Molecular Partners and Orano Med Present Additional Positive Preclinical Data Supporting DLL3 Targeting Radio-DARPin Therapeutic Candidate MP0712 at EANM 2024

October 22, 2024

Dose-dependent efficacy observed with favorable safety profile

Attractive tumor to kidney ratios shown in biodistribution studies

Picomolar affinity and high specificity for DLL3 as precision attributes for alpha radiation therapy

Molecular Partners and Orano Med preparing for clinical entry in 2025

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass. and PARIS, Oct. 22, 2024 (GLOBE NEWSWIRE) -- **Ad hoc announcement pursuant to Art. 53 LR** – Molecular Partners AG (SIX: MOLN; NASDAQ: MOLN), a clinical-stage biotech company developing a new class of custom-built protein drugs known as DARPin therapeutics, and Orano Med, a clinical-stage radiopharmaceutical company developing targeted alpha therapies with lead-212 (^{212}Pb), today announced the oral presentation of the latest preclinical data supporting MP0712 as a Radio-DARPin Therapeutic (RDT) at the European Assocation of Nuclear Medicine (EANM) Congress which runs October 19-23, 2024 in Hamburg, Germany. MP0712 is a co-developed ^{212}Pb-labeled RDT candidate targeting delta-like ligand 3 (DLL3). Molecular Partners and Orano Med anticipate initiating first-in-human studies, pending regulatory clearance, in 2025. Initial clinical data of MP0712 is also anticipated in 2025.

“The latest data on MP0712, our DLL3 RDT co-developed with Orano Med, confirms the high tumor uptake in a model with matched target expression level to the human cancer setting, while keeping kidney exposure low. The additional *in vivo* efficacy and safety data further strengthen the momentum for our planned clinical entry next year, likely constituting the first DLL3-targeting ^{212}Pb agent in development,” said Patrick Amstutz, Ph.D., CEO of Molecular Partners. “Together with our partner Orano Med, we’ve been able to kidney-stealth engineer our DARPins and add tumor uptake by half-life tuning to evolve our Radio-DARPin platform. These learnings are directly being applied to the next candidates in our RDT pipeline.”

“We are very pleased with the results of MP0712, to date. The homogeneous distribution observed through alpha camera imaging not only supports our DLL3 program but also highlights the promising potential of the collaboration between Molecular Partners and Orano Med. Their DARPin vectors are particularly well-suited for Targeted Alpha Therapy (TAT) with lead-212. By leveraging the expertise of both teams, we aim to build a robust platform and significantly shorten development timelines,” said Julien Torgue, Ph.D., Chief Scientific Officer of Orano Med.

Details of this Top-Rated Oral Presentation (TROP):

- **Presentation Title:** Preclinical assessment of lead-212 (^{212}Pb) Radio-DARPin Therapeutic (RDT) targeting delta-like ligand 3 (DLL3) in small cell lung cancer (SCLC)
- **Presentation Number:** OP-535
- **Session Title:** M2M Track - TROP Session: Radiopharmaceutical Sciences + Translational Molecular Imaging & Therapy Committee: From Radionuclide to Clinical Translation (session number: 1204)
- **Session Date, Timing & Location:** 22 October 2024; 8:00-9:30 am CEST; Hall X1-X4

The presentation highlights that attractive tumor to kidney (T:K) ratios of >2 can be achieved in biodistribution studies across several models, including in a disseminated tumor model with clinically relevant DLL3 expression levels. This suggests strong uptake by the targeted tissue while minimally impacting healthy tissues. In addition, *in vivo* data indicated that tumor uptake was specific to DLL3.

Dose-range finding studies in mice confirmed that treatment at a clinically relevant dosage was well tolerated, supporting a favorable safety profile. Finally, MP0712 led to strong and dose-dependent efficacy in mice bearing established tumors with clinically-relevant levels of DLL3 expression and at a clinically-relevant dose, as compared to a positive control of a radiolabelled anti-DLL3 antibody rovalpituzumab (Rova).

DLL3 is a highly relevant target for radiopharmaceutical therapy due to its abundant expression in tumors of patients with small cell lung cancer (present in >85% of tumors) and other aggressive neuroendocrine tumors, while expression in healthy tissues is low. MP0712 has picomolar affinity and high specificity to human DLL3.

Molecular Partners is developing its RDT platform for targeted delivery of radioactive payloads to solid tumors. Due to their small size, high specificity and affinity, DARPins are well-suited as potential vectors for efficient delivery of therapeutic radionuclides. DARPins are also readily designed as multispecifics, making bi-specific (or larger) candidates a promising area of growth for Molecular Partner’s RDT portfolio as additional targeting may help address target heterogeneity in many tumors. The portfolio includes programs being developed in-house as well as via collaborations with Orano Med and Novartis.

The presentation given today will be made available on Molecular Partner’s website in the Scientific Documents section.

