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Navidea Biopharmaceuticals Announces that Results of NAV4694 Clinical Trial Published in the Journal of Nuclear Medicine

- Head-to-head comparison of NAV4694 and β-Amyloid imaging gold standard in Alzheimer's disease and dementia -

DUBLIN, Ohio--(BUSINESS WIRE)-- Navidea Biopharmaceuticals, Inc. (NYSE MKT: NAVB), a biopharmaceutical company focused on precision diagnostic radiopharmaceuticals, today announced the peer-reviewed publication of results from a clinical trial of NAV4694 in healthy subjects and those with diagnosed forms of dementia. The trial assessed the performance of Navidea's Fluorine-18 labeled amyloid imaging candidate, NAV4694, in a head-to-head comparison with the acknowledged benchmark, gold-standard amyloid imaging agent, ^{11}C-labeled Pittsburgh Compound-B (PiB). Results demonstrated that NAV4694 displayed imaging characteristics nearly identical to those of PiB and the authors believe these results show that NAV4694 may be useful in the early and differential diagnosis of Alzheimer's disease (AD). The study, "*Head-to-Head Comparison of ^{11}C-PiB and ^{18}F-AZD4694 (NAV4694) for β-Amyloid Imaging in Aging and Dementia,"* was published in the current online edition of the Journal of Nuclear Medicine and will appear in the June print edition [J Nucl Med 2013; 54:1–7 DOI: 10.2967/jnumed.112.114785].

β-Amyloid imaging has the potential to play an increasingly important role in clinical practice as revised criteria for the diagnosis of probable AD allow for earlier diagnosis and therapeutic intervention. "For this to be a reality, clinicians will need access to reliable, practical and affordable imaging options," said Professor Christopher Rowe, MD, FRACP, Director of the Department of Nuclear Medicine and Centre for PET at Austin Health, Melbourne, Australia and one of the authors. "This study suggests that NAV4694 images may be more easily and reliably read in clinical practice than other F-18 labeled PET tracers. By displaying imaging characteristics nearly identical to those of the gold standard, PiB, NAV4694 provides the same low background needed for earlier differential diagnosis while affording the practicality needed for production logistics."

"With the ongoing movement toward earlier evaluation and treatment of cognitive impairment, it is of increasing importance for an improved diagnostic tool that can identify clinical dementia and cognitive impairment before it has fully developed," commented Cornelia Reininger, MD, PhD, Navidea's Senior Vice President and Chief Medical Officer. "These results add to our conviction that NAV4694, with its outstanding performance characteristics, may afford new opportunities to advance the early diagnosis of cognitive decline. We are very excited about the recent initiation of our Phase 2b study evaluating NAV4694 in the differentiation of Mild Cognitively Impaired (MCI) subjects who are at risk of

developing Alzheimer's disease from those who are not, enabling the potential for early intervention with current and future treatments."

About the NAV4694 Head-to-Head Comparison Clinical Trial and Results

Forty-five participants (25 healthy elderly controls (HC), 10 with Mild Cognitive Impairment (MCI), 7 with AD and 3 with fronto-temporal dementia) underwent PET imaging with both PiB and NAV4694 imaging agents. The PiB and NAV4694 images were virtually indistinguishable by visual inspection and similarly low to no white matter binding was observed with both radiotracers. Low white matter binding coupled with comparatively high binding to target amyloid provide enhanced signal-to-noise ratios, facilitating detection of lower levels of amyloid. This may enable earlier detection of amyloid and therefore earlier diagnosis of the underlying cause of cognitive impairment and dementia. When quantified, there were no significant differences in white matter binding for each tracer in both healthy controls and dementia subjects. The quantitative measures of NAV4694 binding to cortical amyloid plaques showed almost identical results to PIB. There was an excellent linear correlation between PiB and NAV4694 neocortical standardized uptake value ratios, or SUVR, (slope of 0.95, $r = 0.99$, $P < 0.0001$). Both radiotracers showed similar binding kinetics and dynamic range. As expected, the AD group showed higher β-Amyloid detection than the HCs, as measured by both PiB and NAV4694 binding, and provided a robust separation of AD patients from HCs. Of note, the authors state that visually, 16% of the Healthy Controls were deemed positive for β-Amyloid as assessed by both PiB and NAV4694, presenting an almost identical pattern of binding suggesting that β-Amyloid deposition is an early feature of the disease preceding cognitive impairment. No serious adverse events related to the study drugs were observed or reported by any participants as a result of the PiB or NAV4694 scans, and no concerns were raised by the participants or their relatives.

About NAV4694

NAV4694 is a Fluorine-18 labeled precision radiopharmaceutical candidate intended for use in Positron Emission Tomography (PET) imaging and evaluation of patients with signs or symptoms of cognitive impairment such as Alzheimer's disease (AD). NAV4694 binds to β-Amyloid deposits in the brain that can then be imaged in scans. β-Amyloid plaque pathology is widely used in the diagnosis of AD. The ability of NAV4694 imaging to display amyloid plaque pathology may enable earlier identification of AD and improve monitoring of disease progression and interpretation of brain scan images. Navidea plans for a Phase 3 trial of NAV4694 to begin in 2013.

About Alzheimer's

Alzheimer's disease (AD) is a progressive and fatal neurodegenerative disease which affects a person's memory and ability to learn, reason, communicate and carry out daily activities. Increasing age is the greatest risk factor for AD and there is no prevention or cure. The World Health Organization estimates that Alzheimer's disease affects over 24,000,000 people worldwide. Currently in the U.S. alone, there are over 5 million Alzheimer's patients with estimates that by 2050, as many as 14 million Americans could have the disease according to the Alzheimer's Association**.** Among the brain changes believed to contribute to the development of Alzheimer's are the accumulation of the protein β-Amyloid *outside* nerve cells (neurons) in the brain and the accumulation of the protein tau *inside* neurons.

Approximately 75 to 100 experimental pharmaceuticals aimed at diagnosing, slowing or stopping the progression of Alzheimer's are now in human clinical trials.

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®, 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 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.

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