Molecular Partners to Present Data from Localized Immune Agonist (MP0317), T-cell Engager, and Peptide-MHC Immunotherapy Programs at AACR Annual Meeting

March 10, 2021

Zurich-Schlieren, Switzerland, March 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 upcoming presentation of four posters with data supporting three of the company's immunotherapy programs at the American Academy for Cancer Research (AACR) Virtual Annual Meeting running April 10-15, 2021.

The accepted research describes multiple aspects of validation for the unique mechanisms of these therapies in development for treating a wide range of tumor types.

Accepted abstract titles include:

MP0317 (targeting CD40 and FAP)

- MP0317, a FAPxCD40 targeting multi-specific DARPin® therapeutic, drives immune activation and leads to macrophage repolarization in vitro and ex vivo

T-cell engager programs

- Novel multi-specific DARPin® T-cell engager with an improved therapeutic window to overcome dose limiting toxicities in AML therapies.
- 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

Peptide-MHC program

- Application of the DARPin® technology for specific targeting of tumor-associated MHC class I: peptide complexes

For **MP0317**, the company's multi-specific DARPin® candidate targeting both FAP and CD40 to enable tumor-localized immune activation, the research describes how the candidate's activation of immune cells in-vitro, as well as on human tumor samples, was dependent on the presence of the FAP protein, which is highly expressed in the stroma of a broad range of solid tumors. Furthermore, the research observed that immunosuppressive macrophages associated with tumor growth and spread were reverted by MP0317 into an anti-tumor phenotype. These data support MP0317's potential to deliver tumor-localized CD40-mediated immune cell activation avoiding systemic toxicity seen in other agents. MP0317 is anticipated to begin clinical trials in the second half of 2021.

For the **T-cell engager** program, two accepted research abstracts detail the construction of next generation T-cell engager DARPin® molecules designed to overcome the limited tumor specificity and the immune hyperstimulation associated with other T-cell engager approaches. By linking a T cell engaging CD3 DARPin® binder to additional DARPin® binder domains that optimally engage tumor-specific antigens in parallel, the company generated candidates that displayed strong *in vitro* potency, and low levels of cytokine release *ex vivo* – suggesting low systemic immune activation. Furthermore, an anti-CD3 Prodrug DARPin® (CD3-PDD) was successfully designed to have its immunostimulatory effects inactivated by a linked 'blocking' DARPin® domain, and become activated only in the tumor microenvironment, upon cleavage of the linker by tumor-associated proteases. In an in vivo humanized mouse tumor model, this candidate demonstrated anti-tumor activity and no toxicity when administered systemically. Together, the research supports Molecular Partners' DARPin® technology ability to control immunostimulation through a validated mechanism with a heightened level of precision relative to existing approaches.

Finally, for the **peptide-MHC (pMHC)** program, the research provides updates on the development of pMHC binders in the T cell engager format. The successful screening and engineering of the bispecific DARPin® candidates (pMHC-CD3) achieved highly potent and specific T cell activation only in the presence of the target peptide, resulting in T-cell mediated tumor cell killing. A vast majority of tumor or viral antigens are presented as peptides on the cell surface by MHC molecules for immune cell recognition and have potential to be leveraged as versatile targets for immunomodulating therapeutics. However, to-date, antibody and T-cell receptor-based pMHC binders have been challenged by their low target abundance, weak affinity, cross-reactivity to other pMHCs, or challenging biochemical properties.

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.

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