical 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, a first-generation beta-amyloid imaging agent for which Eli Lilly received FDA approval in 2012 and marketing authorization in the EU in January 2013,

florbetaben, from Piramal Enterprises, Imaging Division which received FDA approval in March 2014 and marketing authorization in the EU in February 2014, and flutemetamol from GE Healthcare which received FDA approval in October 2013. In addition, NAV5001, if approved, is expected to compete against a product marketed by GE Healthcare. 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, NAV4694, NAV5001 or NAV1800, 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, NAV4694, NAV5001 and NAV1800. 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, NAV4694, NAV5001 and NAV1800, 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, the NIH 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 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.

Holders of our Series B Preferred Stock may exercise their conversion right, and that could dilute your ownership and the net tangible book value per share of our common stock.

Each share of our Series B Preferred Stock is convertible at any time into 3,270 common shares. If holders of our Series B Preferred Stock exercise any or all of their 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.

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 (the Platinum Loan Agreement) with Platinum-Montaur Life Sciences, LLC (Platinum) 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 related to future drawdowns of debt under the Platinum Loan Agreement which 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, 2013, is not 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 and partisan 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, 2013, the Company had a stockholders' deficit of approximately \$4.0 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 \$1.11 per share and as high as \$3.31 per share during the 12-month period ended April 30, 2014. 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 May 1, 2013 and ending on April 30, 2014, the average daily trading volume for our common stock on the NYSE MKT was approximately 1.0 million 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.

If we make any acquisitions, we will incur a variety of costs and may never realize the anticipated benefits.

If appropriate opportunities become available, we may attempt to acquire businesses and assets that we believe are a strategic fit with our business. While we periodically are engaged in discussions regarding potential business or product acquisitions, we currently have no binding agreements to consummate any material acquisitions. If we pursue any such transaction, the process of negotiating the acquisition and integrating an acquired business and assets may result in operating difficulties and expenditures and may require significant management attention that would otherwise be available for ongoing development of our business whether or not any such transaction is ever consummated. Moreover, we may never realize the anticipated benefits of any acquisition. Future acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or amortization expenses related to goodwill and other intangible assets which could harm our business, financial condition, operating results and prospects and the trading price of our securities.

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.

Risks Relating to the offering of the Warrant Shares

Management will have broad discretion as to the use of the proceeds of any exercise of the September 24, 2013 Warrants, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from any exercise of the September 24, 2013 Warrants and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

Purchasers in this offering will experience immediate dilution in the net tangible book value of their investment.

Purchasers of our common stock upon exercise of the September 24, 2013 Warrants will experience an immediate dilution in the net tangible book value of the common stock issued because the price per share of common stock upon exercise is substantially higher than the net tangible book value of each share of common stock outstanding immediately after exercise. Our net tangible book value on a pro forma basis, assuming the September 24, 2013 Warrants are exercised in full, as of March 31, 2014, is approximately \$5.0 million, or \$0.03 per share of common stock. Based on the exercise price of \$3.83 per share, if a holder of the September 24, 2013 Warrants exercises in full, the holder will suffer immediate and substantial dilution of \$3.80 per share in the net tangible book value of the common stock issued upon exercise.

Holders of our debt or preferred stock have liquidation and other rights that are senior to the rights of the holders of our common stock, and any future issuance of debt or preferred stock could adversely affect the market price of our common stock.

As of March 31, 2014, we had approximately \$33.2 million of outstanding indebtedness, and there were 3,403 shares of our Series B Preferred Stock issued and outstanding. Holders of our debt and preferred stock have liquidation and other rights that are senior to the rights of the holders of our common stock. Upon any voluntary or involuntary liquidation, dissolution or winding up, payment will be made to holders of our debt and preferred stock, including our Series B Preferred Stock, before any payment is made to the holders of our common stock. This will reduce the amount of our assets, if any, available for distribution to holders of our common stock. Because our decision to issue debt and preferred stock is dependent on market conditions and other factors that may be beyond our control, we cannot predict or estimate the amount, timing or nature of our future issuances. Any such future issuance could reduce the market price of our common stock.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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. This prospectus and the information incorporated by reference in this prospectus contain forward-looking statements. We sometimes use words such as “anticipate,” “believe,” “continue,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will” and similar expressions, as the our management and our industry, to identify forward-looking statements. Forward-looking statements relate to our expectations, beliefs, plans, strategies, prospects, future performance, anticipated trends and other future events. Specifically, this prospectus and the information incorporated by reference in this prospectus contain forward-looking statements relating to, among other things:

our revenue;

our primary operating costs and expenses;

capital expenditures;

evaluation of possible acquisitions of, or investments in business, products and technologies; and

sufficiency of existing cash to meet operating requirements.

