Molecular Partners Shares New Preclinical Data from its AML-Focused CD3 T-Cell Engager Program, CD40 Product Candidate MP0317, and Other Novel Immuno-oncology Approaches at AACR

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- **Data support potential of DARPin® CD3 T-cell engager candidate for improved safety window while limiting tumor escape**
- **New data show that the FAP x CD40 product candidate, MP0317, led to a localized macrophage repolarization and reversion of T-cell suppression. Clinical trials expected to initiate in the second half of 2021**
- **Effector control technologies give new potential for enhancing current and future immunotherapies while reducing toxicities**

Zurich-Schlieren, Switzerland, April 10, 2021. Molecular Partners AG (SIX: MOLN), a clinical-stage biotech company that is developing a new class of custom-built protein drugs known as DARPin® therapeutics, today announced the presentation of four posters highlighting research across its immuno-oncology programs at the American Association for Cancer Research (AACR) virtual Annual Meeting. The preclinical data shared include results from the Company's acute myeloid leukemia (AML) CD3 T-cell engager program, new data from the MP0317 (FAP x CD40) tumor localized immune activator, and initial results from the Company's CD3 prodrug programs.

"With our new technologies designed for localized immune activation, targeting of cell surface-displayed peptides derived from intracellular proteins, and T-cell engagement, we believe we have a solid strategy for our new immune-oncology product candidates, and novel design capabilities that have the potential to greatly benefit our own and partnered immuno-oncology programs," said Daniel Steiner, Ph.D., SVP Research of Molecular Partners. "Our first T-cell engager program is focused on AML, where statistically about half of people diagnosed relapse after treatment and die from the disease. Despite the existence of approved therapies, patients are often unable to benefit from these treatments due to intolerable toxicity. We believe we have made significant progress toward finding a way to avoid this trade-off and widen the therapeutic window for T-cell engagers in AML, aiming to deliver deeper and broader anti-tumor effect and reduce the impact on patients' healthy cells."

In preclinical studies, the Company's AML candidates demonstrated substantial activity against different populations of AML cells in vitro, without significant damage to healthy cells. As shown in the poster titled ***Novel multi-specific DARPin® T-cell engager with an improved therapeutic window to overcome dose limiting toxicities in AML therapies***, Molecular Partners is building on the strength of the DARPin® platform to create a single product designed to target three different cancer antigens simultaneously (CD70, CD33, and CD123). The multi-specific DARPin® T-cell engager candidate is designed to deliver highly potent and specific activity on AML cells, with a reduced effect on healthy normal cells, and with the potential to counteract target escape mechanisms expected due to tumor heterogeneity. In an ex vivo assay using fresh blood from healthy donors, the candidate induced profoundly less inflammatory cytokine production and reduction in platelet counts, unlike simultaneously tested T-cell engager candidates in development by other parties. We believe these data support the designed capability of this candidate to kill a broader population of AML cells while decreasing risk of toxicity.

The T-cell engager research presented today also displays the Company's prodrug DARPin® technology for tumor-localized release of immune stimulation, through incorporation of a protease cleavable blocker DARPin® molecule. As CD3-binding T-cell engagers are highly potent and can lead to systemic toxicities, Molecular Partners has developed a DARPin® domain designed to mask the CD3 engager from interacting with T cells systemically/outside of the tumor. This technology is aimed at focusing the power of the effector function and reduce toxicities by controlling the location of activation to the tumor microenvironment. In a poster titled ***A solution to T-cell engager toxicity: An anti-CD3 Prodrug DARPin® (CD3-PDD) shows no toxicity, but potent anti-tumor activity in a humanized mouse model***, Molecular Partners presents an anti-CD3 Prodrug DARPin® molecule, CD3-PDD, consisting of an EGFR-binder and a CD3-binder, linked via a protease-cleavable linker to a DARPin® domain masking the CD3 effector function. This-anti EGFR x anti-CD3 – Blocker Prodrug is shown to be unable to bind and recruit T-cells in its non-cleaved state in circulation, and is designed to become activated in the tumor microenvironment upon cleavage of the linker by tumor-associated proteases.

With respect to MP0317, a multi-specific DARPin® product candidate targeting both FAP and CD40 to enable tumor-localized immune activation, new preclinical data demonstrated a localized activation of immune cells in vitro, as well as ex vivo in human tumor samples, dependent on the presence of the FAP protein, which is highly expressed in the stroma of a broad range of solid tumors. The data presented in the poster titled ***MP0317, a FAPxCD40 targeting multi-specific DARPin® therapeutic, drives immune activation and leads to macrophage repolarization in vitro and ex vivo*** shows that MP0317 led to macrophage repolarization and reversion of T cell suppression: MP0317 led to upregulation of CD80, an M1 marker, and downregulation of CD163, an M2 marker, only in the presence of FAP, indicating macrophage repolarization towards an M1 phenotype. Furthermore, when these repolarized macrophages were co-cultured with T cells, T cell suppression was shown to revert and CD8 T-cell activation was observed, as shown by the increase of CD25. In both assays the killing effect was comparable to that achieved by an anti-CD40 antibody. We believe these data support MP0317's potential to deliver tumor-localized CD40-mediated immune cell activation while avoiding systemic toxicity seen in other agents. MP0317 is anticipated to begin clinical trials in the second half of 2021.

Finally, with respect to the Company's peptide-MHC targeting program, the Company presents preclinical results from a proof of concept study targeting a peptide derived from the NY-ESO-1 protein displayed in the context of a HLA-A2 molecule (a human MHC protein). The poster, ***Application of the DARPin® technology for specific targeting of tumor-associated MHC class I: peptide complexes***, highlights results demonstrating rapid and reliable generation of DARPin® proteins against pMHC which were then formatted into bispecific T-cell engagers, and engineered to enable potent and specific activation of T cells. Further, the results show that the pMHC-targeting DARPin® candidate was able to achieve systemic half-life extension with limited impact on potency.

The posters presented at AACR are available to view in the Scientific Presentations section of Molecular Partners' corporate website.

About Molecular Partners' Immuno-oncology Product Candidates

Molecular Partners is developing several candidates designed to activate the immune system to fight cancer while reducing damage to healthy cells. These candidates use multiple novel DARPin® technologies potentially applicable against a wide range of tumor types, including DARPin® candidates with the ability to restrict immune activation to the tumor microenvironment, the ability to target intracellular disease-associated proteins, and multiple novel control mechanisms for immune activation designed to direct immune attack to the right cells, at the right place, and at the right time. These capabilities can be combined during candidate design through the inherent modularity of the DARPin® platform, to provide precise control over immune activation and potentially enable more effective cancer immunotherapies.

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.

For more information see www.molecularpartners.com and follow the Company on Twitter at @MolecularPrtnrs.

For further details, please contact:

Investors:
Seth Lewis
seth.lewis@molecularpartners.com
Tel: +1 781 420 2361

Media:
Shai Biran, Ph.D.
shai.biran@molecularpartners.com
Tel: +1 978 254 6286

Thomas Schneckenburger, European IR & Media
thomas.schneckenburger@molecularpartners.com
Tel: +41 79 407 9952

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