Repairon Announces Completion of Dose-Finding Part of BioVAT-HF Phase 1/2 Trial in Advanced Heart Failure

- Feasibility and safety demonstrated in patients with advanced heart failure
- Safe maximal dose for continuation into Phase 2 (Proof-of-Concept) identified
- Proof for successful heart remuscularization obtained
- Interim data on 15 patients with 800 million cells dose expected in Q2 2024

Göttingen, Germany, April 4, 2023 - 14:00 CET - Repairon, a clinical-stage German biotech company focused on developing a novel reparative treatment for heart failure, together with the University Medical Center Göttingen (UMG) and the University Medical Center Schleswig-Holstein (UKSH), Campus Lübeck, as well as the German Center for Cardiovascular Research (DZHK) today announced the completion of enrolment and follow-up of patients in the dose-finding cohort of the BioVAT-HF-DZHK20 Phase 1/2 trial. The clinical trial is evaluating the safety and efficacy of iPSC[1] -derived engineered human myocardium (EHM) as Biological Ventricular Assist Tissue (BioVAT) in Advanced Heart Failure (NCT04396899).

Dr. Rainer Knaus, Managing Director of Repairon, emphasized that *"Since 2017 Repairon is the exclusive industry partner of UMG to bring the EHM therapy from the bench to the bedside. Strongly encouraged by the emerging data from the BioVAT-HF study, Repairon will continue the commercial development of the EHM technology with the aim to establish it as the therapeutic option of choice for patients with advanced heart failure."*

"We are very pleased to announce the completion of the dose-finding part of our clinical study, evaluating a fundamentally new clinical strategy in the treatment of patients with advanced heart failure," said Professor Tim Seidler from the Heart Center of the University Medical Center Göttingen and Principal Investigator of the BioVAT-HF study.

"With BioVAT implantation a new therapeutic opportunity for patients with advanced heart failure and a realistic chance to avoid more invasive therapeutic procedures such as the implantation of mechanical circulatory assist devices is evolving," said Professor Ingo Kutschka Director of the Clinic for Cardiothoracic Surgery at the University Medical Center Göttingen and principle surgical investigator of the BioVAT-HF study at UMG.

"After many years of preclinical research we are pleased to see the transition of BioVAT implantation into patients with heart failure and addition of new muscle to the failing human heart," said Professor Stephan Ensminger Director of the Clinic for Cardiac and Thoracic Vascular Surgery at the University Heart Center Lübeck and principle surgical investigator of the BioVAT-HF study at UKSH, Campus Lübeck.

[1] induced pluripotent stem cell

"We are finally seeing true remuscularization in patients with heart failure and look forward to the outcome of BioVAT-HF," said Professor Gerd Hasenfuß Director of the Heart Center at the University Medical Center Göttingen.

"We are excited about our involvement in the first-in-patient, first-in-class BioVAT-HF trial, which addresses a critical unmet medical need in our patients with advanced heart failure," said Professor Ingo Eitel Director of the Medical Clinic II (Cardiology/Angiology/Intensive Care Medicine) at the University Heart Center Lübeck.

"Advanced heart failure treatment requires new reparative therapies; with BioVAT-HF remuscularization of the failing heart is becoming a clinical possibility," said Professor Stefan Anker Charité Berlin.

The open-label, non-randomized, multi-center trial is investigating the hypothesis that cardiomyocyte implantation as BioVAT results in sustainable remuscularization and biological enhancement of myocardial performance in patients with advanced heart failure. As such it is the first of its kind in heart repair by tissue engineered remuscularization.

In the dose ranging part of the study, 10 patients with advanced heart failure with left ventricular ejection fraction ≤35% and NYHA ≤III were implanted with EHM hosting an increasing number of iPSC-derived cardiomyocytes and stromal cells:

- The first 2 patients were implanted with 200 million cells
- Followed with 2 patients implanted with 400 million cells
- Followed with 6 patients implanted with 800 million cells (the maximal dose under the study protocol)

With maximal follow-up of 2 years in the low dose group and 1 year in the high dose group, the study continues to enrol patients during a transition period from Phase 1 to Phase 2 (Proof-of-Concept) based on a positive risk-benefit assessment following an adaptive clinical trial design.

"There is a huge unmet medical need for the development of new reparative treatment options for patients suffering from advanced heart failure," said Professor Wolfram-Hubertus Zimmermann, Director of the Institute of Pharmacology and Toxicology at the University Medical Center Göttingen (UMG), Co-Founder of Repairon, and BioVAT-HF Study Director. *"After more than 25 years of research, the BioVAT-HF study is testing whether the addition of new heart muscle to the failing human heart can offer a new therapeutic solution for patients suffering from advanced heart failure despite optimal medical therapy. Our observation as to long-term remuscularization in BioVAT-HF is aligned with our preclinical data and our strategy to address the root-cause of heart failure."*

This first-in-patient and first-in-class study is conducted by the University Medical Center Göttingen with support from Repairon, the German Center for Cardiovascular Research (DZHK), and the University Heart Center Lübeck. The interim data readout from 15 patients receiving 800 million cells is anticipated for Q2 2024, with then first data on the primary efficacy endpoints (augmentation of the target heart wall with evidence for local and global

enhancement of contractility). The completion of BioVAT-HF with 35 patients treated with the safe maximal dose is expected in H2 2025.

About Repairon

Repairon is a clinical-stage private German biotech company focused on developing a treatment for heart failure. The company was founded in 2014 on the pioneering work of Professor Wolfram-Hubertus Zimmermann and his team, who have developed several tissue engineering technologies with documented applicability in organ repair. Repairon's lead therapeutic candidate, engineered heart muscle (EHM), is being evaluated in a Phase 1/2 clinical trial as Biological Ventricular Assist Tissue in Terminal Heart Failure (BioVAT-HF). Repairon maintains strong partnerships with the University Medical Center in Göttingen and the German Center for Cardiovascular Research (DZHK). The company is headquartered in Göttingen, Germany.

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