Cardiol Therapeutics Announces Year-End 2023 Update on Operations

Completed patient enrollment in the Phase II MAvERIC-Pilot study evaluating CardiolRx™ in patients with recurrent pericarditis, with topline results expected in Q2 2024

CardiolRx™ granted U.S. FDA Orphan Drug Designation for the treatment of pericarditis, which includes recurrent pericarditis

Exceeded 50% enrollment in the Phase II ARCHER trial evaluating CardiolRx™ in patients with acute myocarditis; study expected to reach full enrollment during Q3 2024

Data presented at the HFSA Annual Scientific Sessions 2023 demonstrated that the API in Cardiol's novel CRD-38 formulation attenuates harmful fat distribution and key markers of cardiac inflammation and remodelling in a model of heart failure with preserved ejection fraction

Cash and cash equivalents of $34.9 million as of December 31, 2023, which funds operations into 2026

Toronto, ON – April 2, 2024 – 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 heart disease, today announces its year-end 2023 update on operations following the filing of its audited Financial Statements and Management's Discussion and Analysis for the year ended December 31, 2023. Both are available under the Company's profile on SEDAR+ at sedarplus.ca and on the Company's website at cardiolrx.com.

"Cardiol Therapeutics made important progress in 2023 and early 2024 as we pursued our primary objective of providing new therapeutic options to patients with poorly served heart diseases," said David Elsley, President and Chief Executive Officer of Cardiol Therapeutics. "During 2023, we initiated patient recruitment in our MAvERIC-Pilot study in patients with recurrent pericarditis and are very pleased that this important study recently completed full target enrollment, positioning the Company to report topline results in the second quarter of 2024. Completion of patient enrollment in MAvERIC-Pilot was achieved shortly after receipt of U.S. FDA Orphan Drug Designation for CardiolRx™ for the treatment of pericarditis, a larger indication and potential market exclusivity than originally anticipated by the Company. Another noteworthy clinical milestone of 2023 culminated with reporting that our global ARCHER trial, which is evaluating CardiolRx™ in patients with acute myocarditis, exceeded 50% enrollment, and is now expected to complete full enrollment during the third quarter of 2024 which is ahead of the original timeline. Importantly, CardiolRx™ is also eligible for orphan drug designations for the treatment of acute myocarditis in both the United States and the European Union. In support of our ongoing clinical programs, we were pleased to have pre-clinical results presented by our collaborators at a number of cardiology-focused scientific meetings throughout 2023, providing additional insight into the molecular and cellular mechanisms of action and benefits of our

drug candidates. Looking forward, with operations funded into 2026, Cardiol is well positioned to achieve significant milestones in the MAvERIC, ARCHER, and CRD-38 programs during 2024 that we believe will underpin business development initiatives aimed at accelerating our goal of delivering important new therapeutic options to people affected by underserved debilitating heart diseases."

Key Highlights:

Phase II MAvERIC-Pilot Study in Recurrent Pericarditis

- In January 2023, Cardiol announced the first patient had been enrolled in the Company's Phase II open-label pilot study ("MAvERIC-Pilot") investigating the tolerance, safety, and efficacy of CardiolRx™ in patients with recurrent pericarditis. In addition to standard safety assessments, the study is designed to evaluate improvement in objective measures of disease, and during an extension period, assess the feasibility of weaning concomitant background therapy including corticosteroids, while taking CardiolRx™.

- In November 2023, Cardiol announced that it had exceeded 50% of the patient enrollment target for the MAvERIC-Pilot study. Furthermore, in December, Cardiol announced that Massachusetts General Hospital had been initiated and was eligible to enroll patients; adding to a pre-eminent group of medical research centers participating in the study that includes the Cleveland Clinic and the Mayo Clinic.

