Lantheus Announces Presentation at the 2021 American Urological Association (AUA) Annual Meeting

September 10, 2021

Highlights Piflufolastat F 18's Potential to Change Initial Risk Assessment and Intended Patient Management in High-Risk Prostate Cancer

Identified Regional Lymph Node and/or Distant Metastases in 26.9% of Patients Prior to Definitive Therapy

NORTH BILLERICA, Mass., Sept. 10, 2021 (GLOBE NEWSWIRE) -- Lantheus Holdings, Inc. (the "Company") (NASDAQ: LNTH), an established leader and fully integrated provider committed to innovative imaging diagnostics, targeted therapeutics and artificial intelligence solutions to find, fight and follow serious medical conditions, announced that data from the OSPREY pivotal trial on the utility of piflufolastat F 18 (previously referred to as ^{18}F-DCFPyL or PyL) during initial assessment on men with high risk prostate cancer were presented at the 2021 American Urological Association (AUA) Virtual Annual Meeting. Piflufolastat F 18 is Lantheus' prostate-specific membrane antigen (PSMA)-targeted positron emission tomography (PET) imaging agent.

The OSPREY study evaluated the diagnostic performance of piflufolastat F 18 PET/CT using a histopathology truth standard in men with newly diagnosed prostate cancer. A single dose of 9 mCi (333 MBq) of piflufolastat F 18 was administered via intravenous injection, followed by PET/CT acquisition 1 to 2 hours thereafter. 268 men with a median PSA 9.7 (range 1.2-125.3, n=267) underwent a piflufolastat F 18 PET/CT scan. After a piflufolastat F 18 PET/CT scan, 72 (26.9%) patients had regional lymph node and/or distant metastases identified and were radiographically staged with 39 (14.6%) as N1/M0 and 33 (12.3%) as N0/M1 or N1/M1 disease.

In addition, the Company also presented at the meeting the results of an independent, retrospective review to assess the impact of piflufolastat F 18 imaging on the planned management of the patients in the trial. A multidisciplinary panel, consisting of an independent urologist, medical oncologist and radiation oncologist, assessed the patients' clinical profiles and conventional imaging data before reviewing the patients' piflufolastat F 18 imaging data. Incorporation of the piflufolastat F 18 results led to a potential change in planned management for 43.6% (115/264) of patients. In 39.0% (103/264), a change in surgery or type of surgery was recommended and in 25.8% (68/264), a change in planned radiation therapy was recommended.[1]

"In the OSPREY trial, in patients selected for radical prostatectomy, piflufolastat F 18 was able to detect disease outside of the prostate in nearly one-third of the cases," said Peter Carroll, MD, MPH, Professor of Urology at University of California San Francisco. "These results suggest that PSMA imaging may have a substantial impact on management decisions at the time of initial assessment in men at risk for metastasis."

"Proper patient selection for any therapy is critical," said Bela Denes, MD, Vice President of Medical Affairs at Lantheus. "This analysis of the OSPREY data further supports the utility of piflufolastat F 18 in men with suspected metastasis prior to definitive therapy and its potential impact on treatment recommendations."

OSPREY Phase 2/3 Trial
The OSPREY trial was designed to assess the diagnostic performance of piflufolastat F 18 to detect prostate cancer in pelvic lymph nodes in subjects with high-risk, locally advanced prostate cancer (Cohort A). The primary endpoints for the trial were sensitivity and specificity of piflufolastat F 18 PET/CT imaging to detect metastatic prostate cancer within the pelvic lymph nodes relative to histopathology in Cohort A.

OSPREY enrolled a cohort of 268 men with biopsy-proven prostate cancer who were considered candidates for radical prostatectomy and pelvic lymph node dissection. These patients were all considered to have high risk disease based on criteria such as Gleason score, PSA level, and tumor stage. Each patient received a single piflufolastat F 18 PET/CT scan from mid-thigh to skull vertex.

Three central readers independently interpreted each PET scan for the presence of abnormal piflufolastat F 18 uptake in pelvic lymph nodes in multiple sub-regions, including the common iliac lymph nodes. The readers were blinded to all clinical information. While readers also recorded the presence of piflufolastat F 18 PET-positive lesions in the prostate gland and outside the pelvis, those results were not included in the primary efficacy analysis.

