Perspective Therapeutics Presents Updates at the 37th Annual Congress of the European Association of Nuclear Medicine

SEATTLE, Oct. 23, 2024 (GLOBE NEWSWIRE) -- Perspective Therapeutics, Inc. ("Perspective" or the "Company") (NYSE AMERICAN: CATX), a radiopharmaceutical company that is pioneering advanced treatment applications for cancers throughout the body, today announced six updates on the Company's radiopharmaceutical programs being presented at the 37th Annual Congress of the European Association of Nuclear Medicine ("EANM") held in Hamburg, Germany, from October 19-23, 2024.

"The preclinical studies and first-in-human imaging data presented with [^{212}Pb]Pb-PSV359, our novel cyclic peptide targeting fibroblast activation protein-alpha, are very encouraging and validate the potential of this radiopharmaceutical in treating a variety of epithelial-derived cancers," said Thijs Spoor, Perspective's CEO. "We also note the valuable contributions from our scientists, collaborators and independent investigators to advancing the development of our potential new medicines, including updated safety and efficacy observations of [^{212}Pb]Pb-VMT-α-NET."

[^{212}Pb]Pb-PSV359

Presentation One: Preclinical evaluation and first-in-human imaging of [$^{203/212}$Pb]Pb-PSV359, a novel cyclic peptide targeting fibroblast activation protein-alpha (FAP)

Summary: Lead-212 (^{212}Pb; alpha-particle therapy) and lead-203 (^{203}Pb; SPECT imaging) are an elementally identical isotope pair for image-guided, targeted-alpha-particle therapy. High-throughput screening of approximately 3 billion amino acid sequences and affinity maturation identified PSV359, a cyclic peptide targeting human fibroblast activation protein ("hFAP"), which is commonly overexpressed in a variety of cancers. The purpose of this study was to conduct the in vitro and in vivo evaluation of [^{203}Pb/^{212}Pb]Pb-PSV359, and present first-in-human SPECT/CT imaging of [^{203}Pb]Pb-PSV359.

The findings of the study demonstrated that [^{212}Pb]Pb-PSV359 exhibits strong binding affinity (Kd=1.8 nM, Ki=0.4 nM) and selectivity for hFAP. Preclinical biodistribution and imaging studies revealed strong tumor uptake of [^{212}Pb]Pb-PSV359 with fast renal clearance and low background in off-target tissues. Furthermore, strong anti-tumor efficacy of [^{212}Pb]Pb-PSV359 was found in both HT1080-hFAP (FAP on cancer cells) and U87MG (FAP in stromal tissues) xenograft models. First-in-human SPECT/CT images of [^{203}Pb]Pb-PSV359 from an independent investigator revealed strong tumor uptake, fast clearance through the renal system, low accumulation in normal organs, and long tumor retention in all three patients with FAP expressing cancers.

Presenter: Brianna S. Cagle, PhD, Research Scientist, Perspective Therapeutics

[203Pb]Pb-VMT-α-NET

Presentation Two: Impact of molar activity on [^{203}Pb]Pb-VMT-α-NET biodistribution profile in mice bearing neuroendocrine tumor xenograft

Summary: Hematotoxicity limits radiopharmaceutical therapy (RPT) targeting somatostatin receptor 2 ("SSTR2"). Somatostatin agonists and antagonists bind to bone marrow cells and lymphocytes in humans and mice. The molar activity ("MA") of a given RPT impacts radioactivity absorbed dose to normal tissues and tumors by changing the "hot" to "cold" stoichiometry. The purpose of this study was to develop an understanding of how the MA of SSTR2 agonist [^{203}Pb]Pb-VMT-α-NET (an imaging surrogate for [^{212}Pb]Pb-VMT-α-NET) impacts its biodistribution in tumor-free and SSTR2+ tumor bearing mice.

Overall findings of the study demonstrated that the MA of [^{203}Pb]Pb-VMT-α-NET impacts the uptake in low-SSTR2

expressing organs. Results suggest that a "sweet spot" of total injected mass of [^{203}Pb]Pb-VMT-α-NET (<0.5 nmol) can be found in which the tumor to normal tissue ratios can be found. These findings exemplify a strategy that Perspective uses to optimize the therapeutic window of its proprietary RPTs.

