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Navidea Biopharmaceuticals Announces Agreement with FDA on Special Protocol Assessments for NAV5001 Phase 3 Program

- SPA provides clear pathway to NDA – preparations underway to commence enrollment -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB), a biopharmaceutical company focused on precision diagnostic radiopharmaceuticals, today announced that it has reached agreement with the U.S. Food and Drug Administration (FDA) for two special protocol assessments (SPA) for the Company's pivotal Phase 3 program with NAV5001 as an aid in the differential diagnosis of Parkinsonian Syndromes from non-Parkinsonian tremor. NAV5001 is an investigational imaging agent used to visualize dopamine transporters (DAT) in the brain using single photon emission tomography (SPECT) imaging. The SPAs are written agreements between the Company, as the program's sponsor, and FDA regarding the design, endpoints and statistical analysis for the two pivotal Phase 3 clinical trials to be used in support of a potential NAV5001 New Drug Application (NDA). The Company is actively preparing for the initiation of the pivotal Phase 3 trials later this year.

"Reaching an agreement on the SPAs indicates that FDA considers the design of the program and positive results from the Phase 3 trials will be appropriate for FDA consideration for regulatory approval of NAV5001 as an aid in the diagnosis of Parkinsonian syndromes," said William J. Regan, Navidea Senior Vice President, Global Regulatory Strategy. "In achieving the SPA agreements on a first-cycle review, we are extremely pleased to have more certainty around FDA registration requirements."

The international, open-label, pivotal NAV5001 Phase 3 program consists of two similar clinical trials that will run in parallel and enroll approximately 550 total subjects who exhibit early stage tremor. Each Phase 3 trial was the subject of a SPA with FDA. The primary endpoint of both studies is to evaluate the relative diagnostic efficacy of the NAV5001 SPECT images compared with the diagnosis made by neurologists and that established by a consensus panel of three movement disorder specialists as the 'Standard of Truth'. In one study, each subject will undergo SPECT imaging with NAV5001 only. In the second study, subjects will undergo SPECT imaging with both NAV5001 and an alternative SPECT agent, ioflupane, in a cross-over comparison design.

"Clinicians often struggle with diagnosing neurodegenerative diseases such as Parkinsonian syndromes," said Cornelia Reininger, MD, PhD, Navidea Senior Vice President and Chief Medical Officer. "The differential diagnoses of movement disorders and tremor are extensive,

and the disorders often exhibit similarities, especially early in the initial clinical presentation. The data accumulated to date from NAV5001 clinical trials suggests that it may be an effective, well-tolerated imaging agent with high affinity for DAT and rapid kinetics which enable faster generation of clear images, and may assist physicians in reaching an accurate diagnosis. We are excited to begin this registration program focused on patients with emerging symptoms where diagnostic uncertainty and unmet need are highest. We believe that NAV5001 has the promise to address the needs of a rapidly growing market and will provide another option to the currently marketed diagnostic products and methods."

About NAV5001

Iodine-123 labeled NAV5001 is a patented, novel, small molecule radiopharmaceutical used with single photon emission computed tomography (SPECT) imaging to identify the status of specific regions in the brains of patients suspected of having Parkinson's disease. The agent binds to the dopamine transporter (DAT) on the cell surface of dopaminergic neurons in the striatum and substantia nigra regions of the brain. Loss of these neurons is a widely recognized hallmark of Parkinson's disease and other forms of Parkinsonism.

NAV5001 has been administered to more than 600 subjects in multi-phase clinical trials to date. Results from these clinical trials have demonstrated that NAV5001 has high affinity for DAT and rapid kinetics which enable the generation of clean diagnostic images quickly, beginning within approximately 20 minutes after injection. In addition to its potential use as an aid in the differential diagnosis of Parkinsonian syndromes and movement disorders, NAV5001 may also be useful in the diagnosis of Dementia with Lewy Bodies (DLB), which is the second most common cause of progressive dementia after Alzheimer's disease.

About Parkinsonian Syndromes, Parkinson's Disease and other movement disorders

Parkinsonian syndromes and movement disorders such as Essential Tremor represent a class of neurodegenerative diseases with important diagnostic needs. Parkinsonian syndromes (PS) are neurodegenerative disorders that affect a person's ability to control movement and other muscle functions. Parkinson's Disease (PD) is the most common form of Parkinsonian Syndromes believed to be caused by loss of dopamine producing neurons in the brain and with first symptoms such as tremor, rigidity, or slow movement. Other less common Parkinsonian Syndromes include multiple system atrophy (MSA), Progressive Supranuclear Palsy (PSP), and drug-induced Parkinsonism. The Parkinson's Disease Foundation (PDF) estimates that up to 10 million people worldwide are living with PD, including 1 million people in the U.S. Approximately 60,000 new cases of PD are diagnosed in the U.S. each year.[1] The International Essential Tremor Foundation estimates that as many as 10 million people in the United States are afflicted by essential tremor.

PD is commonly misdiagnosed or completely missed in clinical evaluations as symptoms are often attributed to the normal aging process. Essential tremor and the other similar conditions are also common sources of confusion in PD diagnosis. Collectively, there are over 25 million people in the U.S. and Europe with some type of movement disorder, comprising a large differential diagnosis population.

About Navidea Biopharmaceuticals Inc.

Navidea Biopharmaceuticals, Inc. (NYSE MKT:NAVB) is a biopharmaceutical company

focused on the development and commercialization of precision diagnostics and radiopharmaceutical agents. Navidea is actively developing four radiopharmaceutical agent platforms – Lymphoseek® (technetium 99m tilmanocept) Injection, NAV4694, NAV5001 and RIGScan™ – to help identify the sites and pathways of undetected disease and enable better diagnostic accuracy, clinical decision-making and, ultimately, patient care. Navidea's first commercial agent, Lymphoseek, was approved by the FDA in March 2013. Navidea's strategy is to deliver superior growth and shareholder return by bringing to market novel radiopharmaceutical agents and advancing the Company's pipeline through selective acquisitions, global partnering and commercialization efforts. For more information, please visit www.navidea.com.

The Private Securities Litigation Reform Act of 1995 (the Act) provides a safe harbor for forward-looking statements made by or on behalf of the Company. Statements in this news release, which relate to other than strictly historical facts, such as statements about the Company's plans and strategies, expectations for future financial performance, new and existing products and technologies, anticipated clinical and regulatory pathways, and markets for the Company's products are forward-looking statements within the meaning of the Act. The words "believe," "expect," "anticipate," "estimate," "project," and similar expressions identify forward-looking statements that speak only as of the date hereof. Investors are cautioned that such statements involve risks and uncertainties that could cause actual results to differ materially from historical or anticipated results due to many factors including, but not limited to, the Company's continuing operating losses, uncertainty of market acceptance of its products, reliance on third party manufacturers, accumulated deficit, future capital needs, uncertainty of capital funding, dependence on limited product line and distribution channels, competition, limited marketing and manufacturing experience, risks of development of new products, regulatory risks and other risks detailed in the Company's most recent Annual Report on Form 10-K and other Securities and Exchange Commission filings. The Company undertakes no obligation to publicly update or revise any forward-looking statements.

[1] Parkinson's Disease Foundation. Statistics on Parkinson's: http://www.pdf.org/en/parkinson_statistics. Accessed on August 21, 2013.

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