A total of 252 patients (94%) underwent standard-of-care prostatectomy and template pelvic lymph node dissection and had sufficient histopathology data for evaluation of the pelvic lymph nodes. Surgical specimens were separated into three regions: left hemipelvis, right hemipelvis, and other. For each patient, piflufolastat F 18 PET results and histopathology results obtained from dissected pelvic lymph nodes were compared by surgical region. PET results in locations that were not dissected were excluded from analysis.

For the 252 evaluable patients, the mean age was 64 years (range 46 to 84 years), and 87% were white. The median serum PSA was 9.3 ng/mL. The total Gleason score was 7 for 19%, 8 for 46%, and 9 for 34% of the patients, with the remainder of the patients having Gleason scores of 6 or 10.

In the trial, the diagnostic performance of piflufolastat F 18 in detecting disease in pelvic lymph nodes (Cohort A) was compared with histopathology. When matched by lymph node location, piflufolastat F 18 showed specificity of 95-98%, sensitivity of 28-39%, and positive predictive value (PPV) of 72-81% meeting the specificity but not the pre-established sensitivity co-primary endpoint.

Safety results showed piflufolastat F 18 was well tolerated. The most frequent adverse events reported were dysgeusia (2.6%), headache (1.8%) and fatigue (1.3%).[2]

About Prostate Cancer
Prostate cancer is the second most common form of cancer affecting men in the United States -- an estimated one in eight men will be diagnosed with

prostate cancer in their lifetimes. The American Cancer Society estimates that in 2021, almost 250,000 new cases of prostate cancer will be diagnosed, and more than 30,000 men will die of the disease. Approximately 3.1 million men in the United States currently count themselves as prostate cancer survivors.[3]

About PYLARIFY® (piflufolastat F 18) Injection

PYLARIFY (piflufolastat F 18) injection (also known as ^{18}F-DCFPyL or PyL) is a fluorinated small molecule PSMA-targeted PET imaging agent that enables visualization of lymph nodes, bone and soft tissue metastases to determine the presence or absence of recurrent and/or metastatic prostate cancer. For men with prostate cancer, PYLARIFY PET combines the accuracy of PET imaging, the precision of PSMA targeting and the clarity of an F 18 radioisotope for superior diagnostic performance. The recommended PYLARIFY dose is 333 MBq (9 mCi) with an acceptable range of 296 MBq to 370 MBq (8 mCi to 10 mCi), administered as a bolus intravenous injection.[4-9]

PYLARIFY® (piflufolastat F 18) Injection
Indication

PYLARIFY® (piflufolastat F 18) Injection is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer:

- with suspected metastasis who are candidates for initial definitive therapy.
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.

Important Safety Information
Contraindications

None.

Warnings and Precautions
Risk of Image Misinterpretation

Imaging interpretation errors can occur with PYLARIFY imaging. A negative image does not rule out the presence of prostate cancer and a positive image does not confirm the presence of prostate cancer. The performance of PYLARIFY for imaging of patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels. The performance of PYLARIFY for imaging of metastatic pelvic lymph nodes prior to initial definitive therapy seems to be affected by risk factors such as Gleason score and tumor stage. PYLARIFY uptake is not specific for prostate cancer and may occur with other types of cancer as well as non-malignant processes and in normal tissues. Clinical correlation, which may include histopathological evaluation of the suspected prostate cancer site, is recommended.

Hypersensitivity Reactions

Monitor patients for hypersensitivity reactions, particularly patients with a history of allergy to other drugs and foods. Reactions may be delayed. Always have trained staff and resuscitation equipment available.

Radiation Risks

Diagnostic radiopharmaceuticals, including PYLARIFY, expose patients to radiation. Radiation exposure is associated with a dose-dependent increased risk of cancer. Ensure safe handling and preparation procedures to protect patients and health care workers from unintentional radiation exposure. Advise patients to hydrate before and after administration and to void frequently after administration.

Adverse Reactions

The most frequently reported adverse reactions were headaches, dysgeusia and fatigue, occurring at rate of ≤2% during clinical studies with PYLARIFY. In addition, a delayed hypersensitivity reaction was reported in one patient (0.2%) with a history of allergic reactions.

Drug interactions

Androgen deprivation therapy (ADT) and other therapies targeting the androgen pathway, such as androgen receptor antagonists, may result in changes in uptake of PYLARIFY in prostate cancer. The effect of these therapies on performance of PYLARIFY PET has not been established.