These statements involve known and unknown risks, uncertainties, and other factors that may cause our or our industry's past results, levels of activity, performance, or achievements to be materially different from any future results, levels of activity, performance, or achievements expressed or implied by such forward-looking statements. Actual results may differ materially. Some of the risks, uncertainties and assumptions that may cause actual results to differ from these forward-looking statements are described in "Risk Factors" and elsewhere in this prospectus, and may also be found in an accompanying prospectus supplement and in information incorporated by reference.

You should read this prospectus, the documents that we filed as exhibits to the registration statement of which this prospectus is a part and the documents that we incorporate by reference in this prospectus completely and with the understanding that our future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements, and we assume no obligation to update these forward-looking statements publicly for any reason.

WHERE YOU CAN FIND MORE INFORMATION

AND INCORPORATION BY REFERENCE

We have filed a registration statement on Form S-3 with the Securities and Exchange Commission. This prospectus does not contain all of the information in the registration statement. In addition, we file annual, quarterly and special reports, proxy statements and other information with the Commission. Our Commission filings are available to the public over the Internet at the Commission's web site at <http://www.sec.gov>. You may also read and copy any document we file with the Commission at its public reference facilities at 100 F Street, N.E., Washington, DC 20549. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the Commission at 100 F Street, N.E., Washington, DC 20549. Please call the Commission at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

We "incorporate by reference" into this prospectus the information we file with the Commission (Commission file number 001-35076), which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. Information that we file with the Commission after the date of this prospectus will automatically update this prospectus. We incorporate by reference the documents listed below, and any filings we make with the Commission under Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934 after the initial filing of the registration statement that contains this prospectus (except for information furnished and not filed with the Commission in a Current Report on Form 8-K):

our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the Commission on March 14, 2014;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, filed with the Commission on May 9, 2014;

our Current Reports on Form 8-K, dated January 1, 2014 (filed January 2, 2014), dated January 28, 2014 (filed February 3, 2014), dated February 17, 2014 (filed February 19, 2014), dated March 4, 2014 (filed March 7, 2014), dated March 10, 2014 (filed March 11, 2014), dated April 21, 2014 (filed April 24, 2014), and dated May 15, 2014 (filed May 19, 2014); and

the description of our common stock which is contained in our Form 8-A filed with the Commission pursuant to Section 12 of the Securities Exchange Act of 1934, as amended, as updated in any amendment or report filed for the purpose of updating such description.

Information furnished by us in Current Reports on Form 8-K under Items 2.02 and 7.01 (and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) is expressly not incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge, upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You may request a copy of these filings at no cost, by writing to or telephoning us at:

Navidea Biopharmaceuticals, Inc.

Attn: Brent L. Larson

5600 Blazer Parkway, Suite 200

Dublin, Ohio 43017-7550

(614) 793-7500

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we intend to use the net proceeds from this offering for general corporate purposes, which may include additions to working capital, repayment of indebtedness and financing capital expenditures and licenses or acquisitions.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is only a summary and is subject to the provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which are included as exhibits to the registration statement of which this prospectus forms a part, and provisions of applicable law.

Our certificate of incorporation authorizes our board of directors to issue 200,000,000 shares of common stock, \$0.001 par value per share, and 5,000,000 shares of undesignated preferred stock, \$0.001 par value per share. As of April 30, 2014, 150,724,574 shares of common stock were issued and outstanding, and 3,143 shares of preferred stock were issued and outstanding.

Common Stock

Dividends

Each share of common stock is entitled to receive an equal dividend, if one is declared, which is unlikely. We have never paid dividends on our common stock and do not intend to do so in the foreseeable future. We intend to retain any future earnings to finance our growth. See Risk Factors.

Liquidation

If our company is liquidated, any assets that remain after the creditors are paid, and the owners of preferred stock receive any liquidation preferences, will be distributed to the owners of our common stock pro-rata.

