Molecular Partners Presents Positive Preclinical Data for First Switch-DARPin Candidate MP0621 at EHA 2024

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- Proof-of-concept of Switch-DARPin platform established *in vivo*, enabling the use of logic-gated and reversible immune activators
- Preclinical safety, efficacy, and pharmacokinetics support MP0621's potential to selectively kill cKit-positive cells and conditionally block CD47 with limited systemic side effects
- MP0621 presently in IND-enabling studies with Phase 1 in AML anticipated in 2025

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass., June 14, 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, today announced preclinical proof-of-concept data from MP0621, a multispecific cKit x CD16a x CD47 Switch-DARPin program. The data validates the Switch-DARPin concept *in vivo* and MP0621's potential as a next-generation therapeutic supporting hematopoietic stem cell transplantation (HSCT), initially for the treatment of acute myeloid leukemia (AML) patients. The data will be presented today in a poster session at the European Hematology Association (EHA) 2024 Hybrid Congress taking place June 13-16 in Madrid, Spain.

"We designed our Switch-DARPin platform to unlock undruggable targets and enable safe use of powerful immune activators via logic-gated and reversible immune activation," said Anne Goubier, Ph.D., SVP Research & Early Development. "MP0621 is our first candidate in this series, with the aim to clear HSCs effectively and safely, by targeting cKit, engaging innate immune cells via CD16a, and blocking CD47 only on cKit+ cells. We're thrilled by these results, which validate our Switch-DARPin platform *in vitro* and *in vivo* and pave the way for a new generation of conditionally activated T cell engagers, with the potential to revolutionize therapy in areas of unmet need, such as solid tumors".

HSCT offers a potential cure for patients with AML and other malignant and non-malignant diseases. However, the toxicity of pre-HSCT conditioning often requires that it is carried out with reduced intensity, increasing the likelihood that diseased cells remain in the bone marrow and lead to relapse. Safer and more efficacious treatments are needed to improve HSCT outcomes for more patients with AML and other diseases requiring HSC transplant. MP0621 is intended to maximize the therapeutic potential of HSCT for AML patients, including those with poor cytogenetic risk profile, to extend the access to potentially curative HSCT for more patients, and to increase long term disease control post HSCT.

MP0621 is designed to induce eradication of HSCs while avoiding the toxicity associated with current high-intensity conditioning regimens. MP0621 engages natural killer cells and macrophages via CD16a to selectively kill targeted cKit-positive cells. cKit is critical for stem cell maintenance and renewal and thus an attractive target to select for HSCs as well as leukemic stem cells in AML. CD47 is widely expressed as "don't-eat-me" signal and prevents killing of cells, including HSCs/LSCs. Blocking CD47 can enhance damage to bound stem cells; however systemic anti-CD47 blockers cause significant toxicity, highlighting the need for conditional and targeted blockade of CD47.

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 cells, 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 Company is presently conducting preclinical efficacy and safety studies for MP0621 with data expected in H2 2024.

In the poster presented, preclinical studies demonstrate that:

- MP0621 selectively blocks CD47 on cells expressing cKit
- Conditional blockade of CD47 enhances efficacy of cKit targeting, with phagocytosis comparable to a combo of anti-cKit and anti-CD47 monoclonal antibodies
- MP0621 depleted cKit+ cells in bone marrow of humanized mice without affecting circulating immune cells
- PK profile of MP0621 is suitable for HSCT therapy in humans

Poster details can be found below. The full poster will be made available on Molecular Partners' website after the presentation.

Title: *C-KIT X CD16A X CD47 Switch-DARPin with Conditional Blockade of CD47: A Next-generation Targeted Conditioning for Hematopoietic Stem Cell Transplantation*
Session Title: Stem Cell Transplantation – Experimental
Abstract Number for Publication: P1294
Poster Session Timing: June 14, 2024; 6-7 pm CET

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.

For further details, please contact:
Seth Lewis, SVP Investor Relations & Strategy
Concord, Massachusetts, U.S.
seth.lewis@molecularpartners.com
Tel: +1 781 420 2361

Laura Jeanbart, PhD, Head of Portfolio Management & Communications
Zurich-Schlieren, Switzerland
laura.jeanbart@molecularpartners.com
Tel: +41 44 575 19 35

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