Lantheus Presents Results from the Primary Analysis of Phase 3 Pivotal SPLASH Trial in PSMA-Positive Metastatic Castration-Resistant Prostate Cancer During ESMO Congress 2024

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Study met its primary endpoint, demonstrating significant improvement in radiographic progression-free survival

Overall Response Rate was 38.1% vs. 12.0% for the ARPI switch arm, including 9.3% Complete Responses

Patients demonstrated statistically significant improvement in time to reduction of health-related quality of life (HRQoL) as measured by Functional Assessment of Cancer Therapy—Prostate (FACT-P)

Interim Overall Survival Crossover Adjusted Hazard Ratio was <1.00 when Assessed Using Two-Stage and Inverse Probability Censoring Weighting Methods

Overall Survival data continue to mature, an update is expected once data are available for 75% of protocol-specified target OS events

BEDFORD, Mass., Sept. 15, 2024 (GLOBE NEWSWIRE) -- Lantheus Holdings, Inc. (“Lantheus”) (NASDAQ: LNTH), the leading radiopharmaceutical-focused company committed to enabling clinicians to Find, Fight and Follow disease to deliver better patient outcomes, presented additional clinical data from initial topline results of the SPLASH Phase 3 trial evaluating the efficacy of ^{177}Lu-PNT2002, a prostate-specific membrane antigen (PSMA)-targeted radioligand therapy (RLT), administered at 6.8 GBq every 8 weeks for up to 4 cycles in patients with metastatic castration-resistant prostate cancer (mCRPC) following progression on androgen receptor pathway inhibitor (ARPI). Data were presented during the European Society of Medical Oncology (ESMO) Congress 2024, which is taking place in Barcelona, Spain.

“We are encouraged by the initial results from the SPLASH trial, with ^{177}Lu-PNT2002 demonstrating improvement compared to ARPI change in radiographic progression-free survival, positive interim crossover-adjusted overall survival hazard ratios, as well as improved quality of life,” said Oliver Sartor, M.D., Director of Radiopharmaceutical Trials and Professor of Medical Oncology at the Mayo Clinic in Rochester, Minnesota. “These initial data underscore the importance of PSMA-targeted RLTs, including ^{177}Lu-PNT2002, as potential treatment options for patients who have limited choices after progressing on ARPI therapy.”

Efficacy Endpoint	**^{177}Lu-PNT2002 vs. ARPI**
Radiographic Progression-Free Survival (rPFS)	HR 0.71 (CI: 0.55, 0.92; *p=0.0088*)
Median rPFS	9.5 vs. 6.0 months
OS HR (46% of protocol-specified target OS events reached)	1.11 (0.73, 1.69; *p=0.6154*)
OS HR crossover adjusted: prespecified RPSFTM*	1.14 (0.54, 2.53)
Two-Stage Method: no recensoring**	0.68 (0.44, 1.04)
Two-Stage Method: recensoring**	0.85 (0.53, 1.36)
Inverse Probability Censoring Weighting (IPCW)**	0.72 (0.48, 1.12)
Objective Response Rate (ORR) by BICR***	38.1% vs. 12.0% (*p=0.0021*)
Median Duration of Response (DOR)	9.4 vs. 7.3 months
PSA50 Response****	35.7% vs. 14.6%
Biochemical Progression Free Survival (bPFS)	7.0 vs. 3.9 months (HR 0.58; CI: 0.44, 0.76; *p*<0.0001)
Median time to deterioration by FACT-P	8.1 vs. 5.3 months (HR 0.59; CI: 0.44, 0.80; *p*=0.0005)
Time to Opioid Use for Cancer-Related Pain	HR 0.64 (CI: 0.42, 0.98; *p*=0.0366)

*Overlapping OS curves suggest potential violation of statistical assumptions in RPSFTM method; **exploratory analyses; ***confirmed and unconfirmed ORR; ****evaluable subjects with baseline PSA value

The pivotal SPLASH trial met its primary endpoint, demonstrating a median radiographic progression-free survival (rPFS) per blinded independent central review of 9.5 months for patients treated with ^{177}Lu-PNT2002, compared to 6.0 months for patients treated with ARPI in the control arm, a statistically significant 29% reduction in the risk of radiographic progression or death (hazard ratio [HR] 0.71; *p*=0.0088). In the SPLASH study, ^{177}Lu-PNT2002 patients demonstrated significantly improved ORR, PSA50 reduction, time to reduction of HRQoL, and time to opioid use for cancer-related pain in PSMA-positive mCRPC patients who had progressed on an ARPI. At the time of the analysis, 84.6% of patients who experienced progressive disease in the

control arm subsequently crossed over to receive ^{177}Lu-PNT2002. The overall survival (OS) results at 46% of protocol-specified target OS events reached had a HR of 1.11, with additional crossover adjusted HRs for rank preserving structural failure time model (RPSFTM): (1.14); Two-Stage: no recensoring (0.68); Two-Stage recensoring (0.85); and Inverse Probability Censoring Weighting (0.72).