Voting Rights

Each share of our common stock entitles the owner to one vote. There is no cumulative voting. A simple majority can elect directors at a given meeting and the minority would not be able to elect any directors at that meeting.

Preemptive Rights

Owners of our common stock have no preemptive rights. We may sell shares of our common stock to third parties without first offering it to current stockholders.

Redemption Rights

We do not have the right to buy back shares of our common stock except in extraordinary transactions such as mergers and court approved bankruptcy reorganizations. Owners of our common stock do not ordinarily have the right to require us to buy their common stock. We do not have a sinking fund to provide assets for any buy back.

Conversion Rights

Shares of our common stock cannot be converted into any other kind of stock except in extraordinary transactions, such as mergers and court approved bankruptcy reorganizations.

Preferred Stock

Our certificate of incorporation authorizes our board of directors to issue “blank check” preferred stock. The board of directors may divide this stock into series and set their rights. On December 26, 2007, the board of directors designated 3,000 shares of preferred stock as Series A 8% Cumulative Convertible Preferred Stock. On December 5, 2008, we issued 3,000 shares of Series A 8% Cumulative Convertible Preferred Stock (Series A Preferred Stock) to Platinum-Montaur Life Sciences, LLC (Platinum). On June 22, 2010, the board of directors designated 10,000 shares of preferred stock as Series B Convertible Preferred Stock, \$0.001 par value (Series B Preferred Stock), and 1,000 shares of preferred stock as Series C Convertible Preferred Stock, \$0.001 par value (Series C Preferred Stock). On June 22, 2010, Platinum surrendered all 3,000 shares of Series A Preferred Stock issued to it on December 5, 2008. On June 22, 2010, we issued 10,000 shares of Series B Preferred Stock to Platinum, and 1,000 shares of Series C Preferred Stock to David C. Bupp, our former president and chief executive officer, and Cynthia B. Gochoco, both individually and as co-executors of the Estate of Walter H. Bupp, referred to as the Bupp Investors. During 2011 and 2012, Platinum converted 917 and 3,063 shares, respectively, of Series B Preferred Stock into 2,998,590 and 10,016,010 shares, respectively, of the Company’s common stock. On November 27, 2012, pursuant to a Securities Exchange Agreement with the Company, Platinum Partners Value Arbitrage Fund, L.P. (PPVA), an affiliate of Platinum, exchanged 3,001,860 shares of our common stock for 918 shares of Series B Preferred Stock. On December 31, 2012, all issued and outstanding shares of Series C Preferred Stock automatically converted into 3,226,000 shares of common stock pursuant to the terms of the Company’s Series C certificate of designations. On June 25, 2013, the Company and Platinum entered into a Warrant Exercise Agreement, pursuant to which Platinum exercised its Series X Warrant and Series AA Warrant for 2,364.9 shares of our Series B Preferred Stock, which are convertible into 7,733,223 shares of our common stock in the aggregate (3,270 shares of common stock per preferred share). During 2013 and in 2014 through April 30, 2014, Platinum converted 1,737.9 and 4,422 shares, respectively, of Series B Preferred Stock into 5,682,933 and 14,459,940 shares, respectively, of the Company’s common stock.

The Series B Preferred Stock ranks senior to our common stock.

Shares of our Series B Preferred Stock have class voting rights which limit our ability to carry out certain corporate actions. If 25% or more of our Series B Preferred Stock is outstanding, we must obtain the affirmative vote of a majority of the shares of such series to repurchase, redeem or pay dividends on our common stock, or effect any distribution with respect to common stock. In addition, if 25% of our Series B Preferred Stock is outstanding, subject to certain exceptions described in the Series B certificate of designations, we may not issue common stock or a common stock equivalent for a per share effective price less than \$1.35. Except as otherwise provided in the Series B

certificate of designations, we may not amend, alter or repeal the provisions of such series so as to adversely affect any right, preference or voting power of the Series B Preferred Stock without obtaining the affirmative vote or consent of the holders of a majority of such series.

Platinum and PPVA currently hold an aggregate of 3,143 shares of Series B Preferred Stock, which they may convert at any time into an aggregate of 10,277,610 shares of our common stock. Each share of Series B Preferred Stock converts into 3,270 common shares. The applicable certificate of designations provides for adjustments to the conversion rate upon certain corporate events, including stock splits, combinations, substitutions and certain other distributions. The Series B Preferred Stock is automatically convertible upon the occurrence of certain automatic conversion events described in the Series B certificate of designations.

