Molecular Partners Announces Publication in Cancer Immunology Research of Preclinical Data Supporting MP0533's Proposed Mechanism of Action

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- *Preclinical data of tetra-specific T cell engager MP0533 demonstrate preferential T cell mediated killing of AML cells, while sparing healthy cells*
- *Results highlight MP0533-mediated T-cell activation and tumor regression, as well as cytokine release in AML models without systemic adverse effects*
- *Published data build on results previously presented at ASH 2021 and 2022, and support the rationale for the clinical development of MP0533 as monotherapy and in combination with azacitidine/venetoclax*
- *Ongoing Phase 1/2a clinical study continues to progress well, currently dosing patients in cohort 7*

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass., April 29, 2024 (GLOBE NEWSWIRE) -- 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, today announced a comprehensive, peer-reviewed publication of preclinical data supporting MP0533's proposed unique mechanism of action (MoA) for the treatment of acute myeloid leukemia (AML) in *Cancer Immunology Research*, a journal of the American Association for Cancer Research. The publication collates and discusses multiple studies undertaken to characterize MP0533's preclinical profile and evaluate its therapeutic potential.

Developing safe and efficacious targeted therapies for patients with AML has proven challenging as AML cells share many of the relevant target antigens with healthy cells. Through its unique MoA, MP0533 was designed to simultaneously target the proteins CD33, CD123, and CD70, which are commonly co-expressed on AML cells and rarely on healthy cells. MP0533's binding strength increases with the number of target proteins present, leading to increased engagement of T cells when at least two of the targets are present. This results in preferential killing of AML cells.

The data published by Bianchi et al in *Cancer Immunology Research* in collaboration with the University of Bern build on the results presented at the American Society of Hematology (ASH) Annual Meeting and Exposition in December 2021 and 2022, and support MP0533's intended MoA. MP0533 induces selective T cell-mediated killing of AML cell lines, as well as patient bone marrow-derived AML blasts and leukemic stem cells (LSCs) expressing two or three of the target antigens, while sparing healthy hematopoietic stem cells, blood and endothelial cells. MP0533 also demonstrated reduced risk of T cell fratricide observed with other CD70-targeting agents related to CD70's upregulation on activated T cells. MP0533 was equivalent to non-CD70 targeting therapies in terms of impact on T cell count and viability, further supporting its potentially favorable on-target, off-tumor profile.

MP0533 led to tumor-localized T-cell activation and efficacious tumor regression in an antigen-dependent manner across different *in vivo* models. Notably, when compared to other T cell engagers that target single antigens, MP0533 led to lower levels of cytokine release, findings that were confirmed through *in vitro*, *in vivo*, and *ex vivo* studies. This included IL-6, a cytokine known as a primary driver of cytokine release syndrome, a systemic toxicity that has so far limited the development of T cell engagers as potential treatment options of AML. Finally, an evaluation of MP0533 in combination with azacitidine and venetoclax, two chemotherapeutic drugs used in AML, suggest the MoAs may be synergistic in terms of LSC killing.

MP0533 is currently being evaluated in a Phase 1/2a trial in patients with relapsed/refractory AML or myelodysplastic syndrome (MDS/AML), and the Company presented positive initial data from the first four dosing cohorts at the ASH Annual Meeting and Exposition in December 2023. The trial is currently dosing patients in cohort 7. The Company expects to present an update from the study in H1 2024.

For more information about the publication, visit:

The CD33xCD123xCD70 Multispecific CD3-Engaging DARPin MP0533 Induces Selective T Cell–Mediated Killing of AML Leukemic Stem Cells

Reference:
Bianchi M et al. *Cancer Immunol Res* 2024. Epub ahead of print April 29, 2024.

About MP0533
MP0533 is a novel tetra-specific T cell-engaging DARPin, which simultaneously targets the antigens CD33, CD123 and CD70 on AML cells as well as the immune activator CD3 on T cells. AML cells commonly co-express at least two of the three target antigens, whereas most healthy cells only have one or none. MP0533 binds with increasing avidity as the number of its target antigens present increases, dramatically favoring binding to AML cells over healthy cells. This unique avidity-driven mode of action is designed to enable T cell-mediated killing of AML cells while preserving a therapeutic window that minimizes damage to healthy cells.

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 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 Molecular Partners
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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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, the selection and development of future programs, and Molecular Partners' expected business and financial outlook, including anticipated expenses and cash utilization for 2024 and its expectation of its current cash runway. These statements may be identified by words such as "guidance", "believe", "expect", "may", "plan", "potential", "will", "would" 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 may cause Molecular Partners' actual results and outcomes to materially differ from its 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. 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.