



Lantheus Presents New Data on the Effectiveness of Novel PET Cardiac Imaging Agent Flurpiridaz F 18 in Obese Patients with Suspected Heart Disease at ACC Scientific Session

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Flurpiridaz F 18 Demonstrates Improved Coronary Artery Disease Detection and Reduced Radiation Exposure in Difficult to Image, High BMI Patients Compared to SPECT MPI

NORTH BILLERICA, Mass.--(BUSINESS WIRE)--Apr. 4, 2016-- Lantheus Holdings, Inc. (NASDAQ: LNTN), the parent company of Lantheus Medical Imaging, Inc. ("LMI"), a global leader in the development, manufacture and commercialization of innovative diagnostic imaging agents, today announced that new data from a sub-analysis of its first Phase 3 study of flurpiridaz F 18 for myocardial perfusion imaging (MPI) in obese patients will be presented at the American College of Cardiology's Annual Scientific Session today in Chicago. The findings show the superiority of flurpiridaz F 18, an investigational positron emission tomography (PET) agent for MPI, compared to MPI with single photon emission computed tomography (SPECT) for the assessment of coronary artery disease (CAD) in patients with a body mass index (BMI) of 30 or higher.

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An example of a 59-year-old male subject with a BMI of 30 in Lantheus' first Phase 3 clinical trial of flurpiridaz F 18 PET imaging, studied using exercise stress. Quantitative angiography showed a stenosis of 72% in the left circumflex coronary artery and smaller stenoses (<50%) in the left anterior descending and the right coronary arteries. Three expert readers blinded to all clinical information and without knowledge that the two studies were from the same subject assessed the SPECT study as "normal" but correctly assessed the flurpiridaz F 18 PET study as abnormal. (Graphic: Business Wire)

The moderated poster entitled, "Improved Assessment of CAD in Obese Subjects with Flurpiridaz F 18 PET Myocardial Perfusion Imaging: A Subset Analysis of the Flurpiridaz F 18 301 Phase 3 Study," will be presented by Timothy Bateman, M.D. of Mid America Heart Institute on Monday, April 4, 2016 at 9:45 a.m.

CT in the Non-invasive Imaging session of the meeting.

"Nearly 70% of American adults are either overweight or obese, putting this patient population at a greater risk of heart disease, stroke, high blood pressure, diabetes, and other potential health problems," said Dr. Bateman, the lead author of the poster. "Obese patients present a significant imaging challenge, and improved imaging modalities are needed to accurately and reliably assess this patient population. The results of this study provide evidence of the particular utility and future potential of flurpiridaz F 18 PET imaging for the diagnosis of coronary artery disease in people with a BMI of 30 or higher."

Based on a blinded read of PET and SPECT data, flurpiridaz F 18 PET imaging demonstrated a statistically greater sensitivity (71.1%) versus SPECT (51.7%) ($p < 0.001$) and similar specificity (79.8%) versus SPECT (77.5%) ($p = 0.002$ for non-inferiority testing). The diagnostic superiority of flurpiridaz F 18 PET imaging versus SPECT was demonstrated by ROC analysis ($p < 0.001$).

A significantly higher percentage of images were rated as either excellent or good quality with flurpiridaz F 18 PET imaging, compared to SPECT 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 imaging compared to SPECT ($p < 0.001$). No drug-related serious adverse events were observed. Importantly, radiation exposure associated with flurpiridaz F 18 PET imaging was reduced to less than 50% of that associated with standard SPECT.

The data are from a multicenter, international (United States, Canada, and Finland) Phase 3 study of flurpiridaz F 18 PET imaging. The study enrolled approximately 800 patients with known or suspected CAD who were scheduled for coronary angiography and conventional SPECT. Of these patients, 413 obese patients with a BMI ≥ 30 and suspected CAD underwent both rest and stress flurpiridaz F 18 PET and SPECT imaging and coronary angiography. The subset had a mean BMI of 35 ± 6 with a range of 30-87. Flurpiridaz F 18 PET imaging was performed at rest and during pharmacologic or exercise stress testing.

