Molecular Partners Presents New Preclinical Data Supporting its MP0533 DARPin T-Cell Engager for the Treatment of AML

December 13, 2022

- New data indicates potential to expand the therapeutic window and improve safety compared to existing T-cell engagers
- Tri-specific T-cell engager resulted in AML cell-specific cytotoxicity with minimal off-tumor toxicity
- Phase I clinical trial evaluating safety and dose of MP0533 in patients with Relapsed/Refractory AML and high-risk MDS to start imminently

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass., Dec. 12, 2022 (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, presented today new preclinical data showing its DARPin T-cell engager MP0533 can induce preferential killing of cells expressing two or three tumor-associated antigens (TAAs) compared to cells expressing a single TAA. The data was disclosed in an oral presentation at the 64th Annual American Society of Hematology Meeting in New Orleans.

MP0533 engages CD3 on T cells while binding up to three tumor-associated antigens (CD33, CD70, and CD123) on AML cells. By modulating the affinity to each TAA, Molecular Partners designed MP0533 to induce T cell-mediated killing preferentially when the cancer cells express two or three of the TAAs. This avidity-driven T cell activation ensures preferential killing of AML cells, that consistently expresses two or three of the target antigens. At the same time, it reduces the damage to healthy cells, which tend to express only one of the target antigens. Such damages have been a recurrent issue with other T-cell engagers in AML.

“Our preclinical data provides a strong base for MP0533’s clinical entry. Its design strategy is to focus the proven power of CD3-mediated T-cell killing onto AML cells and eliminate the systemic toxicity that has been a challenge for CD3 T-cell engagers as a class in this disease. The ability of multi-specific DARPins to exploit the natural differentiation in antigen expression between healthy and cancerous cells supplies a powerful platform for highly targeted immuno-oncology solutions,” said Nicolas Leupin, MD, Ph.D., CMO of Molecular Partners. “We look forward to the MP0533 PhI study which, on top of the recent encouraging Phase I data presented at SITC (Society for Immunotherapy of Cancer) for MP0317 (targeting FAP and CD40, enabling tumor-localized immune activation), illustrates the strength and uniqueness of our DARPin portfolio.”

As presented today, MP0533 was able to activate T-cells and destroy AML cells in samples from newly diagnosed and previously treated AML patients with different TAA expressions. Humanized mouse models confirmed MP0533’s ability to activate intra-tumoral T-cells and control tumor growth. The research also showed that MP0533 was able to directly target and kill LSCs while sparing a variety of healthy cells including hematopoietic stem cells. The unique safety profile of MP0533 was further supported by several other parameters including a lower level of cytokine release relative to benchmark mono-targeted T cell engagers, both in vitro in a whole blood assay and in vivo in the humanized mouse AML models.

These results have been disclosed at ASH 2022 in a podium presentation, which will also be made available on Molecular Partners’ website.

Presentation: “A Multispecific DARPin CD3 Engager Targeting CD33, CD123, and CD70 for the Treatment of AML and MDS Designed to Selectively Target Leukemic Stem Cells”
Session: 604
Timing: December 12, 2022: 5:45PM Central Time
Presenter: Anne Goubier, DVM

A Phase I clinical trial to evaluate safety and dose of MP0533 has been authorized to proceed by Swiss regulatory authorities’ and ethics committees. Patient enrollment is planned to initiate in the near future.

About Molecular Partners AG
Molecular Partners AG is a clinical-stage biotech company developing DARPin therapeutics, a new class of custom-built protein drugs designed to address challenges current modalities cannot. The Company has formed partnerships with leading pharmaceutical companies to advance DARPin therapeutics in the areas of ophthalmology, oncology, and infectious disease, and has compounds in various stages of clinical and preclinical development across multiple therapeutic areas. www.molecularpartners.com; Find us on Twitter - @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 antiviral or other programs, and Molecular Partners’ expected expenses and cash utilization for 2022 and its expectation that its current cash resources will be sufficient to fund its operations and capital expenditure requirements into 2026. These statements may be identified by words such as “believe”, “expect”, “may”, “plan”, “potential”, “will”, “would” and similar expressions, and are based on Molecular Partners AG’s 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 impact of the COVID-19 pandemic 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; 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, 2021 filed with Securities and Exchange Commission (SEC) on March 15, 2022 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.

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