



## Lantheus Presents New Data on the Effectiveness of Novel PET Cardiac Imaging Agent Flurpiridaz F 18 in Women with Suspected Heart Disease at AHA Scientific Sessions 2015

Nov 8, 2015

### ***Flurpiridaz F 18 Demonstrates Improved Coronary Artery Disease Detection and Reduced Radiation Exposure in Women over Standard SPECT MPI***

NORTH BILLERICA, Mass.--(BUSINESS WIRE)--Nov. 8, 2015-- [Lantheus Holdings, Inc.](#) (the "Company") (NASDAQ:LNTH), the parent company of [Lantheus Medical Imaging, Inc.](#) ("LMI"), a global leader in developing, manufacturing, selling and distributing innovative diagnostic imaging agents and products, today announced data from a sub-analysis of its first Phase 3 study of flurpiridaz F 18 for myocardial perfusion imaging (MPI) presented at the American Heart Association Scientific Sessions on November 8, 2015 in Orlando, Florida. The findings show the superiority of flurpiridaz F 18 over standard single photon emission computed tomography (SPECT) MPI for the assessment of coronary artery disease (CAD) in women. Flurpiridaz F 18 is an investigational positron emission tomography (PET) MPI agent in Phase 3 development.

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The moderated poster (#4424) titled, "Improved Assessment of CAD in Women with Flurpiridaz F 18 PET Myocardial Perfusion Imaging: A Subset Analysis of the Flurpiridaz F 18 301 Phase 3 Study," will be presented by Gary V. Heller, M.D., of Morristown Medical Center on Sunday, November 8, 2015 at 2:00 p.m. Eastern Time in the Nuclear Cardiology: Advances in SPECT and PET Imaging session of the meeting.

"While coronary heart disease is the leading cause of death in women, coronary artery disease remains under-diagnosed and under-treated in this population," said Dr. Heller, the lead author of the sub-analysis. "The results of this study provide evidence of the usefulness and future potential of flurpiridaz F 18 PET imaging for the diagnosis of coronary artery disease in women."

The data are from a multicenter, international (United States, Canada, and Finland) study enrolling approximately 800 patients with known or suspected CAD and scheduled for coronary angiography and conventional nuclear SPECT imaging.

In this flurpiridaz F 18 Phase 3 trial, 235 women with suspected CAD underwent rest and stress PET and SPECT MPI and coronary angiography. Flurpiridaz F 18 PET MPI was performed at rest and during pharmacologic or exercise stress testing. It is important to note that flurpiridaz F 18 can be used in conjunction with treadmill exercise, which is not generally feasible with currently used PET tracers for MPI. Results showed a statistically greater sensitivity for flurpiridaz F 18 (67.8%) versus SPECT (37.3%) ( $p < 0.001$ ). Similar specificity was shown for flurpiridaz F 18 (81.3%) versus SPECT (80.1%) ( $p = 0.017$  for non-inferiority testing). The diagnostic superiority of flurpiridaz F 18 versus SPECT was also demonstrated by ROC analysis ( $p < 0.001$ ).

Superior diagnostic accuracy was observed with flurpiridaz F 18 versus SPECT (77.9% vs. 69.4%,  $p = 0.014$ ). A significantly higher percentage of images were rated as either excellent or good quality with PET imaging, compared to SPECT imaging for stress images ( $p < 0.001$ ) and rest images ( $p < 0.001$ ). Diagnostic certainty of interpretation (the percentage of cases with definitely abnormal or definitely normal interpretation) was significantly higher for flurpiridaz F 18 PET compared to SPECT (89.8% vs. 74.5%,  $p < 0.001$ ). The agent was safe and well tolerated. Importantly, radiation exposure associated with flurpiridaz F 18 PET imaging was reduced to less than 50% of that associated with standard SPECT MPI.

"While one in every four female deaths is related to heart disease, there remains an established need to provide clinicians with tools for better and earlier detection to reduce the number of women who would potentially go untreated," said Jennifer H. Mieres, M.D., a leading expert and patient advocate in the field of cardiovascular disease in women, Senior Vice President, Office of Community and Public Health, North Shore-LIJ Health System and Professor of Cardiology at Hofstra North Shore-LIJ School of Medicine. "These results suggest that flurpiridaz F 18 is uniquely poised to advance the delivery, timeliness and precision needed to accurately diagnose and manage outcomes for the underserved population of women with coronary artery disease."