To report suspected adverse reactions for PYLARIFY, call 1-800-362-2668 or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For important risk and use information about PYLARIFY Injection, please see Full Prescribing information.

About Lantheus Holdings, Inc.

Lantheus Holdings, Inc. is the parent company of Lantheus Medical Imaging, Inc., Progenics Pharmaceuticals, Inc. and EXINI Diagnostics AB and an established leader and fully integrated provider committed to innovative imaging diagnostics, targeted therapeutics and artificial intelligence solutions to Find Fight and Follow® serious medical conditions. Lantheus provides a broad portfolio of products, including the echocardiography agent DEFINITY® Vial for (Perflutren Lipid Microsphere) Injectable Suspension; PYLARIFY®, a PSMA PET imaging agent for the detection of suspected recurrent or metastatic prostate cancer; TechneLite® (Technetium Tc99m Generator), a technetium-based generator that provides the essential medical isotope used in nuclear medicine procedures; AZEDRA® for the treatment of certain rare neuroendocrine tumors; and RELISTOR® for the treatment of opioid-induced constipation, which is partnered with Bausch Health Companies, Inc. The Company is headquartered in North Billerica, Massachusetts with offices in New York, New Jersey, Canada and Sweden. For more information, visit 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, as amended, that are subject to risks and uncertainties and are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements may be identified by their use of terms such as "anticipate," "believe," "confident," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "will" and other similar terms. Such forward-looking statements are based upon current plans, estimates and expectations that are subject to risks and uncertainties that could cause actual results to materially differ from those described in the forward-looking statements. The inclusion of forward-looking statements should not be regarded as a representation that such plans, estimates and expectations will be achieved. 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. Risks and uncertainties that could cause our actual results to materially differ from those described in the forward-looking statements include (i) the Company's ability to successfully launch PYLARIFY as a commercial product, including (A) Lantheus' ability to obtain FDA approval for additional PET manufacturing facilities (PMFs) that could manufacture PYLARIFY, (B) the ability of those PMFs to supply PYLARIFY to customers, and (C) Lantheus' ability to sell PYLARIFY to customers; and (ii) the risks and uncertainties discussed in our filings with the Securities and Exchange Commission (including those described in the Risk Factors section in our Annual Reports on Form 10-K and our Quarterly Reports on Form 10-Q), including, but not limited to those related to PYLARIFY.

[1]Changes in treatment plan do not necessarily lead to improved patient outcomes.

[2]Pienta KJ et al. A Phase 2/3 Prospective Multicenter Study of the Diagnostic Accuracy of Prostate Specific Membrane Antigen PET/CT with 18F-DCFPyL in Prostate Cancer Patients (OSPREY). *J Urol*. 2021;206(1):52-61.

[3]American Cancer Society. Facts & Figures 2021. American Cancer Society. Atlanta, GA. 2021.

[4]Mena et al. 18 F-DCFPyL PET/CT Imaging in Patients with Biochemically Recurrent Prostate Cancer After Primary Local Therapy J Nucl Med 2020 Jun;61(6):881-889. doi: 10.2967/jnumed.119.234799. Epub 2019 Nov 1.

[5]Alipour et al. Guiding management of therapy in prostate cancer: time to switch from conventional imaging to PSMA PET? Ther Adv Med Oncol. 2019; 11: 1758835919876828.

[6]Werner et al 18F-Labeled, PSMA-Targeted Radiotracers: Leveraging the Advantages of Radiofluorination for Prostate Cancer Molecular Imaging Theranostics 2020; 10(1):1-16. doi:10.7150/thno.37894.

[7]Petersen LJ, Zacho HD. PSMA PET for primary lymph node staging of intermediate and high-risk prostate cancer: an expedited systematic review. Cancer Imaging. 2020;20(1):1-8. doi:10.1186/s40644-020-0290-

[8]Tan N, Oyoyo U, Bavadian N, et al. PSMA-targeted radiotracers versus 18F fluciclovine for the detection of prostate cancer biochemical recurrence after definitive therapy: a systematic review and meta-analysis. Radiology. 2020;296:44-55. doi:10.1148/radiol.2020191689

[9]PYLARIFY® [package insert]. North Billerica, MA: Progenics Pharmaceuticals, Inc., a Lantheus company

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