APEIRON Biologics' APN01 selected for large-scale US trial in COVID-19

- APEIRON´s APN01 to participate in US Phase 2 COVID-19 trial ACTIV-4d RAAS
- Further clinical study in preparation with inhalative drug delivery of APN01 to directly target respiratory tract and lung tissue
- Additional pre-clinical data show highly promising results with APN01 in various mutation variants
- Financing round planned to secure funding of further upcoming development steps

Vienna, Austria, 19 May 2021: APEIRON Biologics AG announced today the next development steps for APN01 (alunacedase alfa) for the treatment of COVID-19. Based on the recently announced clinical results from APEIRON's Phase 2 trial with APN01 in COVID-19, APN01 will be developed in further international clinical trials with different COVID-19 patient populations and drug delivery routes.

APEIRON was invited to participate in the US ACTIV-4d RAAS trial, part of Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), initiated and funded by the National Heart Lung and Blood Institute (NHLBI), part of the United States' National Institutes of Health (NIH). ACTIV is a public-private partnership that unites partners from government, industry, academic and non-profit organizations to prioritize and speed development of the most promising COVID-19 treatments. APEIRON's specific recombinant human ACE2 (rhACE2), APN01, was prioritized for study by a broad panel of clinical trial experts through the Collaborative Network of Networks for Evaluating COVID-19 Therapeutic Strategies (CONNECTS). The trial is anticipated to begin in Q2-2021. The trial is largely funded by public grants.

APEIRON's recently completed Phase 2 trial showed significant improvement in certain parameters of the Renin Angiotensin Aldosterone System (RAAS) with APN01 treatment compared to placebo. Data also suggested that APN01 will confer greatest therapeutic benefit to patients with lower WHO scores. The randomized, double-blinded, placebo controlled ACTIV-4d RAAS trial will enroll approximately 1,600 hospitalized patients with COVID-19, at more than 50 individual sites. APN01 will be one of at least three agents to be evaluated in the trial.

"We are highly motivated and honored, that APN01 was selected for this government funded US program. The ACTIV-4d RAAS trial perfectly fits our strategy to address larger patient populations and various disease states based on our recent convincing results. Administering APN01 earlier in the course of COVID-19 potentially protects patients from progressing to a severe stage of the disease with uncontrollable inflammation and organ damage," **said Peter Llewellyn-Davies, Chief Executive Officer of APEIRON Biologics AG.** "We are confident that this Phase 2 US trial will confirm the clinical benefits of APN01 in the treatment of COVID-19 patients and opens the US and international markets for our promising drug candidate."

Sean Collins, MD, MSc, professor of Emergency Medicine at Vanderbilt University Medical Center (VUMC) and principal investigator of the ACTIV-4d study commented: "While RAAS is central to both the mechanism of viral entry and the multiple organ dysfunctions associated with COVID-19, RAAS-targeted therapies remain understudied. The ACTIV-4d RAAS platform has tremendous potential to clarify the impact of restoring RAAS balance in patients hospitalized with COVID-19 and to identify a therapy for patients affected by the disease."

In parallel to the US clinical trial with APN01 as intravenous application, APEIRON is preparing a company-sponsored Phase 1 trial to evaluate drug delivery of APN01 through inhalation in order to target all infected or at-risk patients earlier in the course of the disease. Preliminary data from ongoing evaluations with inhalation of ACE2 based therapeutics show high efficacy in SARS-CoV-2 animal models. A Phase 1 inhalation study will form the basis for further development in chronic respiratory diseases with high unmet medical need such as Chronic Obstructive Pulmonary Disease (COPD) and Pulmonary Arterial Hypertension (PAH). Study start of the inhalation trial is anticipated for Q3-2021.

Romana Gugenberger, Head of R&D at APEIRON Biologics comments: "Both of our study approaches ensure we drive the development of APN01 forward to provide patients a safe and efficacious treatment option. Delivery of our drug candidate directly to the respiratory tract could block viral entry into the lung cells and control inflammation. Importantly, APN01 may also be suitable against infections with variants of SARS-CoV-2 as already preclinically shown."

In parallel, an improved manufacturing process for a commercially viable mass scale production of good manufacturing practice (GMP) material of APN01 is under preparation.

In order to secure funding of APEIRON's next development steps, APEIRON will initiate a financing round within the next months.

About ACTIV-4d RAAS trial

The Vanderbilt Institute for Clinical and Translational Research (VICTR) has received a $60 million federal grant to lead a national trial of treatments targeting the Renin Angiotensin Aldosterone System (RAAS) in patients hospitalized with COVID-19. ACTIV-4d will test agents that operate through distinct mechanisms to restore balance to RAAS in COVID-19 patients. Primary endpoint is oxygen free days through 28 days. Secondary endpoints include in hospital mortality, use of mechanical ventilation, and WHO scale scores. For more information about this and other ACTIV therapeutic trials, visit the ACTIV website.

About APN01 (alunacedase alfa)

APN01 is a soluble recombinant human Angiotensin Converting Enzyme 2 (rhACE2) which mimics ACE2, a receptor identified as the critical cellular entry receptor for the SARS-CoV-2 virus and therefore plays a crucial role in combating COVID-19. The virus' spike uses the ACE2 protein on the cell membrane to enter the cells. APN01 as a soluble form of ACE2,

potentially prevents binding of the virus spike protein to the cell surface receptor and thereby preventing infection of cells.

In addition, as shown in several studies human ACE2 is a key enzyme regulator of the Renin Angiotensin Aldosterone System (RAAS), a peptide system involved in blood pressure, lung disorders, diabetic kidney disease, inflammation, or cardiovascular diseases. ACE2 dials down the RAAS and thereby reduces blood pressure, diminishes inflammation, and protects multiple organs such as the heart, kidney, liver, lung or vasculature from damage. Thus, in addition to blocking the access of SARS-CoV-2 to its cell membrane-bound entry gate, the enzyme function of APN01, engineered into the same drug, potentially leads to reduction of organ injuries in COVID-19.

Additionally, due to the unique therapeutic approach of using the soluble form of the SARS-CoV-2 entry receptor ACE2, APN01 is inherently resilient to viral escape, thus an optimal drug candidate for novel variants of concern, as already shown for the UK, the South African, the Brazilian variant and projected to be demonstrated for further variants.

APN01 was first discovered and developed in response to the first SARS outbreak by the founder of APEIRON Biologics, Prof. Josef Penninger MD in 2003.

About APEIRON Biologics AG

APEIRON Biologics is a privately held European biotech company based in Vienna, Austria, focused on the discovery and development of treatments for respiratory diseases and novel cancer immunotherapies.

APN01 (rhsACE2, alunacedase alfa), a soluble recombinant version of the SARS-CoV-2 cell entry receptor ACE2, has three distinct potential clinical benefits for COVID-19 and has completed a double blind, placebo-controlled Phase 2 trial in Europe and Russia.

APEIRON received EU marketing approval for APN311 (dinutuximab beta, Qarziba®) in 2017 for the treatment of pediatric neuroblastoma patients and out-licensed global, exclusive rights for this product to EUSA Pharma Ltd.

APN401´s proprietary cellular therapy process brings in a paradigm change in cancer treatment to fight hematological and solid tumors. The clinical program is a first-in-class ambulatory autologous transient therapy to strengthen immune reactivity via an intracellular master checkpoint inhibitor, Cbl-b.

APEIRON Biologics´ projects and technologies are based on a strong patent portfolio and partnerships with leading pharmaceutical companies and academic institutions.

Further information, visit www.apeiron-biologics.com and connect with us on Twitter and LinkedIn.

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