"We are very pleased with the additional Phase 3 data presented at the AHA meeting showing the advantages of flurpiridaz F 18 PET MPI for coronary artery disease detection in women," said Cesare Orlandi, M.D., Chief Medical Officer of Lantheus Medical Imaging. "The study demonstrated a substantial gain in sensitivity without a loss of specificity over standard SPECT MPI. We believe the improved diagnostic accuracy of the agent coupled with reduced radiation exposure and the potential for quantification of coronary flow reserve provide great promise for flurpiridaz F 18 to become the diagnostic imaging tool of choice for evaluating coronary artery disease in women."

The Company is poised to move to completion its Phase 3 development program for flurpiridaz F 18 with a revised protocol being initiated under a Special Protocol Assessment agreed upon with the U.S. Food and Drug Administration. Lantheus also remains in active discussions with prospective strategic partners for completion of the development and commercialization of this promising agent.

### **About the Flurpiridaz F 18 First Phase 3 Study**

The first flurpiridaz F 18 Phase 3 study was designed to assess the diagnostic efficacy of flurpiridaz F 18 with positron emission tomography (PET) imaging versus single photon emission computed tomography (SPECT) with Tc99m-labeled agents for coronary artery disease (CAD) detection in the same patients. Patients with known or suspected CAD who were either scheduled for or had completed invasive coronary angiography (without intervention) were included in the study. Each patient was studied using both one-day rest/stress flurpiridaz F 18 PET MPI and Tc99m-labeled SPECT MPI (one-day rest/stress or two-day protocol). Images were interpreted by three expert readers blinded to all clinical information. Quantitative coronary angiography (QCA) was used as the truth standard, with patients considered CAD positive with a stenosis  $\geq 50\%$  in at least one major vessel by QCA. Flurpiridaz F 18 substantially outperformed SPECT MPI, in sensitivity, one of the study's primary endpoints, but did not meet the study's other primary endpoint, non-inferiority for specificity, implying a substantial and unexpected under-diagnosis of CAD with SPECT imaging in the trial. Unlike flurpiridaz F 18, SPECT imaging results were skewed with low sensitivity and high specificity when compared to the truth standard. In secondary endpoints, flurpiridaz F 18 outperformed SPECT imaging in image quality and diagnostic certainty with less than half of the radiation exposure for patients. Subsequent to the initial read of the data, the Company performed a re-read which confirmed the initial results as well as showed improved performance of PET MPI as compared to SPECT imaging in women and subjects with high body mass index. Based on the results of the first Phase 3 study, the Company redesigned the protocol for its second Phase 3 study, including different primary endpoints – namely, the performance of flurpiridaz F 18 on its own merit versus coronary angiography as the truth standard – and the Company has received a Special Protocol Assessment from the FDA in connection with its second study.

### **About Flurpiridaz F 18 Injection and Coronary Artery Disease**

Flurpiridaz F 18 injection, a fluorine 18-labeled agent that binds to mitochondrial complex 1 (MC-1)<sup>1</sup>, was designed to be a novel myocardial perfusion positron emission tomography imaging agent that may better evaluate patients with known or suspected coronary artery disease (CAD), which is the most common form of heart disease<sup>2</sup>, affecting an estimated 15.4 million Americans 20 years of age or older<sup>3</sup>. CAD is the leading cause of death in the United States for both men and women<sup>2</sup>. Each year more than 400,000 Americans die from CAD<sup>2</sup>. Despite increases in awareness over the past decade, only 54% of women recognize that heart disease is their number one killer, accounting for one in every four female deaths<sup>4</sup>. Heart disease and related risk factors are often missed in women and symptoms of CAD are often different in women than their male counterparts<sup>5</sup>. In the first phase 3 study, **flurpiridaz F 18 demonstrated improved CAD detection and reduced radiation exposure in women over standard single photon emission computed tomography (SPECT) MPI.**

### **About PET and MPI**

Positron emission tomography (PET), also called PET imaging or a PET scan, is a type of nuclear medicine imaging procedure<sup>6</sup> that provides information about the function and metabolism of the body's organs, unlike computed tomography (CT) or magnetic resonance imaging (MRI), which primarily show anatomy and structure<sup>7</sup>. Myocardial perfusion imaging (MPI) is a minimally invasive test that utilizes a small amount of radioactive material (radiopharmaceutical) injected into the body to depict the distribution of blood flow to the heart. MPI is used to identify areas of reduced blood flow (perfusion) to the heart muscle. The test is typically conducted under both rest and stress conditions, after which physicians examine and compare the two scans and predict whether the patient has significant coronary artery disease<sup>8</sup>. Although single photon emission computed tomography (SPECT) is most commonly used for MPI<sup>9</sup>, PET imaging has gained considerable support and use in the field of cardiovascular imaging, as it offers many advantages to SPECT, including higher spatial and contrast resolution, which results in higher image quality and improved diagnostic accuracy, accurate attenuation correction and risk stratification<sup>10</sup>.

