Molecular Partners presents new preclinical data on Radio-DARPin and Switch-DARPin programs at AACR 2025

April 25, 2025

- *Positive IND-enabling data on MP0712 targeting DLL3, the most advanced Radio-DARPin program in co-development with Orano Med, entering clinical development in 2025*
- *First preclinical data of novel targeted Radio-DARPin against mesothelin (MSLN), in co-development with Orano Med*
- *Additional preclinical proof-of-concept data on logic-gated CD3 Switch-DARPin T cell engager with CD2 co-stimulation*

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass., April 25, 2025 (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 ("Molecular Partners" or the "Company"), today announced the presentation of three posters at the American Association for Cancer Research (AACR) Annual Meeting 2025, taking place April 25–30 in Chicago, IL. The first poster includes positive Investigational New Drug (IND)-enabling data for MP0712, a Radio-DARPin targeting DLL3 and labeled with ^{212}Pb for small cell lung cancer patients. The second poster presents initial preclinical data on the second ^{212}Pb-based Radio-DARPin, targeting mesothelin (MSLN) in solid tumors – both programs are co-developed with Orano Med. The third poster includes additional preclinical proof-of-concept data on the logic-gated CD3 Switch-DARPin T cell engager with CD2 co-stimulation in solid tumors.

"Our presentations at AACR highlight the breadth of Molecular Partners' DARPin innovation and the progress in our strategic Radio-DARPin partnership with Orano Med. Our first Radio-DARPin program, MP0712, targeting DLL3, is well advanced and on track to provide initial clinical data in the second half of 2025. Additionally, we are proud to present the first preclinical data from our second program with Orano Med, targeting MSLN. The results show substantial uptake into MSLN-positive tumors, with limited accumulation in other organs, justifying continued investment in our RDT x MSLN program for solid tumors," said Patrick Amstutz, Ph.D., CEO of Molecular Partners.

"Furthermore, we continue to advance our wholly-owned logic-gated and co-stimulated T cell engager program. Our SWITCH approach activates CD3/T-cells only when binding to tumor-associated antigens, while remaining inactive in circulation. This gating allows us to add a CD2 DARPin for co-stimulation without the risk of fratricide. This project demonstrates the value of our platform, which can be used for any target combination."

Preclinical data presented on MP0712, a DLL3-targeting and ^{212}Pb-labeled Radio-DARPin, show a high tumor uptake and a favorable safety profile for MP0712, with good efficacy and tumor reduction in mouse models matching clinically relevant DLL3 expression levels. With these data, the IND-enabling package is complete; IND filing and initial first-in-human clinical data are expected in 2025. DLL3 is a promising target for radioligand therapy as it is highly upregulated in small cell lung cancer and other high-grade neuroendocrine tumors, while not expressed in healthy tissues.

The MSLN x ^{212}Pb Radio-DARPin poster outlines how MSLN may be a promising target for ovarian cancer due to its differentiated expression profiles - high in tumor, and lower in healthy tissues. High levels of shed MSLN, however, can act as a decoy receptor and have historically hampered the development of MSLN-targeted therapeutics. Molecular Partners has leveraged the unique properties of DARPins to develop a Radio-DARPin able to selectively bind membrane-bound MSLN without being impacted by shed MSLN. *In vivo* results show a favorable biodistribution with strong tumor accumulation of the Radio-DARPin in a MSLN-overexpressing model in mice.

Preclinical proof-of-concept data on Molecular Partners' conditionally activated CD3 Switch-DARPin shows it activates T cells specifically in the presence of cells co-expressing MSLN and epithelial cell adhesion molecule (EpCAM), increasing tumor specificity. Concurrent CD2 co-engagement leads to sustained T cell activation and cytotoxic capacity, preventing T cell dysfunction. The Switch-DARPin effectively induces significant tumor regression in mice engrafted subcutaneously with MSLN- and EpCAM-expressing cells, without signs of T cell activation in the periphery, indicating a favorable safety profile.

Click here to access the poster presentations, which will be made available on Molecular Partners' website.

Details of the presentations:

MP0712, the first anti-DLL3 ^{212}Pb Radio-DARPin (RDT) candidate for targeted radiotherapy of small cell lung cancer (SCLC)
Session Category: Experimental and Molecular Therapeutics
Session Title: Biochemical Modulators of Cancer / Differentiation Therapeutic Strategies
Session Timing: Sunday April 27 at 2:00pm - 5:00pm CST
Location: Poster Section 16, Poster Board Number: 13
Published Abstract Number: 346

Development of ^{212}Pb-based Radio-DARPin therapy (RDT) for the treatment of mesothelin (MSLN)-positive solid tumors
Session Category: Experimental and Molecular Therapeutics
Session Title: Biochemical Modulators of Cancer / Differentiation Therapeutic Strategies
Session Timing: Sunday April 27 at 2:00 – 5:00pm CST
Location: Poster Section 16, Poster Board Number: 6
Published Abstract Number: 339

Next-generation multi-specific and conditionally activated CD3 Switch-DARPins with CD2 co-stimulation to tackle the current limitations of T cell engagers in solid tumors
Session Category: Experimental and Molecular Therapeutics
Session Title: Therapeutic Approaches to Attack the Tumor Microenvironment
Session Timing: Monday April 28 at 2:00pm – 5:00pm CST
Location: Poster Section 24, Poster Board Number: 3
Published Abstract Number: 3119

About Molecular Partners AG
Molecular Partners AG (SIX: MOLN, NASDAQ: MOLN) 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

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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; expectations regarding timing for reporting data from ongoing clinical trials or the initiation of future 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' collaboration with Orano Med including the benefits and results that may be achieved through the collaboration; and Molecular Partners' expected business and financial outlook, including anticipated expenses and cash utilization for 2025 and its expectation of its current cash runway and the expected use of proceeds from the October 2024 offering. These statements may be identified by words such as "aim", "anticipate", "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 cause Molecular Partners' actual results to differ from its financial and business projections and guidance; and other risks and uncertainties set forth in Molecular Partners' Annual Report on Form 20-F for the year ended December 31, 2024 and other filings Molecular Partners makes with the SEC from time to time. 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.