Pursuant to the Series B certificate of designations, a conversion of shares of Series B Preferred Stock cannot result in the number of shares of common stock when aggregated with all other shares of common stock owned by such holder, to exceed 9.99% of all of our common stock outstanding at such time, unless such holder provides us with 61 days' notice that such holder would like to waive this restriction with respect to any or all of the shares of common stock issuable upon conversion of Series B Preferred Stock.

The board of directors may, without prior stockholder approval, issue any of the remaining 4,996,857 shares of authorized preferred stock with dividend, liquidation, conversion, voting or other rights which could adversely affect the relative voting power or other rights of the common stock. Preferred stock could be used as a method of discouraging, delaying, or preventing a take-over of our company. If we do issue preferred stock in the future, it could have a dilutive effect upon the common stock. See "Risk Factors."

DESCRIPTION OF WARRANTS

The material terms and provisions of the September 24, 2013 Warrants, referred to throughout this section as the warrant, are summarized below. The Form of the warrant is filed as exhibit 4.1 to our form 8-K filed September 24, 2013, and is incorporated herein by reference.

Exercisability

The number of shares of common stock that may be issued upon the exercise of the warrant is up to an aggregate of 3,848,340 shares of our common stock. The warrant is exercisable until September 24, 2016. The holder of the warrant may exercise its warrant to purchase shares of our common stock on or before the expiration date by delivering an exercise notice, appropriately completed and duly signed, and payment of the aggregate exercise price by wire transfer (unless the cashless exercise procedure described below is permissible and specified in the exercise notice), for the number of shares with respect to which the warrant is being exercised. The warrant may be exercised in whole or in part, but only for full shares of common stock. Any portion of the warrant not exercised prior to the termination date shall be and become void and of no value. The absence of an effective registration statement or applicable exemption from registration does not alleviate our obligation to deliver common stock issuable upon exercise of the warrant.

The shares of common stock issuable on exercise of the warrant will be, when issued and paid for in accordance with the terms of the warrant, duly authorized, validly issued and fully paid and non-assessable. We will authorize and reserve at least that number of shares of common stock equal to the number of shares of common stock issuable upon exercise of the warrant.

Exercise Price

The exercise price per share of common stock purchasable upon exercise of the warrant is \$3.83 per share of common stock being purchased, which equals approximately 135% of the last reported bid price of our common stock on the

NYSE MKT as of the trading date prior to the date of closing of the offering of the warrant. The exercise price and number of shares issuable upon exercise are subject to appropriate adjustment in the event of stock dividends and distributions, stock splits, stock combinations, reclassifications and similar events affecting our common stock.

Exchange of Warrant

As an alternative to exercising the warrant in whole or in part, beginning six months after the date of issuance, if our common stock is then trading at a price at or lower than the warrant exercise price per share, a holder may, without the payment of additional consideration, exchange all or any portion of the warrant based on a formula for a number of shares of our common stock equal to the negotiated Black-Scholes value as defined below divided by the closing bid price of our common stock as of two trading days prior to such exchange (provided that if such closing bid price is less than \$2.00 per common share, it shall be deemed to be \$2.00 for purposes of this calculation).

The negotiated Black-Scholes value is defined as the value of an option for the number of shares equal to the portion of the warrant being exchanged at the applicable exchange date as such value is determined calculated using the Black Scholes Option Pricing Model obtained from the “OV” function on Bloomberg utilizing (i) an underlying price per share equal to the closing bid price of the common stock as of the trading day immediately preceding the date of issuance of the warrant, (ii) a risk-free interest rate corresponding to the 5-Year U.S. Treasury Note Swap Rate, (iii) a strike price equal to the exercise price in effect at the time of the applicable exchange, (iv) an expected volatility equal to 135% and (v) a deemed remaining term of the warrant of five years (regardless of the actual remaining term of the warrant). The negotiated Black-Scholes value would only change based on changes in the risk-free interest rate corresponding to the 5-Year U.S. Treasury Note Swap Rate at the time of an exchange.

Limitations on Exercise

The number of shares of common stock that may be acquired by the holder upon any exercise of the warrant will be limited to the extent necessary to ensure that, following such exercise (or other issuance), the total number of shares of common stock then beneficially owned by the holder and its affiliates and any other persons whose beneficial ownership of common stock would be aggregated with the holder’s for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended, does not exceed 9.9% of the total number of issued and outstanding shares of common stock (including for such purpose the shares of common stock issuable upon such exercise), which we refer to as the beneficial ownership limitation.