### **About Lantheus Holdings, Inc. and Lantheus Medical Imaging, Inc.**

Lantheus Holdings, Inc. is the parent company of Lantheus Medical Imaging, Inc. ("LMI"), which is a global leader in developing, manufacturing, selling and distributing innovative diagnostic imaging agents and products. LMI provides a broad portfolio of products, which are primarily used for the diagnosis of cardiovascular diseases. LMI's key products include the echocardiography contrast agent DEFINITY® Vial for (Perflutren Lipid Microsphere) Injectable Suspension; TechnoLite® (Technetium Tc99m Generator), a technetium-based generator that provides the essential medical isotope used in nuclear medicine procedures; and Xenon (Xenon Xe 133 Gas), an inhaled radiopharmaceutical imaging agent used to evaluate pulmonary function and for imaging the lungs. The Company is headquartered in North Billerica, Massachusetts, and has offices in Puerto Rico, Canada and Australia. For more information, visit [www.lantheus.com](http://www.lantheus.com).

### **Safe Harbor for Forward-Looking and Cautionary Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements are subject to risks and uncertainties that may be described from time to time in our filings with the Securities and Exchange Commission. Readers are cautioned not to place undue reliance on the forward-looking statements

contained herein, which speak only as of the date hereof. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law.

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<sup>1</sup> Yalamanchili, P, Wexler, E, Hayes, M, Yu, M, MD, Bozek J, Radeke, H, Azure, M, Purohit, A, Casebier, DS, and Robinson, SP. Mechanism of uptake and retention of 18F BMS-747158-02 in cardiomyocytes: A novel PET myocardial imaging agent. *Journal Nuclear Cardiology* 2007 Nov-Dec;14(6):782-8.

<sup>2</sup> National Institutes of Health, National Heart, Lung, and Blood Institute. Coronary Artery Disease: Who Is At Risk. [http://www.nhlbi.nih.gov/health/dci/Diseases/Cad/CAD\\_WholsAtRisk.html](http://www.nhlbi.nih.gov/health/dci/Diseases/Cad/CAD_WholsAtRisk.html). Accessed October 2015.

<sup>3</sup> Heart Disease and Stroke Statistics. 2014 Update: A Report From the American Heart Association. *Circulation*. 2014;129:e28-e292.

<sup>4</sup> National Center for Chronic Disease Prevention and Health Promotion. Division for Heart Disease and Stroke: Women and Heart Disease Fact Sheet. [http://www.cdc.gov/dhdsp/data\\_statistics/fact\\_sheets/fs\\_women\\_heart.htm](http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_women_heart.htm). Accessed October 2015.

<sup>5</sup> American College of Cardiology. Women and Coronary Artery Disease. <https://www.cardiosmart.org/Heart-Conditions/Women-and-Coronary-Artery-Disease>. Accessed October 2015.

<sup>6</sup> Radiology Info. What is Positron Emission Tomography – Computed Tomography (PET/CT) Scanning. <http://www.radiologyinfo.org/en/info.cfm?pg=PET>. Accessed October 2015.

<sup>7</sup> National Institutes of Health. NIH Clinical Center. Positron Emission Tomography Department Overview. <http://clinicalcenter.nih.gov/pet/>. Accessed October 2015.

<sup>8</sup> Society of Nuclear Medicine. Procedure Guidelines for Myocardial Perfusion Imaging. Version 3.0 June 2002. [http://interactive.snm.org/docs/pg\\_ch02\\_0403.pdf](http://interactive.snm.org/docs/pg_ch02_0403.pdf).

<sup>9</sup> Salerno, M and Beller, GA, Noninvasive Assessment of Myocardial Perfusion. *Circ Cardiovasc Imaging*. 2009; 2:412-424.

<sup>10</sup> Heller, G, Calnon, D and Dorbala, S. Recent Advances in Cardiac PET and PET/CT Myocardial Perfusion Imaging. *J Nucl Cardiol* 2009; 16:962-9.



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Lantheus Holdings, Inc.  
Investor Relations  
John Bakewell, 978-436-7073  
or  
Media Relations  
Meara Murphy, 978-671-8508