Cardior Announces First Patient Dosed in Phase 2 Study Evaluating Efficacy and Safety of Non-coding RNA-Based Lead Candidate CDR132L in Heart Failure Patients Post-Myocardial Infarction

Hanover, Germany, July 20, 2022 – Cardior Pharmaceuticals, a clinical-stage biotech company developing non-coding RNA (ncRNA)-based therapeutics for patients with cardiac diseases, today announced the dosing of the first patient in their multicenter Phase 2 trial assessing efficacy and safety of CDR132L in 280 patients with reduced left ventricular ejection fraction after myocardial infarction (HF-REVERT). CDR132L is an oligonucleotide-based ncRNA inhibitor that targets microRNA-132, a central regulator of pathological cardiac remodeling processes. Cardiac remodeling is a debilitating and often life-threatening consequence of myocardial infarction that contributes to the development of heart failure.

Myocardial infarction (MI), commonly known as a heart attack, is an extremely severe condition caused by a blockage in the coronary arteries limiting the blood supply to the heart. Even if resolved, MI can lead to permanent damage of the heart cells initiating pathological cardiac remodeling resulting in the development of heart failure. Heart failure remains one of the leading causes of death globally with only limited intervention options. Cardior's lead candidate is designed to address the root cause of the pathological remodeling of the heart following MI to halt and reverse the detrimental signaling cascade and restore normal function of the heart. CDR132L is the first-ever ncRNA-based therapy to enter Phase 2 studies in heart disease.

CDR132L's target is the well-established microRNA, miR-132, which plays a key role in pathological cardiac remodeling processes. Levels of miR-132 are elevated in the cardiac tissue of heart failure patients, triggering well-defined molecular pathways. Inhibition of miR-132 by CDR132L normalizes those pathways leading to a transformational change at the tissue level aiming to restore normal cardiac muscle function.

"RNA therapies have a tremendous potential to fundamentally change the treatment paradigm for many diseases. Achieving Phase 2 initiation for CDR132L marks a meaningful step towards validating a disease-modifying therapeutic that inhibits a master regulator of cardiopathology. This innovation is based on our in-depth expertise in developing non-coding RNA-based treatments," **said Rahul Agrawal, MD, Chief Medical Officer of Cardior.** *"Our antisense oligonucleotide-based inhibitor addresses key molecular mechanisms to prevent or reverse heart failure following myocardial infarction and we look forward to documenting the impact it can provide to improve patients' quality of life and reduce mortality."*

HF-REVERT (NCT05350969) is a multicenter, randomized, parallel, three-arm, placebo-controlled clinical proof-of-concept study designed to evaluate the safety and efficacy of CDR132L in 280 patients with heart failure and reduced left ventricular ejection fraction (LVEF) after MI. The study consists of a 6-month double-blind period, and a 6-month extension period. Patients enrolled in the Phase 2 study will be randomized to receive three intravenous CDR132L infusions at either 5 mg/kg, 10 mg/kg or placebo, administered 28 days apart as an add-on to Standard of Care (SoC) treatment.

The primary endpoint of the study is defined as percentage change from baseline in the left ventricular end-systolic volume assessed by echocardiography (ECHO). The left ventricular end-systolic volume index is used as a clinical assessment of the systolic function of the heart. Additional outcome measures include changes in biomarkers such as NT-proBNP, as well as safety assessments including frequency of adverse events and quality of life questionnaires.

The study will be conducted at locations across Europe involving approximately 60 clinical study centers. The Phase 2 HF-REVERT trial has been designed in collaboration with Cardior's Scientific Advisory Board including renowned cardiology experts Prof. Johann Bauersachs, who is also the trial's coordinating investigator, and Prof. Scott Solomon, Co-Chair of the trial. Cardior will initiate subsequent clinical trials for CDR132L in the U.S. following discussions with the U.S. Food and Drug Administration (FDA).

"Cardior has focused exclusively on meeting this clinical development milestone and reaching the next stage of our development as a leader in ncRNA therapeutics. By applying our insight on using ncRNA through an unprecedented mechanism of action that transcends the cellular level to modulate well-defined pathways, our goal is to move closer to a curative approach for cardiac diseases. Dosing the first patient in the Phase 2 HF-REVERT study is a first step that could enable the treatment of other indications including ischemic heart failure and genetic cardiomyopathies," **commented Claudia Ulbrich, MD, CEO and Co-Founder of Cardior.** *"I would like to thank the Cardior team and the clinicians involved in the HF-REVERT trial for the collaboration that has brought us to this trial initiation and another step closer to addressing a large and growing unmet medical need*."

"The Phase 2 clinical proof-of-concept study builds upon the promising results from our Phase 1b clinical study that demonstrated not only a favorable safety profile but also beneficial cardiac effects in heart failure patients treated with CDR132L versus placebo. The data to date paved the way for our ncRNA approach as the first therapy to reverse cellular pathology and potentially restore normal function in millions of cardiac disease patients," **added Prof. Dr. Dr. Thomas Thum, CSO and Founder of Cardior.** *"It is exciting that we have moved from candidate selection to Phase 2 initiation within just five years and we look forward to leveraging the Phase 2 trial in preparations of a future pivotal trial as well as exploring the further potential in additional indications."*

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About Heart Failure
Heart failure (HF) is a common complication of myocardial infarction and is a result of multiple structural and functional abnormalities that result in the failure of the heart to pump blood through the body. The global burden of HF is significant, with an estimated prevalence of >60 million cases. Post-MI HF is associated with a high risk of death with an estimated median survival of only 4 years and thus represents a high burden for patients and their quality of life.

About CDR132L
CDR132L is a synthetic antisense oligonucleotide-based inhibitor directed against the microRNA-132 (miR-132), that is up-regulated in cardiac tissue of heart failure patients leading to a pathological expression of genes that are crucially involved in cardiac function thus leading to pathological remodeling. By blocking miR-132 with its selective inhibitor CDR132L, Cardior is able to restore healthy levels of miR-132 and trigger a concerted therapeutic effect against key hallmarks of heart disease including pathological remodeling processes, impaired contractility and fibrosis. CDR132L has the potential to restore heart function thereby prolonging the patient's life span as well as improving quality of life. The candidate is currently under evaluation in the company's Phase 2 HF-REVERT trial and has successfully completed Phase 1b clinical studies demonstrating a favorable safety profile and beneficial cardiac effects in heart failure patients. Results were published in the *European Heart Journal* in 2021.

About Cardior
Cardior Pharmaceuticals is a leading clinical-stage biopharmaceutical company pioneering the discovery and development of RNA-based therapeutics designed to prevent, repair and reverse diseases of the heart. Cardior's therapeutic approach uses distinctive non-coding RNAs as an innovative platform for addressing the root causes of cardiac dysfunctions. The

company aspires to bring transformative therapeutics and diagnostics to patients and thereby make a lasting impact on the treatment of cardiac diseases worldwide.

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