In addition, the number of shares of common stock that may be acquired by the holder upon any exercise or exchange of the warrant will be limited (subject to certain exceptions) to the extent necessary to ensure that, following such exercise or exchange, the total number of shares of common stock issued in the applicable offering (including shares issued in connection with prior warrant exercises or exchanges) does not exceed 19.99% of our total issued and outstanding shares immediately preceding the closing of the applicable offering. We refer to the 19.99% limitation as the share cap.

Cashless Exercise

If we do not meet certain conditions, including (i) there is no effective registration statement registering, or the prospectus contained therein is not available for, the issuance of the shares of common stock underlying the warrant to the holder, (ii) the shares of common stock underlying the warrant are not freely tradeable by the holder without restriction, (iii) there is a limitation applicable with respect to the issuance of any shares of common stock underlying the warrant (other than the beneficial ownership limitation or the share cap described above), (iv) we are not fully reporting under the Exchange Act, or (v) other conditions set forth in the warrant, then the holder may, in its sole discretion, elect a cashless exercise in the exercise notice. The number of shares to be issued would be determined by a formula based on the total number of shares with respect to which the warrant is being exercised, the closing sale price for a share of our common stock on the trading day immediately preceding the warrant exercise notice is

received and the applicable exercise price of the warrant.

Mandatory Exercise

Under certain circumstances, in the event that our common stock trades at a price that is 25% or more above the exercise price of the warrant for a period of 20 of 30 consecutive trading days (with an average daily volume equal to or greater than \$1.0 million), we may require the holder of the warrant to fully exercise the warrant for cash (subject to certain additional conditions).

No Short Sales

For as long as the warrant is outstanding, the holder shall not engage in any short sales of our common stock, except certain short sales may be permissible if made one trading day prior to the exercise of such warrant.

No Established Public Trading Market

There is no established public trading market for the warrant, and we do not expect a market to develop. We do not intend to apply to list the warrant on any securities exchange. Without an active market, the liquidity of the warrant will be limited.

Anti-Takeover Charter Provisions and Laws

Some features of our certificate of incorporation and bylaws and the Delaware General Corporation Law (DGCL), which are further described below, may have the effect of deterring third parties from making takeover bids for control of our company or may be used to hinder or delay a takeover bid. This would decrease the chance that our stockholders would realize a premium over market price for their shares of common stock as a result of a takeover bid. See Risk Factors.

Limitations on Stockholder Actions

Our certificate of incorporation provides that stockholder action may only be taken at a meeting of the stockholders. Thus, an owner of a majority of the voting power could not take action to replace the board of directors, or any class of directors, without a meeting of the stockholders, nor could he amend the bylaws without presenting the amendment to a meeting of the stockholders. Furthermore, under the provisions of the certificate of incorporation and bylaws, only the board of directors has the power to call a special meeting of stockholders. Therefore, a stockholder, even one who owns a majority of the voting power, may neither replace sitting board of directors members nor amend the bylaws before the next annual meeting of stockholders.

Advance Notice Provisions

Our bylaws establish advance notice procedures for the nomination of candidates for election as directors by stockholders, as well as for other stockholder proposals to be considered at annual meetings. Generally, we must receive a notice of intent to nominate a director or raise any other matter at a stockholder meeting not less than 120 days before the first anniversary of the mailing of our proxy statement for the previous year's annual meeting. The notice must contain required information concerning the person to be nominated or the matters to be brought before the meeting and concerning the stockholder submitting the proposal.

Delaware Law

We are incorporated in Delaware, and as such are subject to Section 203 of the DGCL, which provides that a corporation may not engage in any business combination with an interested stockholder during the three years after the stockholder becomes an interested stockholder unless:

the corporation's board of directors approved in advance either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
the interested stockholder owned at least 85 percent of the corporation's voting stock at the time the transaction commenced; or
the business combination is approved by the corporation's board of directors and the affirmative vote of at least two-thirds of the voting stock which is not owned by the interested stockholder.