"The Phase 3 data sub-analysis presented at ACC show the advantages of flurpiridaz F 18 PET imaging for coronary artery disease detection in obese patients," said Cesare Orlandi, M.D., Chief Medical Officer of Lantheus Medical Imaging. "Flurpiridaz F 18 PET imaging shows superiority over SPECT in an obese population and provides images with better quality, and less attenuation, which can lead to increased diagnostic certainty by physicians. We believe the improved diagnostic accuracy, utility in stress imaging, reduced radiation exposure and 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 obese patients."

Lantheus is poised to commence the second of the two Phase 3 trials for flurpiridaz F 18 PET imaging with a revised protocol in place under an FDA-approved Special Protocol Assessment and is 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 PET imaging versus SPECT with Tc99m-labeled agents for 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 imaging and Tc99m-labeled SPECT imaging (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 PET imaging substantially outperformed SPECT, 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 in the trial. Unlike flurpiridaz F 18 PET imaging, SPECT results were skewed with low sensitivity and high specificity when compared to the truth standard. In secondary endpoints, flurpiridaz F 18 PET imaging outperformed SPECT in image quality and diagnostic certainty with less than half of the radiation exposure for patients. Subsequent to the initial read of the data, LMI performed a re-read which confirmed the initial results as well as showed improved performance of flurpiridaz F 18 PET imaging as compared to SPECT 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 and Coronary Artery Disease

Flurpiridaz F 18, a fluorine 18-labeled agent that binds to mitochondrial complex 1 (MC-1)¹, was designed to be a novel PET imaging agent that may better evaluate patients with known or suspected CAD, which is the most common form of heart disease², affecting an estimated 15.4 million Americans 20 years of age or older³. CAD is the leading cause of death in the United States for both men and women². Each year more than 400,000 Americans die from CAD². In the first phase 3 study, flurpiridaz F 18 demonstrated improved CAD detection and reduced radiation exposure over standard SPECT. In subgroup analyses, the risk-benefit profile of flurpiridaz F 18 PET imaging appeared to be favorable in women, obese patients and patients with multivessel disease. It is important to note that, with a 110 minute half-life, flurpiridaz F 18 can be used in conjunction with treadmill exercise, which is not feasible with other currently used PET tracers for MPI.

About PET and MPI

PET imaging or a PET scan is a type of nuclear medicine imaging procedure⁴ 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 structure⁵. MPI is a non-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 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 disease⁶. Although SPECT is most commonly used for MPI⁷, 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, resulting in higher image quality and improved diagnostic accuracy, accurate attenuation correction and risk stratification⁸.

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

Lantheus Holdings, Inc. is the parent company of Lantheus Medical Imaging, Inc., which is a global leader in the development, manufacture and commercialization of 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. LMI is headquartered in North Billerica, Massachusetts with offices in Puerto Rico, Canada and Australia. For more information, visit www.lantheus.com.

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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. Lantheus 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.

¹ 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.

² 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. Accessed April 2016.

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

⁴ Radiology Info. What is Positron Emission Tomography – Computed Tomography (PET/CT) Scanning. <http://www.radiologyinfo.org/en/info.cfm?pg=PET>. Accessed October 2015.

⁵ National Institutes of Health. NIH Clinical Center. Positron Emission Tomography Department Overview. <http://clinicalcenter.nih.gov/pet/>. Accessed April 2016.

⁶ Society of Nuclear Medicine. Procedure Guidelines for Myocardial Perfusion Imaging. Version 3.0 June 2002. http://interactive.snm.org/docs/pg_ch02_0403.pdf.

⁷ Salerno, M and Beller, GA, Noninvasive Assessment of Myocardial Perfusion. *Circ Cardiovasc Imaging*. 2009; 2:412-424.

⁸ 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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