



2265 Upper Middle Road East, Suite 602
Oakville, ON L6H 0G5, Canada

Cardiol Therapeutics Announces Pre-Clinical Study Results Demonstrating CardiolRx™ Inhibits and also Promotes Reversal of Mechanisms Leading to Cardiac Fibrosis

Data Presented at The Annual Scientific Meeting of the Heart Failure Society of America September 30th, 2022

Oakville, ON – October 3, 2022 – Cardiol Therapeutics Inc. (**NASDAQ: CRDL**) (**TSX: CRDL**) (“**Cardiol**” or the “**Company**”), a clinical-stage life sciences company focused on the research and clinical development of anti-inflammatory and anti-fibrotic therapies for the treatment of cardiovascular diseases (“CVD”), announced today that study results demonstrate the active pharmaceutical ingredient (“API”) in CardiolRx™ inhibits and also promotes the reversal of mechanisms known to play a role in the occurrence and development of fibrotic CVD. The data were presented by its research collaborators from Houston Methodist DeBakey Heart & Vascular Center at The Annual Scientific Meeting of the Heart Failure Society of America (“HFSA2022”).

The poster entitled “Cannabidiol Inhibits Endothelial-to-Mesenchymal Transition and also Promotes the Reverse Process *in vitro*” was presented within the “Basic and Translational Science” category of the HFSA2022 Scientific Programme. The authors concluded that the API in CardiolRx™ protects cardiac function and exhibits an anti-fibrotic effect, possibly mediated by endothelial-to-mesenchymal transition (“EndoMT”).

“Our research collaborators from Houston Methodist DeBakey Heart & Vascular Center have previously shown that CardiolRx™ preserves cardiac function in a pre-clinical model of heart failure. The results of the present study provide further evidence of the cardioprotective properties of CardiolRx™ that suggest anti-fibrotic mechanisms with therapeutic potential in heart failure,” stated Dr. Andrew Hamer, Cardiol Therapeutics’ Chief Medical Officer and Head of Research & Development. “These results, together with previously reported pre-clinical *in vivo* data demonstrating anti-inflammatory activity, underpin our plan to advance the development of a novel subcutaneous formulation of CardiolRx™ for use in heart failure.”

EndoMT is a complex biological process whereby an endothelial cell, the main cell type found in the inside lining of blood vessels, undergoes a series of molecular events that alter its characteristics towards a mesenchymal cell, such as a myofibroblast. Myofibroblast cells are the primary cells during wound healing and fibrosis. Mounting evidence indicates EndoMT is involved in adult CVD, and the mechanism has been described to contribute to myocardial fibrosis, an important part of heart remodelling that can lead to heart failure.

In the study, EndoMT was induced in HUVEC cells, a model system for studying human endothelial cell function, using a combination of agents (L-NAME and angiotensin-II). EndoMT was characterized through immunofluorescence (“IF”) for endothelial (CD31) and mesenchymal (Vimentin) markers. CardioliRx™ was added during the EndoMT induction process, and on Day 4 following induction IF studies were performed. CardioliRx™ was shown to reduce the expression of the mesenchymal marker Vimentin in a dose dependent manner. Separately, CardioliRx™ was added to EndoMT transitioned cells (after Day 4 of EndoMT), and IF studies were performed on Day 8. In this experiment CardioliRx™ was shown to reduce Vimentin expression, suggesting reversal of EndoMT *in vitro*. This provides evidence that the cardioprotective properties of CardioliRx™ are due, in part, to the modulation of EndoMT.

About The Heart Failure Society of America

The Heart Failure Society of America (“HFSA”) is a multidisciplinary organization working to improve and expand heart failure care through collaboration, education, research, innovation, and advocacy. Members include physicians, scientists, nurses, nurse practitioners, pharmacists, and patients. The Annual Scientific Meeting of the HFSA brings together these members to communicate progress in basic science and the clinical management of heart failure.

About Cardioli Therapeutics

Cardioli Therapeutics Inc. (NASDAQ: CRDL) (TSX: CRDL) is a clinical-stage life sciences company focused on the research and clinical development of anti-inflammatory and anti-fibrotic therapies for the treatment of cardiovascular diseases (“CVD”). The Company's lead product candidate, CardioliRx™, is an oral pharmaceutical that is being clinically developed for use in CVD.

Cardioli has received IND authorization from the FDA to conduct clinical studies to evaluate the efficacy and safety of CardioliRx in two orphan drug indications: (i) a Phase II multi-national, randomized, double-blind, placebo-controlled trial (the “*ARCHER*” trial) in acute myocarditis, an important cause of acute and fulminant heart failure in young adults and a leading cause of sudden cardiac death in people less than 35 years of age; and (ii) a Phase II multi-center open-label pilot study in recurrent pericarditis (inflammation of the pericardium), which is associated with symptoms including debilitating chest pain, shortness of breath, and fatigue, and results in physical limitations, reduced quality of life, emergency department visits, and hospitalizations.

In addition, CardioliRx is being evaluated in a Phase II/III multi-national, randomized, double-blind, placebo-controlled study (the “*LANCER*” trial). *LANCER* is designed to evaluate the efficacy and safety of CardioliRx as a cardioprotective therapy to reduce major cardiovascular and respiratory events in patients hospitalized with COVID-19 who have a prior history of, or risk factors for, CVD, and to investigate the influence CardioliRx has on key biomarkers associated with heart disease.

Cardioli is also developing a subcutaneous formulation of cannabidiol targeting the inflammation and fibrosis associated with the development and progression of heart failure – a leading cause of death and hospitalization in the developed world, with associated healthcare costs in the U.S. exceeding \$30 billion annually.

For more information about Cardioli Therapeutics, please visit cardiolrx.com.

Cautionary statement regarding forward-looking information:

This news release contains "forward-looking information" within the meaning of applicable securities laws. All statements, other than statements of historical fact, that address activities, events, or developments that Cardiol believes, expects, or anticipates will, may, could, or might occur in the future are "forward-looking information". Forward looking information contained herein may include, but is not limited to, statements relating to the Company's focus on developing anti-inflammatory and anti-fibrotic therapies for the treatment of cardiovascular disease and the Company's plan to advance the development of a novel subcutaneous formulation of CardiolRx™ for use in heart failure. Forward-looking information contained herein reflects the current expectations or beliefs of Cardiol based on information currently available to it and is based on certain assumptions and is also subject to a variety of known and unknown risks and uncertainties and other factors that could cause the actual events or results to differ materially from any future results, performance or achievements expressed or implied by the forward-looking information, and are not (and should not be considered to be) guarantees of future performance. These risks and uncertainties and other factors include the risks and uncertainties referred to in the Company's Annual Information Form dated March 23, 2022, as well as the risks and uncertainties associated with product commercialization and clinical studies. These assumptions, risks, uncertainties, and other factors should be considered carefully, and investors should not place undue reliance on the forward-looking information. Any forward-looking information speaks only as of the date on which it is made and, except as may be required by applicable securities laws, Cardiol disclaims any intent or obligation to update or revise such forward-looking information, whether as a result of new information, future events, or results, or otherwise.

For further information, please contact:

Trevor Burns, Investor Relations +1-289-910-0855
trevor.burns@cardiolrx.com