^{177}Lu-PNT2002 also demonstrated a favorable safety profile compared to patients treated with ARPI in the control arm. Only 3.0% of patients treated with ^{177}Lu-PNT2002 halted or reduced therapy as a result of treatment-emergent adverse events (TEAEs), compared to 11.5% of patients treated with ARPI, and 17.1% of ^{177}Lu-PNT2002 patients experienced serious TEAEs compared to 23.1% of ARPI patients.

Adverse Events	**^{177}Lu-PNT2002**	**ARPI**
Treatment-related AEs grade ≥ 3	9.7% (26/269)	11.5% (15/130)
Treatment-related serious AEs	2.2% (6/269)	3.8% (5/130)
Treatment-related AEs leading to death	0.0% (0/269)	0.0% (0/130)

"^{177}Lu-PNT2002 is outperforming the control arm and showing an improved quality of life for patients based on this interim analysis," said Jeff Humphrey, M.D., Chief Medical Officer at Lantheus. "We are grateful to the patients and investigators who participated in this trial thereby helping to advance this important potential treatment option."

About the SPLASH Trial

The Phase 3 SPLASH trial is a multicenter, randomized, open-label assessment of ^{177}Lu-PNT2002 administered at 6.8 GBq for up to 4 cycles in patients with PSMA-expressing mCRPC who have progressed on ARPI therapy and refuse, or are not eligible for, chemotherapy. The randomization phase of the study randomized 412 patients across North America, Europe, and the United Kingdom. Patients were randomized 2:1 with those in arm A receiving ^{177}Lu-PNT2002 and those in arm B receiving either abiraterone or enzalutamide. Patients in arm B who experience centrally assessed radiographic progression and meet protocol eligibility have the option to crossover and receive ^{177}Lu-PNT2002. Patients will be followed for up to 5 years from their first ^{177}Lu-PNT2002 dose. The primary endpoint of the study is radiographic progression-free survival.

At the time of the primary analysis, 84.6% of patients who experienced progressive disease in the control arm subsequently crossed over to receive ^{177}Lu-PNT2002. SPLASH was conducted across the United States, Canada, Europe, and the United Kingdom. Eighty percent of SPLASH patients resided in North America and approximately 10% of all participants were Black or African American. More information about the trial is accessible at www.ClinicalTrials.gov, identifier NCT04647526.

About ^{177}Lu-PNT2002

^{177}Lu-PNT2002 is a PSMA-targeted, lutetium 177-based radioligand therapy candidate that combines a PSMA-targeted ligand, PSMA-I&T, with the beta-emitting radioisotope no-carrier-added lutetium-177. Lantheus in-licensed exclusive worldwide commercialization rights (excluding certain Asian territories) to ^{177}Lu-PNT2002 from POINT Biopharma (a Lilly company) in December of 2022. In April of 2023, the FDA granted Fast Track designation for ^{177}Lu-PNT2002 for the treatment of mCRPC. Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and address unmet medical needs.

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 2024, almost 299,010 new cases of prostate cancer will be diagnosed, and about 35,250 men will die of the disease.[1]

About Lantheus

Lantheus is the leading radiopharmaceutical-focused company, delivering life-changing science to enable clinicians to Find, Fight and Follow disease to deliver better patient outcomes. Headquartered in Massachusetts with offices in Canada and Sweden, Lantheus has been providing radiopharmaceutical solutions for more than 65 years. For more information, visit www.lantheus.com.

Safe Harbor for Forward-Looking and Cautionary Statements

This press release contains "forward-looking statements" that are subject to risks and uncertainties. Forward-looking statements include, but are not limited to, statements relating to the potential of PNT2002 and statements regarding Lantheus' expectations, hopes, beliefs, intentions or strategies regarding the future. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. Forward-looking statements may be identified by their use of terms such as "expected," "look," "planned," "potential," "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. Risks and uncertainties that could cause our actual results to materially differ from those described in the forward-looking statements include (i) the outcome of the SPLASH trial after full data is available; (ii) a delay in obtaining, or failure to obtain, a positive regulatory outcome from the FDA and regulatory authorities for PNT2002; (iii) the additional costs and risks associated with Lantheus' ability to successfully launch PNT2002 as a commercial product; (iv) the market and patient receptivity to PNT2002 as a radiopharmaceutical therapy; (v) the existence, availability and profile of competing products and therapies; (vi) Lantheus'

ability to obtain and maintain adequate coding, coverage and payment for PNT2002; (vii) the intellectual property protection of PNT2002; (viii) POINT Biopharma's ability to successfully develop and scale the manufacturing capabilities to support the launch of PNT2002; and (ix) the risks and uncertainties discussed in Lantheus' filings with the Securities and Exchange Commission (including those described in the Risk Factors section in its Annual Reports on Form 10-K and its Quarterly Reports on Form 10-Q). 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. 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.

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[1] American Cancer Society. Facts & Figures 2023. American Cancer Society. Atlanta, GA. 2023

Source: Lantheus Holdings, Inc.