About DARPin Therapeutics
DARPin (Designed Ankyrin Repeat Protein) therapeutics are a new class of custom-built protein drugs based on natural binding proteins that open new dimensions of multi-functionality and multi-target specificity in drug design. The flexible architecture, intrinsic potential for high affinity and specificity, small size and high stability of DARPins offer benefits to drug design over other currently available protein-based therapeutics. DARPin candidates can be radically simple, with a single DARPin unit acting as the delivery vector to a specific target; or multispecific, with the possibility of engaging more than five targets, and combining multiple and conditional functionalities in a unique DARPin drug candidate. The DARPin platform is designed to be a rapid and cost-effective drug discovery engine, producing drug candidates with optimized properties and high production yields. DARPin therapeutics have been clinically validated across several therapeutic areas and developed through to the registrational stage.

About Targeted Alpha Therapy
Targeted alpha therapy (TAT) relies on a simple concept: combining the ability of biological molecules to target cancer cells with the short-range and highly energetic cell-killing capabilities of alpha-emitting radioisotopes, such as lead-212. Alpha decay consists of the emission of a helium nucleus (alpha particle) together with very high linear energy transfer and a range emission of only few cell layers, resulting in irreparable double strand DNA breaks in cells adjacent only to area of alpha emission. This approach results in an increased cytotoxic potential toward cancer cells while limiting toxicity to nearby healthy cells. As a result, alpha emitters are considered as the most powerful payloads to be found for targeted therapies.

About Molecular Partners AG
Molecular Partners AG is a clinical-stage biotech company pioneering the design and development of DARPin therapeutics for medical challenges other drug modalities cannot readily address. The Company has programs in various stages of pre-clinical and clinical development, with oncology as its main focus. Molecular Partners leverages the advantages of DARPins to provide unique solutions to patients through its proprietary programs as well as through partnerships with leading pharmaceutical companies. Molecular Partners was founded in 2004 and has offices in both Zurich, Switzerland and Concord, MA, USA. For more information, visit www.molecularpartners.com and find us on LinkedIn and Twitter/X @MolecularPrtnrs

About Orano Med
Orano Med is a clinical-stage biotechnology company which develops a new generation of targeted therapies against cancer using the unique properties of lead-212 (^{212}Pb), a rare alpha-emitting radioisotope and one of the more potent therapeutic payloads against cancer cells known as Targeted Alpha-Emitter Therapy (TAT). The company develops several treatments using ^{212}Pb combined with various targeting agents. Orano Med has ^{212}Pb manufacturing facilities, laboratories, and R&D centers in France and in the US and is currently investing to further expand its GMP-manufacturing capacities for ^{212}Pb radiolabeled pharmaceuticals in North America and Europe. For more information, please visit: www.oranomed.com.

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Cautionary Note Regarding Forward-Looking Statements
Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation: implied and express statements regarding the clinical development of Molecular Partners' current or future product candidates, including MP0712; expectations regarding timing for reporting data from ongoing preclinical studies and clinical trials or the initiation of future preclinical studies and clinical trials; the potential therapeutic and clinical benefits of Molecular Partners' product candidates and its RDT and Switch-DARPin platforms; the selection and development of future programs; Molecular Partners' collaborations with Orano Med and Novartis, including the benefits and results that may be achieved through those collaborations; the timing of regulatory filings and the likelihood of favorable regulatory outcomes and approvals, including the IND for MP0712; and Molecular Partners' expected business and financial outlook. These statements may be identified by words such as "aim", "expect", "guidance", "intend", "outlook", "plan", "potential", "will" and similar expressions, and are based on Molecular Partners' current beliefs and expectations. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Some of the key factors that could cause actual results to differ from Molecular Partners' expectations include its plans to develop and potentially commercialize its product candidates; Molecular Partners' reliance on third party partners and collaborators over which it may not always have full control; Molecular Partners' ongoing and planned clinical trials and preclinical studies for its product candidates, including the timing of such trials and studies; the risk that the results of preclinical studies and clinical trials may not be predictive of future results in connection with future clinical trials; the timing of and Molecular Partners' ability to obtain and maintain regulatory approvals for its product candidates; the extent of clinical trials potentially required for Molecular Partners' product candidates; the clinical utility and ability to achieve market acceptance of Molecular Partners' product candidates; the potential that Molecular Partners' product candidates may exhibit serious adverse, undesirable or unacceptable side effects; the impact of any health pandemic, macroeconomic factors and other global events on Molecular Partners' preclinical studies, clinical trials or operations, or the operations of third parties on which it relies; Molecular Partners' plans and development of any new indications for its product candidates; Molecular Partners' commercialization, marketing and manufacturing capabilities and strategy; Molecular Partners' intellectual property position; Molecular Partners' ability to identify and in-license additional product candidates; unanticipated factors in addition to the foregoing that may impact Molecular Partners' financial and business projections and guidance; and other risks and uncertainties that are described in the Risk Factors section of Molecular Partners' Annual Report on Form 20-F for the fiscal year ended December 31, 2023, filed with Securities and Exchange Commission (SEC) on March 14, 2024 and other filings

Molecular Partners makes with the SEC. These documents are available on the Investors page of Molecular Partners' website at www.molecularpartners.com. In addition, this press release contains information relating to interim data as of the relevant data cutoff date, results of which may differ from topline results that may be obtained in the future. Any forward-looking statements speak only as of the date of this press release and are based on information available to Molecular Partners as of the date of this release, and Molecular Partners assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.