An interested stockholder is anyone who owns 15 percent or more of a corporation's voting stock, or who is an affiliate or associate of the corporation and was the owner of 15 percent or more of the corporation's voting stock at any time within the previous three years; and the affiliates and associates of any those persons. Section 203 of the DGCL makes it more difficult for an interested stockholder to implement various business combinations with our Company for a three-year period, although our stockholders may vote to exclude it from the law's restrictions.

Classified Board

Our certificate of incorporation and bylaws divide our board of directors into three classes with staggered three year terms. There are currently seven directors. Two classes are comprised of two directors each and a third class is comprised of three directors. At each annual meeting of stockholders, the terms of one class of directors will expire and the newly nominated directors of that class will be elected for a term of three years. The board of directors will be able to determine the total number of directors constituting the full board of directors and the number of directors in each class, but the total number of directors may not exceed nine nor may the number of directors in any class exceed six. No reduction in the total number of directors or in the number of directors in a given class will have the effect of removing a director from office or reducing the term of any then sitting director. Stockholders may only remove directors for cause. If the board of directors increases the number of directors in a class, it will be able to fill the vacancies created for the full remaining term of a director in that class even though the term may extend beyond the next annual meeting. The directors will also be able to fill any other vacancies for the full remaining term of the director whose death, resignation or removal caused the vacancy.

A person who has a majority of the voting power at a given meeting will not in any one year be able to replace a majority of the directors since only one class of the directors will stand for election in any one year. As a result, at least two annual meeting elections will be required to change the majority of the directors by the requisite vote of stockholders. The purpose of classifying the board of directors is to provide for a continuing body, even in the face of a person who accumulates a sufficient amount of voting power, whether by ownership or proxy or a combination, to have a majority of the voting power at a given meeting and who may seek to take control of our Company without paying a fair premium for control to all of the owners of our common stock. This will allow the board of directors time to negotiate with such a person and to protect the interests of the other stockholders who may constitute a majority of the shares not actually owned by that person. However, it may also have the effect of deterring third parties from making takeover bids for control of our Company or may be used to hinder or delay a takeover bid.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company, located in New York, New York.

PLAN OF DISTRIBUTION

The common stock referenced on the cover page of this prospectus will be offered solely by us and will be issued and sold upon the exercise or exchange of the warrants described herein.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, has been passed upon for us by Porter, Wright, Morris & Arthur LLP, 41 South High Street, Columbus, Ohio 43215.

EXPERTS

The financial statements as of December 31, 2013 and 2012 and for each of the three years in the period ended December 31, 2013 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2013 incorporated by reference in this Prospectus have been so incorporated in reliance on the reports

of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the expenses expected to be incurred by our Company in connection with the issuance and distribution of the securities being registered.

Commission registration fee	\$7,478
Legal fees and expenses	**
Accounting fees	**
Printing expenses	**
Miscellaneous	**
Total	\$**

** Estimated expenses are presently not known and cannot be estimated.

Item 15. Indemnification of Directors and Officers.

Section 145 of the General Corporation Law of the State of Delaware (Section 145) provides that directors and officers of Delaware corporations may, under certain circumstances, be indemnified against expenses (including attorneys' fees) and other liabilities actually and reasonably incurred by them as a result of any suit brought against them in their capacity as a director or officer, if they acted in good faith and in a manner they reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, if they had no reasonable cause to believe their conduct was unlawful. Section 145 also provides that directors and officers may also be indemnified against expenses (including attorneys' fees) incurred by them in connection with a derivative suit if they acted in good faith and in a manner they reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification may be made without court approval if such person was adjudged liable to the corporation.

Article V of the Company's bylaws contains provisions which require that the Company indemnify its officers, directors, employees and agents, in substantially the same language as Section 145.

Article Nine, section (b), of the Company's certificate of incorporation further provides that no director will be personally liable to the Company or its stockholders for monetary damages or for any breach of fiduciary duty except for breach of the director's duty of loyalty to the Company or its stockholders, for acts or omissions not in good faith or involving intentional misconduct or a knowing violation of law, pursuant to Section 174 of the Delaware General Corporation Law (which imposes liability in connection with the payment of certain unlawful dividends, stock purchases or redemptions), or any amendment or successor provision thereto, or for any transaction from which a director derived an improper personal benefit.

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Item 16. Exhibits.