Presenter: D. Liu, PhD, Senior Research Scientist, Perspective Therapeutics

Presentation Three: Interim results of [^{212}Pb]VMT-α-NET Targeted Alpha Therapy in Metastatic Gastro-entero-pancreatic Neuroendocrine Tumors: First In-human Clinical Results on Safety and Efficacy

Summary: This is an investigator led, exploratory first-in-human use of [^{212}Pb]Pb-VMT-α-NET in adult patients with unresectable or metastatic SSTR2-positive neuroendocrine tumors ("NETs") and medullary thyroid carcinomas in a compassionate setting in India. This presentation, with a data cutoff date of September 15, 2024, focused on 10 patients with well-differentiated gastroenteropancreatic NETs ("GEP-NETs"). These patients were treated with [^{212}Pb]Pb-VMT-α-NET at a dosage of 67 μCi/kg body weight, with an interval of 8 weeks for up to 6 cycles.

Treatment was well-tolerated with a modest and manageable adverse effect profile. Confirmed tumor responses per RECIST 1.1 were observed in six of ten GEP-NETs patients. The investigator concluded that the toxicity profile suggests the potential for dose escalation to achieve optimal treatment responses. Long term survival data will mature with continued follow-up.

Presenter: Ishita B. Sen, DNB, Director and Head of the Department of Nuclear Medicine & Molecular Imaging at Fortis Memorial Research Institute (FMRI), Gurgaon

Presentation Four: Image guided evaluation of [^{212}Pb]VMT-α-NET in metastatic Neuroendocrine tumors: Bio distribution and Dosimetry

Summary: The aim of this analysis was to assess the biodistribution and image-guided dosimetric estimates of [^{212}Pb]Pb-VMT-α-NET peptide used for targeted alpha therapy in patients with GEP-NETs.

Dosimetry estimates were collected from five of the patients as described in Presentation Three. The results demonstrated that the SPECT/CT imaging with [^{212}Pb]Pb-VMT-α-NET showed prompt tumor accumulation, high tumor retention, and rapid renal excretion in all patients. Overall, the findings suggest that post-treatment imaging of [^{212}Pb]Pb-VMT-α-NET is feasible and can serve as a valuable tool to evaluate and monitor patients through a full course of treatment. Further investigation in a greater number of patients is needed to develop and validate post-treatment Pb-212 imaging and dosimetry for clinical translation.

Presenter: Dharmender Malik, MD, Fortis Memorial Research Institute (FMRI)

Investigator-Led Preclinical Research

Presentation Five: Evaluation and Design of New Chelators using Density Functional Theory Modeling: Implications for Improved Performance of ^{203}Pb/^{212}Pb-based Theranostic for Cancers

Summary: One of the key factors leading to the success of targeted theranostics is the sophisticated matching of the chelator to the specific radionuclide, ensuring stability and targeted delivery. The purpose of this study was to evaluate multiple chelators for imaging and therapeutic radionuclides, and newly designed chelator compositions to potentially optimize for the Pb isotopes. Multiple chelators extensively used in targeted theranostics (i.e., DOTA, NOTA, and TETA) were investigated with imaging (e.g., ^{68}Ga, ^{64}Cu, ^{111}In) and therapeutic radionuclides (e.g., ^{177}Lu, ^{90}Y).

The study revealed how each chelator reacts with imaging and therapeutic radionuclides, optimizing the chelating form for the respective radionuclides. The results confirmed the superior performance of the modified chelators when compared to conventional forms and thus validated this computational strategy to be an effective tool for customizing

chelators for targeted theranostics. Ongoing studies are expected to suggest novel chelator compositions designed for improved stability and specificity for ^{203}Pb/^{212}Pb theranostic radionuclides.

Presenter: Dongyoul Lee, PhD, Department of Physics and Chemistry, Korea Military Academy

Presentation Six: Development of ^{203}Pb Labeled SSTR-Targeting Peptides as Surrogates for ^{212}Pb Labeled Radiopharmaceuticals

Summary: SSTR2 is a key target molecule for peptide receptor radionuclide therapy (PRRT) in NETs. The purpose of this study was to assess the feasibility of ^{203}Pb labeled peptides as surrogates for ^{212}Pb labeled radiopharmaceuticals. SSTR2 agonists (i.e., DOTATATE, PSC-PEG2-TOC) and antagonists (i.e., DOTA-LM3, DOTA-PEG2-LM3) were radiolabeled with ^{203}Pb and evaluated to identify the most promising candidate for PRRT.

