Molecular Partners Completes GMP Manufacturing of Anti-COVID-19 DARPin® Candidate MP0420 for Clinical Use

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- **High yields in bacterial fermentation systems support ability of DARPin® manufacturing to rapidly scale for global supply**
- **First and only, tri-specific antiviral demonstrating potential best-in-class potency in vivo**
- **First-in-human clinical trial initiation planned for November 2020**

Zurich-Schlieren, Switzerland, September 14, 2020. 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 completion of initial Good Manufacturing Practice (GMP) manufacturing runs of its tri-specific, antiviral DARPin® candidate for COVID-19, named MP0420. More than 1 kg of DARPin® material was produced in each of the 100 liter E.coli-based bacterial fermenter runs. This fermentation approach is relatively simple, rapid and scalable compared to typical antibody manufacturing approaches, further differentiating the DARPin® approach as a potential therapeutic and prophylactic option for COVID-19.

"We believe the highly distinct manufacturing profile of DARPin® candidates is a crucial element for successful therapeutic efforts underway. Given the number of teams pursuing therapeutic approaches to the novel coronavirus, and considering the need to make a drug available on a global basis, it is essential to demonstrate the ability to manufacture and deploy these medicines," said Patrick Amstutz, PhD, chief executive officer of Molecular Partners. "Beyond the unique tri-specific mechanism and sub-picomolar potency demonstrated in vitro, our first GMP batches now support a target product profile for a COVID-19 candidate with simple, scalable manufacturing that could rapidly meet global need. We will further evaluate optimal dosage in our Phase 1 study initiating this fall."

Characteristics of DARPin® Therapeutics make them ideally suited for antiviral therapies, particularly at time of global need. Offering logistical solutions that other potential therapeutics in development may not possess, including:

- Sub-picomolar potency, allowing investigation of subcutaneous administration as both early intervention and potential prophylaxis*
- Highly scalable microbial manufacturing, allowing for up to 4 production runs on the same fermenter, per month
- High temperature stability of DARPin® drugs (>80°C) which may allow for avoidance of cumbersome cold chain storage

Bacterial fermenters can range upwards of 10,000L in size. A single such fermenter could enable the delivery of hundreds of thousands of doses of MP0420 on a monthly basis, if initial GMP yields and production speed are maintained.

First in human studies for MP0420 are anticipated to begin in November, 2020. Additional manufacturing slots have been secured over the next 6 months, including production in 1000L fermenters. These slots will be used to produce additional doses for MP0420, as well as for our second antiviral candidate for COVID-19, MP0423, with clinical studies anticipated in H1 2021.

About Molecular Partners' anti-COVID-19 program

Molecular Partners has developed a series of tri-specific antiviral DARPin® candidates with strong binding and neutralizing potency targeting multiple epitopes on the SARS-CoV-2 spike protein that are crucial for infection. The source of these constructs is a pool of hundreds of mono-DARPin® binders which individually bind and inhibit the virus with high potency. The construction of multi-specific candidates from monospecific proteins is the foundation of Molecular Partners' drug discovery engine and has yielded multiple clinical candidates in other indications.

These building blocks are designed to target different sites on the virus for multiple concurrent effects. These include blocking viral binding to the human ACE2 receptor (Receptor Binder Domain or RBD), the primary docking mechanism to host cells, as well as allosteric inhibition or "molecular handcuffing", of the spike protein, preventing the conformational change it undergoes prior to injection of viral RNA into the human cell.

The formatting as tri-specific candidates is designed for cooperative binding, extremely high potencies and prevention of viral escape via mutations. The candidates are formatted with a half-life enhanced DARPin® domain that binds to human serum albumin (HSA) to support long-acting activity. All DARPin® candidates are constructed to benefit from high-yield and low-cost microbial manufacturing. Molecular Partners is investigating whether the high thermal stability of DARPin® molecules can be used to overcome cold-chain requirements.

The ability of DARPin® products to be produced in E.coli-based biofermentation is a major advantage over antibodies, which often require substantial manufacturing process optimization and protein modification, significantly increasing cost and complexity. By contrast, DARPin® molecules are much smaller molecules that do not require glycosylation or extensive post-translational modification by producer cells, making simple, highly scalable bacterial fermentation feasible.

Molecular Partners is collaborating with AGC Biologics to support development of its anti-COVID-19 program, and has reached an agreement with the Swiss Government regarding rights to purchase up to 3.2 million doses of MP0420, if it is approved in Switzerland.

About Molecular Partners AG

Molecular Partners AG is a clinical-stage biotech company developing a new class of custom-built protein drugs known as DARPin® therapeutics, designed to address challenges current modalities cannot. The company has compounds in various stages of clinical and preclinical development with a focus on oncology. Molecular Partners has formed partnerships with leading pharmaceutical companies to advance DARPin® therapeutics across multiple therapeutic areas.

For more information regarding Molecular Partners AG, go to: www.molecularpartners.com

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