### Lantheus Medical Imaging Presents Phase I Study Results of Novel Pet Myocardial Perfusion Imaging Tracer

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# Data Presented at the SNM Annual Meeting Demonstrate BMS747158's Potentialas Promising PET Tracer for Clinical Use

N. Billerica, MASSACHUSETTS (June 17, 2008) – Lantheus Medical Imaging, Inc., a worldwide leader in diagnostic imaging, today presents Phase I data relating to the safety and tolerability in human subjects of BMS747158, its novel fluorine 18-labeled Positron Emission Tomography (PET) tracer for myocardial perfusion imaging. The presentation was made by the Principal Investigator, Dr. Jamshid Maddahi, at the 55th Annual Meeting of the SNM in New Orleans, Louisiana. The preliminary clinical findings indicate that when used with PET technology, BMS747158 demonstrates a favorable radiation dosimetry profile and is generally well-tolerated. Exploratory analyses from this study showed high myocardial uptake that was stable over time with favorable myocardial to background ratios. These findings will be further expanded on in subsequent studies.

"We are encouraged by these preliminary findings about the safety and biodistribution profile of BMS747158 which illustrate its potential in myocardial perfusion PET imaging as we move to the next phase of the clinical development process," said D. Scott Edwards, Vice President, Global Research & Development, Lantheus Medical Imaging. "We remain committed to investing in the field of nuclear cardiology and developing innovative imaging agents that give physicians improved options for diagnosing and managing their patients."

The Phase I clinical trial was designed to estimate radiation dosimetry of a single dose of BMS747158 in healthy subjects at rest. Secondary objectives included assessing human safety, tolerability and biodistribution. Thirteen subjects were injected with 150-260 MBq of BMS747158 intravenously at UCLA. Whole body imaging using PET technology was conducted for five hours to collect data for radiation dosimetry calculation. Extensive safety monitoring was conducted with clinical labs, ECG, EEG, neurological, heart rate and blood pressure assessment at several time points during the study.

Preliminary results of this first in human, Phase I study show that intravenous injection of BMS747158 was safe and well-tolerated. No adverse events attributed to the study drug were reported. Mean effective dose was 0.073 rem/mCi, with standard deviation (SD) of 12 percent. Biodistribution results showed high myocardial uptake with favorable target to background ratios. Although non-optimized, heart imaging data collected over the first 10 minutes demonstrated that BMS747158 used in combination with PET imaging could provide high quality cardiac images.

"We are pleased that BMS747158 demonstrated a favorable radiation dosimetry and safety profile and was well-tolerated in human subjects. The possibility of using a fluorine 18-labeled tracer that binds to the mitochondrial complex 1 inhibitor and results in higher myocardial uptake, better uptake ratios and potentially higher quality cardiac images could fulfill the well-recognized need for a radiopharmaceutical that broadens the use of PET technology as a major modality for myocardial perfusion imaging," said the Principal Investigator, Jamshid Maddahi, M.D., F.A.C.C., Professor of Molecular and Medical Pharmacology (Nuclear Medicine) and Medicine (Cardiology) at David Geffen School of Medicine at UCLA.

"The initial PET studies performed by Lantheus Medical Imaging and Dr. Maddahi at UCLA demonstrate attractive imaging characteristics for BMS747158 as a cardiac perfusion tracer – high and rapid unidirectional capillary extraction and retention required for it to accurately represent cardiac perfusion in a short time after administration," said Dr. Michael E. Phelps, Norton Simon Professor, Chair, Department of Molecular and Medical Pharmacology, Director, Institute for Molecular Medicine, and Director, Crump Institute for Molecular Imaging, at UCLA. "Because of this, and the low surrounding background, the image quality is excellent. In terms of practicalities, BMS747158 is prepared from a one step fluorination and the precursor has a stable shelf lifetime for facilitating distribution from commercial PET radiopharmacies to clinical PET services. I am very excited about the prospects for BMS747158 as it continues to advance through clinical trials."

#### About BMS747158

BMS747158 is a fluorine 18-labeled pyridaben derivative that binds to the mitochondrial complex 1 (MC-1) inhibitor and designed as a novel myocardial perfusion PET imaging agent.

Preclinical studies show BMS747158's unique potential to serve as a new class of PET agent for myocardial perfusion imaging, based on its high, rapid and sustained cardiac uptake proportional to blood flow, slower washout, higher target to non-target

uptake ratios, ability to image perfusion deficits and capability to produce high quality of images taken in multiple species compared to currently marketed tracers.

Findings of preclinical studies describing BMS747158's promise for use in combination with PET/CT (Computed Tomography) imaging were published in the November/December 2007 edition of *The Journal of Nuclear Cardiology* (JNC)and the April 2008 edition of *The Journal of Nuclear Medicine* (JNM).

The work leading to the Investigational New Drug application of BMS747158 was conducted in collaboration with Siemens Medical Solutions of Siemens AG (NYSE: SI) utilizing resources and expertise at the company's Molecular Imaging Biomarker Research facility in Culver City, California, with support from its site in Knoxville, Tennessee. Through its existing agreement with Lantheus Medical Imaging, Inc. (formerly Bristol-Myers Squibb Medical Imaging), Siemens will distribute the new tracer if the clinical process continues to be successful and FDA approval is obtained.

## **About Positron Emission Tomography (PET)**

A positron emission tomography (PET) scan is an imaging test that can detect changes within certain tissues or organs early, often before disease progresses. In particular, PET images provide information about the function and metabolism of the body's organs, unlike computed tomography (CT) or magnetic resonance imaging (MRI), which show the body's anatomy and structure. PET scanning is useful in evaluating a variety of conditions — including neurological disease, heart disease, infections, certain inflammatory diseases and cancer. For myocardial perfusion imaging, single photon emission tomography (SPECT) remains the dominant modality at this time; however, there is increasing interest in the actual use of PET for this purpose. In contrast with SPECT, PET instrumentation offers higher spatial resolution, greater sensitivity and accurate, well-validated attenuation correction. 3

### **About Myocardial Perfusion Imaging (MPI)**

Myocardial perfusion imaging (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. 4 MPI is used to identify areas of reduced blood flow to the heart muscle 4 to determine whether or not the heart is working properly. Following the administration of the radiopharmaceutical, the heart rate is raised to induce myocardial stress, either by exercise or pharmacologically. 5 Using PET or SPECT technology, images of the heart muscle are then obtained and examined. In patients with known or suspected coronary artery disease (CAD), MPI is often used to determine the presence and severity of physiologically significant CAD. 4 CAD is the leading cause of death in the U.S. for both men and women. 6 Each year, more than half a million Americans die from CAD. 6 Of the estimated 16 million imaging and therapeutic procedures performed each year in the U.S., 40-50 percent are cardiac-related. 7

#### **About Lantheus Medical Imaging**

Lantheus Medical Imaging, Inc., a worldwide leader in diagnostic medicine for the past 50 years, is committed to advancing and investing in the field of diagnostic imaging. The company's proven success in discovering, developing and marketing innovative medical imaging agents provides a solid platform from which to bring forward breakthrough new tools for the diagnosis and management of disease. The company is home to leading cardiac imaging brands, including Cardiolite® (Kit for the Preparation of Technetium Tc99m Sestamibi for Injection), DEFINITY® Vial For (Perflutren Lipid Microsphere) Injectable Suspension, and TechneLite® (Technetium Tc99m Generator) and has nearly 700 employees worldwide with headquarters in North Billerica, Massachusetts, and offices in Puerto Rico, Canada, and Australia. For more information, visit www.lantheus.com.

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