The SSTR2-targeting peptides investigated exhibited excellent radiolabeling performance and stability with ^{203}Pb. Imaging data suggested the feasibility of using ^{203}Pb-labeled radiopharmaceuticals as surrogates for ^{212}Pb counterparts, potentially enabling ^{203}Pb image-guided ^{212}Pb therapy for NETs. Further studies are planned to evaluate the therapeutic potential of ^{212}Pb labeled radiopharmaceutical candidates in NET mouse models.

Presenter: Jung Woo Byun, Department of Nuclear Medicine, Seoul National University

For more details on the presentations, the abstract book is available online at https://link.springer.com/article/10.1007/s00259-024-06838-z.

About Perspective Therapeutics, Inc.
Perspective Therapeutics, Inc., is a radiopharmaceutical development company that is pioneering advanced treatment applications for cancers throughout the body. The Company has proprietary technology that utilizes the alpha emitting isotope ^{212}Pb to deliver powerful radiation specifically to cancer cells via specialized targeting peptides. The Company is also developing complementary imaging diagnostics that incorporate the same targeting peptides, which provide the opportunity to personalize treatment and optimize patient outcomes. This "theranostic" approach enables the ability to see the specific tumor and then treat it to potentially improve efficacy and minimize toxicity.

The Company's melanoma (VMT01) and neuroendocrine tumor (VMT-α-NET) programs have entered Phase 1/2a imaging and therapy trials for the treatment of metastatic melanoma and neuroendocrine tumors at several leading academic institutions. The Company has also developed a proprietary ^{212}Pb generator to secure key isotopes for clinical trial and commercial operations.

For more information, please visit the Company's website at www.perspectivetherapeutics.com.

Safe Harbor Statement
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Statements in this press release that are not statements of historical fact are forward-looking statements. Words such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "estimate," "believe," "predict," "potential," or "continue" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, though not all forward-looking statements contain these identifying words. Forward-looking statements in this press release include express or implied statements concerning, among other things, the Company's ability to pioneer and develop advanced treatment applications for cancers throughout the body; expectations regarding the timing and advancement of the Company's clinical and preclinical programs; the potential of [^{212}Pb]Pb-PSV359 to treat a variety of epithelial-derived cancers; the feasibility of post-treatment imaging of [^{212}Pb]Pb-VMT-α-NET to evaluate and monitor patients; the potential to modify chelators for targeted theranostics; the potential identification of novel chelator compositions to offer improved stability and specificity for ^{203}Pb/^{212}Pb theranostic radionuclides; the feasibility of using ^{203}Pb-labeled radiopharmaceuticals as surrogates for

^{212}Pb counterparts, potentially enabling ^{203}Pb image-guided ^{212}Pb therapy for NETs; plans for future studies to evaluate the therapeutic potential of ^{212}Pb labeled radiopharmaceutical candidates; the ability of the Company's proprietary technology that utilizes the alpha-emitting isotope ^{212}Pb to deliver powerful radiation specifically to cancer cells via specialized targeting peptides; the opportunity to personalize treatment and optimize patient outcomes using the Company's complementary imaging diagnostics that incorporate the same targeting peptides; the Company's expectation that its "theranostic" approach enables the ability to see specific tumors and then treat them to potentially improve efficacy and minimize toxicity; the Company's ability to develop a proprietary ^{212}Pb generator to secure key isotopes for clinical trial and commercial operations; expectations regarding the potential market opportunities for the Company's product candidates; the potential functionality, capabilities, and benefits of the Company's product candidates and the potential application of these product candidates for other disease indications; the Company's expectations, beliefs, intentions, and strategies regarding the future; the Company's intentions to improve important aspects of care in cancer treatment; and other statements that are not historical fact.

The Company may not actually achieve the plans, intentions, or expectations disclosed in the forward-looking statements, and you should not place undue reliance on the forward-looking statements. These forward-looking statements involve risks and uncertainties that could cause the Company's actual results to differ materially from the results described in or implied by the forward-looking statements. Certain factors that may cause the Company's actual results to differ materially from those expressed or implied in the forward-looking statements in this press release are described under the heading "Risk Factors" in the Company's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC"), in the Company's other filings with the SEC, and in the Company's future reports to be filed with the SEC and available at www.sec.gov. Forward-looking statements contained in this news release are made as of this date. Unless required to do so by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.

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