Exhibit Number	Footnote	Exhibit Description
1.1	*	Form of Underwriting Agreement.
4.1	(a)	Amended and Restated Certificate of Incorporation of Navidea Biopharmaceuticals, Inc., as corrected February 18, 1994, and amended June 27, 1994, July 25, 1995, June 3, 1996, March 17, 1999, May 9, 2000, June 13, 2003, July 29, 2004, June 22, 2005, November 20, 2006, December 26, 2007, April 30, 2009, July 27, 2009, August 2, 2010, January 5, 2012, and June 26, 2013.
4.2	(b)	Amended and Restated Bylaws dated July 21, 1993, as amended July 18, 1995, May 30, 1996, July 26, 2007, and November 7, 2013.
4.3	(c)	Amended and Restated Certificate of Designations, Voting Powers, Preferences, Limitations, Restrictions, and Relative Rights of Series B Cumulative Convertible Preferred Stock.
4.4	*	Form of Certificate of Designation for the Preferred Stock (together with Preferred Stock Certificate)
4.5	*	Form of Warrant Agreement (together with form of Warrant Certificate)
4.6	(d)	Form of September 24, 2013 Warrants.
4.7	*	Form of Subscription Rights Agreement (together with Subscription Rights Certificate)
4.8	*	Form of Purchase Contract (together with form of Purchase Contract Certificate)
4.9	*	Form of Unit Agreement (together with form of Unit Certificate)
5.1	***	Opinion of Porter, Wright, Morris & Arthur LLP.
23.1	***	Consent of Porter, Wright, Morris & Arthur LLP (included in Exhibit 5).
23.2	***	Consent of Independent Registered Public Accounting Firm.
24.1	**	Power of Attorney is contained on the signature pages.

*To be subsequently filed, if applicable, by an amendment to the Registration Statement or by a Current Report on Form 8-K.

** Filed herewith.

*** Previously filed with this Registration Statement.

(a) Incorporated by reference to Exhibit 3.1 previously filed on March 14, 2014, with the Company's Annual Report on Form 10-K.

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(b) Incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q filed November 12, 2013.

(c) Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 26, 2013.

(d) Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed September 24, 2013.

Item 17. Undertakings.

(a) The undersigned hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high and of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement.

Provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

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(i) If the registrant is relying on Rule 430B:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

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(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(d) The undersigned hereby undertakes that, for purposes of determining any liability under the Securities Act:

(1) the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of the registration statement as of the time it was declared effective; and

(2) each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Dublin, State of Ohio, on May 23, 2014.

NAVIDEA BIOPHARMACEUTICALS, INC.

/s/ Brent L. Larson
Brent L. Larson, Executive Vice President and
Chief Financial Officer

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints Mark J. Pykett and Brent L. Larson, and each of them severally, as true and lawful attorneys-in-fact and agents, with full powers of substitution and resubstitution, for them and in their name, place and stead, in any and all capacities, to sign any and all amendments (including pre-effective and post-effective amendments) to this registration statement, and to sign any registration statement for the same offering covered by this registration statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, and generally to do all such things in their names and behalf in their capacities as officers and/or directors to enable Navidea Biopharmaceuticals, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Mark J. Pykett Mark J. Pykett	Chief Executive Officer and Director (principal executive officer)	May 8, 2014

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/s/ Brent L. Larson Brent L. Larson	Executive Vice President and Chief Financial Officer (principal financial officer and principal accounting officer)	May 8, 2014
/s/ Gordon A. Troup Gordon A. Troup	Chairman of the Board of Directors	May 8, 2014
/s/ Peter Drake, Ph.D. Peter Drake, Ph.D.	Director	May 8, 2014
/s/ Brendan A. Ford Brendan A. Ford	Director	May 8, 2014
/s/ Michael M. Goldberg Michael M. Goldberg	Director	May 8, 2014
/s/ Eric K. Rowinsky, M.D. Eric K. Rowinsky, M.D.	Director	May 8, 2014
/s/ Perry A. Karsen Perry A. Karsen	Director	May 8, 2014

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Exhibit Index

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23.1	***	Consent of Porter, Wright, Morris & Arthur LLP (included in Exhibit 5).
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** Filed herewith.

*** Previously filed with this Registration Statement.

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- (a) Incorporated by reference to Exhibit 3.1 previously filed on March 14, 2014, with the Company's Annual Report on Form 10-K.

- (b) Incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q filed November 12, 2013.

- (c) Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 26, 2013.

- (d) Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed September 24, 2013.