Molecular Partners Presents Clinical Data Supporting its Ongoing MP0533 Study and Preclinical Data on Next-Gen Conditioning Agent MP0621 at ASH 2024

December 8, 2024

MP0533 phase 1/2a dose escalation study continues with overall acceptable safety profile to date as well as initial antileukemic and pharmacodynamic activity

Clinical protocol amendment in process with optimized dosing scheme to overcome target-mediated drug disposition and test the full potential of MP0533

Switch-DARPin MP0621 demonstrates intended mechanism in vivo, achieving killing of cKit+ cells while reducing off-target effects seen with systemic anti-CD47 blockade

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass., Dec. 08, 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 ("Molecular Partners" or the "Company"), today announced the presentation of additional data pertaining to two programs, including preclinical data on MP0621, a potential next-generation conditioning regimen for patients undergoing hematopoietic stem cell transplantation, and comprehensive data from the first seven cohorts of the ongoing phase 1/2a dose-escalation study of MP0533. The data are presented in two posters at the American Society of Hematology (ASH) annual meeting, being held December 7-10, 2024 in San Diego, CA.

"We are at a unique crossroads with the MP0533 program. Data from our Ph1/2a study indicate antitumor and pharmacodynamic activity despite currently sub-optimal exposure levels, mostly driven by target-mediated drug disposition," said Patrick Amstutz, Ph.D., CEO of Molecular Partners. "The sum of these data, reviewed in close collaboration with our KOLs, allowed us to define a clear hypothesis that introducing a loading-dose-phase will improve MP0533 exposure, thereby testing the full therapeutic potential of MP0533 in AML patients. We are happy to report that these amendments are submitted, while patient treatment is still ongoing. We look forward to providing updates to the program in 2025."

MP0533: Acceptable safety profile, exposure being optimized via protocol amendment

MP0533 is a novel tetraspecific T cell engaging DARPin which simultaneously targets the three tumor-associated antigens (TAAs) CD33, CD123 and CD70, as well as CD3 on T cells. The mechanism of action of MP0533 is designed to preferentially kill AML cells that express any combination of these three TAAs while sparing healthy cells, which express only one or none of these targets. The immune activation against the malignant cells is achieved through CD3-mediated T cell-engagement.

The data presented at ASH 2024 are from the ongoing first-in-human dose-escalation phase 1/2a study of MP0533 in patients with relapsed/refractory acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS)/AML. MP0533 continues to show an acceptable safety profile in 37 patients up to dose cohort 7, with the majority of adverse events reported being infusion-related reactions and cytokine release syndrome. Initial pharmacodynamic data provide evidence of MP0533 target engagement and resulting immune activation. Despite lower than anticipated drug exposure, four responders in total were reported in cohorts 1-7 and encouraging blast reductions were observed in patients bone marrow, particularly in patients with lower disease burden.

Based on these observations Molecular Partners is amending the protocol of this study to further optimize the dosing schedule and improve the exposure profile of MP0533 in subsequent dosing cohorts. The goal is to achieve higher response rates, as well as an improved quality and duration of response in this heterogeneous patient population.

MP0621: Intended mechanism of HSC depletion confirmed preclinically

MP0621 is a Switch-DARPin candidate designed to induce killing of hematopoietic stem cells (HSCs) as a next-generation conditioning regimen for HSC transplantation (HSCT). The Switch-DARPin platform provides a logic-gated "on/off" function (the "Switch") to multispecific DARPin candidates leading to target activation only in the presence of defined antigens. In MP0621, the Switch-DARPin binds to either cellular cKit or to the anti-CD47 DARPin binder. Upon MP0621 binding to cKit on HSCs, the Switch-DARPin will unmask the anti-CD47 DARPin, which in turn will bind CD47 and block the "don't-eat-me" signal, leveraging the power of CD47 inhibition without its associated toxicity to healthy cells

The preclinical results presented support the intended MP0621 mechanism of action and provide further evidence for its potential as a viable approach for HSC depletion in patients. The blockade of CD47 exclusively on target cells allows MP0621 to enhance efficacy of cKit-targeting, while reducing off-target effects seen with systemic anti-CD47 blockade. The currently available non-human primate data however do not allow Molecular Partners to conclude that MP0621 would serve as a treatment for AML patients, as previously hypothesized. As Molecular Partners' portfolio strategy prioritizes therapeutic candidates for oncology, MP0621 is being evaluated for partnering.

Details of the poster presentations at ASH 2024:

Session Name: 616. Acute Myeloid Leukemias: Investigational Drug and Cellular Therapies: Poster II
Publication Number: 2881
Title: MP0533 (CD33 x CD123 x CD70 x CD3), a Tetra-Specific CD3-Engaging DARPin for the Treatment of Patients with Relapsed/Refractory AML or MDS/AML: Results of an Ongoing Phase 1/2a Study
Session Location: San Diego Convention Center, Halls G-H
Presentation Date & Time: Sunday, December 8, 2024, 6:00–8:00 pm PT

Session Name: 701. Experimental Transplantation: Basic and Translational: Poster III
Publication Number: 4775
Title: MP0621 (cKit x CD16a x CD47), a Multi-Specific Switch-DARPin with Conditional Blockade of CD47 Targeting Hematopoietic Stem Cells: Preclinical Evaluation of a Next-Generation Conditioning Agent for Stem Cell Transplantation
Session Location: San Diego Convention Center, Halls G-H
Presentation Date & Time: Monday, December 9, 2024, 6:00–8:00 pm PT

Both posters 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 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

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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 2024 and its expectation of its current cash runway. 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.