APEIRON Biologics launches next clinical trial with innovative cancer therapy APN401

Important development step for promising cell therapy

- Paradigm shift in cancer treatment: process developed by APEIRON uses immune system to treat solid tumors
- Innovative new manufacturing and treatment process enables outpatient treatment within one day from cell collection to reinfusion
- Phase Ib clinical trial evaluates immunological effects as well as safety and tolerability of APN401 in patients with advanced-stage solid tumors
- APN401 is an autologous cell therapy designed to inhibit the immune checkpoint Cbl-b using RNAi technology

Vienna, Austria, 06 July 2021: APEIRON Biologics AG announced today the start of a Phase Ib clinical trial with its product candidate APN401 for the treatment of solid tumors. The principle of cell therapy with APN401 by inhibiting the immune checkpoint Cbl-b aims at the patient's own immune cells. These are modified to recognize and destroy cancer cells without being permanently genetically altered.

The open-label, multi-center Phase Ib clinical trial is expected to enroll approximately 60 patients at multiple sites in Austria. The study objective is to evaluate the safety, tolerability and immunological effects of the treatment on patients with various solid tumors. This will build on the experience of the two previous Phase I clinical studies, which already successfully demonstrated good tolerability and the first signs of clinical efficacy by activating the immune cells that are crucial to tumor defense.

The clinical study is divided into two parts. Part A of the study aims to determine the optimal dosing, i.e. the quantity of treated cells reinfused back to the patient. Patients will receive APN401 treatment every three weeks. In part B of the study, patients with specific tumor indications (three groups of 15 patients each) will be treated to generate further efficacy signals, which will be used to determine the tumor indication for a subsequent Phase II clinical study. The Phase I clinical study will start at the Medical University of Vienna (MUW) where the GMP-certified production of the cell therapy and treatment of the patients will take place.

For the treatment, the patient's own peripheral blood mononuclear cells (PBMCs) are collected, specifically modified outside the body using RNAi technology and then reinfused into the patient. APEIRON uses a specially developed system for this purpose, which enables an automated process from cell processing to reinfusion within just one day. This GMP-certified system increases patient safety and the reproducibility of the manufacturing process. APEIRON's technology thus enables personalized cell therapy in solid tumors.

Peter Llewellyn-Davies, CEO of APEIRON Biologics AG, says: “We are thrilled to be contributing a groundbreaking cancer treatment with this truly pioneering step in development of our APN401 cell therapy. The short outpatient administration process,

which can also be used for solid tumors, plays a key advantage compared to other autologous cell therapies. APN401 could offer critically ill patients, with previously difficult-to-treat cancers, new individualized treatment options and thus new hope. The APEIRON team is highly motivated to develop much needed new treatment options with this major next step."

Dr. Romana Gugenberger, Chief Medical & Scientific Officer (CMSO) of APEIRON Biologics AG, explains: "The immune system is the most effective weapon against tumor disease and offers many advantages over conventional therapies such as chemotherapy. Cbl-b is a master checkpoint in the immune system that controls important processes of the immune response, especially in cancer. APN401, by blocking Cbl-b using RNA interference (RNAi), is designed to reactivate the patient's immune system, allowing it to fight solid tumors. The flexibility of RNAi technology could expand the applicability of cell therapy to additional immune checkpoints and holds enormous potential for new therapeutic approaches."

Prof. Dr. Nina Worel, Head of Cell Therapy at the Department of Transfusion Medicine at AKH / Medical University of Vienna and lead investigator of the study, adds: "Patients with advanced solid tumors urgently need new, safe and effective therapeutic options. Using cell therapy to enable the patient's immune system to directly attack the tumor is a very promising approach. APEIRON's APN401 could become superior in safety and efficacy to standard oncology therapies as well as to currently available cell therapies, due to its rapid applicability and central immune activation. We are excited to initiate this study here in Vienna and other sites and gain new insights."

About APN401

Immune checkpoints are receptors with immunoregulatory activity. Tumor cells can make use of these immune checkpoints to escape recognition by the immune system. Cbl-b represents a new class of intra-cellular immune checkpoints in contrast to the immune checkpoint molecules PD-1/PD-L1 and CTLA-4, which are localized at cell surfaces.

APN401, an autologous cell therapy, was designed to transiently, i.e. temporarily, inactivate Cbl-b ex-vivo in autologous PBMCs. These altered autologous PBMCs are then returned to the patient, with the entire procedure performed on an outpatient basis over one day. APN401 is well tolerated, has a good safety profile, and has shown early evidence of clinical activity in patients with advanced solid tumors in two Phase I studies.

More information on checkpoint inhibition of Cbl-b and APN401 can also be found on our website.

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.

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.

APEIRON is developing a promising drug for COVID-19: APN01 (rhsACE2, alunacedase alfa), a soluble recombinant version of the SARS-CoV-2 cell entry receptor ACE2. APN01 has three distinct potential clinical benefits for COVID-19 and has completed a double blind, placebo-controlled Phase II trial in Europe and Russia. Based on promising results, APN01 was selected for a publicly funded, large-scale study in COVID-19 by the U.S. government which is scheduled to start in Q3 2021.

APN401´s proprietary cellular therapy process brings in a paradigm change in cancer treatment to fight 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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