Lantheus Announces Presentation Featuring AZEDRA® (iobenguane I 131) at ENDO 2021

March 22, 2021

- Statistically Significant Correlation Between Biomarker Responses and Objective Tumor Response -

NORTH BILLERICA, Mass.--(BUSINESS WIRE)--Mar. 22, 2021-- Lantheus Holdings, Inc. (NASDAQ: LNTH) (Lantheus), an established leader and fully integrated provider of innovative imaging diagnostics, targeted therapeutics and artificial intelligence solutions to find, fight and follow serious medical conditions, announced today that updated biochemical tumor marker data from its pivotal Phase 2 trial of AZEDRA® (iobenguane I 131) were presented at the Endocrine Society's 2021 Annual Meeting, ENDO 2021.

Dr. Camilo Jimenez, Professor of Endocrine Neoplasia and Hormonal Disorders at the University of Texas MD Anderson Cancer Center, delivered an oral presentation entitled: "Biochemical Tumor Marker Status and Its Role in Treatment Response in Patients Who Received High-Specific-Activity I-131 MIBG in Advanced Pheochromocytoma and Paraganglioma (PPGL): Results from a Pivotal Phase 2 Clinical Trial" on Saturday, March 20, 2021.

"AZEDRA yielded reductions in hypersecreted tumor biomarkers in a majority of patients in this pivotal study of advanced pheochromocytoma and paraganglioma," said Dr. Jimenez. "In addition, the overall tumor biomarker response correlated significantly with both the primary and secondary endpoint responses in the study, underscoring the clinical utility and relevance of this important biochemical endpoint to the therapeutic benefit of AZEDRA in patients with these life-threatening tumors."

Tumor biomarkers were analyzed in patients with hypersecreting tumors (tumor biomarkers 1.5x above the upper limit of normal at baseline). The best biochemical responses (complete response (CR) or partial response (PR) at any time after treatment as evidenced by significant biomarker reductions) were observed in 80% (Chromogranin A), 70% (total metanephrines) and 64% (vanillylmandelic acid) of patients administered at least one therapeutic dose of AZEDRA. The overall tumor biomarker response correlated significantly with the best confirmed objective tumor response by Response Evaluation Criteria in Solid Tumors (RECIST) v.1.0 (including PR and stable disease; r=0.35, p=0.006). Importantly, none of the responders with an overall biomarker response (CR or PR) had progressive disease as best response per RECIST.

"AZEDRA is the first and only approved treatment option for patients with advanced or metastatic PPGL," said Istvan Molnar, M.D., Chief Medical Officer of Lantheus. "Elevated neuroendocrine markers are the hallmark of these diseases and are responsible for many of the signs and symptoms of PPGL. We believe these data support the established efficacy of AZEDRA in its approved indication by demonstrating that after treatment with AZEDRA, the majority of patients with elevated baseline neuroendocrine markers had a reduction of these markers."

Indication

AZEDRA® (iobenguane I 131) is indicated for the treatment of adult and pediatric patients 12 years and older with iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma who require systemic anticancer therapy.

Important Safety Information

Warnings and Precautions:

Risk from radiation exposure: AZEDRA contributes to a patient's overall long-term radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. These risks of radiation associated with the use of AZEDRA are greater in pediatric patients than in adults. Minimize radiation exposure to patients, medical personnel, and household contacts during and after treatment with AZEDRA consistent with institutional good radiation safety practices and patient management procedures.

Myelosuppression: Severe and prolonged myelosuppression occurred during treatment with AZEDRA. Among the 88 patients who received a therapeutic dose of AZEDRA, 33% experienced Grade 4 thrombocytopenia, 16% experienced Grade 4 neutropenia, and 7% experienced Grade 4 anemia. Five percent of patients experienced febrile neutropenia. Monitor blood cell counts weekly for up to 12 weeks or until levels return to baseline or the normal range. Withhold and dose reduce AZEDRA as recommended in the prescribing information based on severity of the cytopenia.

Secondary myelodysplastic syndrome, leukemia, and other malignancies: Myelodysplastic syndrome (MDS) and acute leukemias were reported in 6.8% of the 88 patients who received a therapeutic dose of AZEDRA. The time to development of MDS or acute leukemia ranged from 12 months to 7 years. Two of the 88 patients developed a non-hematological malignancy.

Hypothyroidism: Hypothyroidism was reported in 3.4% of the 88 patients who received a therapeutic dose of AZEDRA. Initiate thyroid-blocking medications starting at least 1 day before and continuing for 10 days after each AZEDRA dose to reduce the risk of hypothyroidism or thyroid neoplasia. Evaluate for clinical evidence of hypothyroidism and measure thyroid-stimulating hormone (TSH) levels prior to initiating AZEDRA and annually thereafter.

Elevations in blood pressure: Eleven percent of the 88 patients who received a therapeutic dose of AZEDRA experienced a worsening of pre-existing hypertension defined as an increase in systolic blood pressure to ≥160 mmHg with an increase of 20 mmHg or an increase in diastolic blood pressure to ≥100 mmHg with an increase of 10 mmHg. All changes in blood pressure occurred within the first 24 hours post infusion. Monitor blood pressure frequently during the first 24 hours after each therapeutic dose of AZEDRA.

Renal toxicity: Of the 88 patients who received a therapeutic dose of AZEDRA, 7% developed renal failure or acute kidney injury and 22% demonstrated a clinically significant decrease in glomerular filtration rate (GFR) measured at 6 or 12 months. Monitor renal function during and after treatment with AZEDRA. Patients with baseline renal impairment may be at greater risk of toxicity; perform more frequent assessments of renal function in patients with mild or moderate impairment. AZEDRA has not been studied in patients with severe renal impairment.

Pneumonitis: Fatal pneumonitis occurred 9 weeks after a single dose in one patient in the expanded access program. Monitor patients for signs and symptoms of pneumonitis and treat appropriately.

Embryo-fetal toxicity: Based on its mechanism of action, AZEDRA can cause fetal harm. Verify pregnancy status in females of reproductive potential prior to initiating AZEDRA. Advise females and males of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with AZEDRA and for 7 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the final dose.

Risk of infertility: Radiation exposure associated with AZEDRA may cause infertility in males and females. Radiation absorbed by testes and ovaries from the recommended cumulative dose of AZEDRA is within the range where temporary or permanent infertility can be expected following external beam radiotherapy.

Adverse Reactions: The most common severe (Grade 3–4) adverse reactions observed in AZEDRA clinical trials (≥10%) were lymphopenia (78%), neutropenia (59%), thrombocytopenia (50%), fatigue (26%), anemia (24%), increased international normalized ratio (18%), nausea (16%), dizziness (13%), hypertension (11%), and vomiting (10%). Twelve percent of patients discontinued treatment due to adverse reactions (thrombocytopenia, anemia, lymphopenia, nausea and vomiting, multiple hematologic adverse reactions).

Drug Interactions: Based on the mechanism of action of iobenguane, drugs that reduce catecholamine uptake or that deplete catecholamine stores may interfere with iobenguane uptake into cells and therefore interfere with dosimetry calculations or the efficacy of AZEDRA. These drugs were not permitted in clinical trials that assessed the safety and efficacy of AZEDRA. Discontinue the drugs listed in the prescribing information for at least 5 half-lives before administration of either the dosimetry dose or a therapeutic dose of AZEDRA. Do not administer these drugs until at least 7 days after each AZEDRA dose.

For important risk and use information about AZEDRA, 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 of 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; 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.

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