- In February 2024, CardiolRx™ was granted Orphan Drug Designation ("ODD") by the United States Food and Drug Administration ("FDA") for the treatment of pericarditis, a rare inflammatory heart disease. The FDA grants ODD to a drug or biological product to prevent, diagnose, or treat a rare disease or condition that affects fewer than 200,000 people in the United States. ODD provides benefits to sponsors including potential seven-year marketing exclusivity, exemptions from certain FDA fees, and tax credits for qualified clinical trials. Products with ODD may also qualify for accelerated regulatory review via Fast Track, Breakthrough Therapy, or Priority Review designations.

- In February 2024, Cardiol announced the completion of patient enrollment in MAvERIC-Pilot. In addition, the Company announced that it expects to report topline results from MAvERIC-Pilot in Q2 2024.

Phase II ARCHER Trial in Acute Myocarditis

- In September 2023, Cardiol announced that all collaborating research centers had been initiated and were eligible to enroll patients in ARCHER, the Company's Phase II, multi-center, international, double-blind, randomized, placebo-controlled trial designed to study the safety and tolerability of CardiolRx™, as well as its impact on myocardial recovery, in patients presenting with acute myocarditis. ARCHER is expected to enroll approximately 100 patients at major cardiac centers in North America, Europe, Latin America, and Israel.

- In January 2024, Cardiol announced that ARCHER had exceeded 50% patient enrollment and was progressing ahead of the original study timeline. The Company anticipates completing full enrollment in

Q3 2024. Given there are no FDA-approved therapies for acute myocarditis, Cardiol believes there is a significant opportunity to develop an important new therapy for acute myocarditis that would also be eligible for orphan designation in the United States and the European Union.

Pre-Clinical/Clinical Developments

- In March, Cardiol announced study results were presented at the American College of Cardiology's 72nd Annual Scientific Session together with World Congress of Cardiology demonstrating that the active pharmaceutical ingredient ("API") in CardiolRx™ and CRD-38 (a novel subcutaneously administered formulation), significantly prevents cardiac dysfunction and the development of fibrosis and cardiomyocyte hypertrophy in a pre-clinical model of heart failure and reduces expression of key inflammatory and fibrotic markers. This work builds upon existing knowledge by confirming the cardioprotective properties of Cardiol's lead small molecule drug candidate and, in this model, its ability to reduce inflammation and prevent hypertrophy and fibrosis in heart tissue.

- A second poster presented data related to the role of the API in mitochondrial calcium dynamics in hypertrophic cells. The API was shown to prevent hypertrophy-induced mitochondrial calcium overload and prevent hypertrophy-induced increase of several mitochondrial function markers such as reactive oxygen species and calcium uptake. In addition, this work suggests that the API effects may rely on PPAR-γ activation, which in turn can inhibit NF-κB, a transcription factor that regulates pro-inflammatory and pro-hypertrophic genes. Together, these findings further clarify the API's mode of action in combatting cardiac hypertrophy.

- In October, Cardiol announced study results presented at the Heart Failure Society of America ("HFSA") Annual Scientific Meeting 2023 demonstrating that the subcutaneously administered formulation of the API slowed increases in body weight and heart weight and prevented increases in key cardiac inflammatory and remodelling markers in a pre-clinical model of heart failure with preserved ejection fraction.

  These findings expand the understanding of the cardioprotective effects of CRD-38 and suggest new therapeutic potential in heart failure, which remains a leading cause of death and hospital admissions in the United States and throughout the developed world, with associated healthcare costs in the United States exceeding US$30 billion annually.

- In November, Cardiol announced results from experiments conducted by its research collaborators at the University of Virginia and Houston Methodist DeBakey Heart & Vascular Center, that in an experimental model of pericarditis, the API induces mesothelial to mesenchymal transition ("MMT") and that this process is inhibited by treatment. The results presented were a continuation of a research collaboration between Cardiol and the University of Virginia, which previously reported at the American Heart Association Scientific Sessions 2022 that the API reduces pericardial effusion and thickness in the same experimental model of pericarditis.

MMT is a complex and stepwise biological process whereby a mesothelial cell, the main cell type lining internal organs and several of the body's internal cavities including the pericardium, undergoes molecular reprogramming. This alters its characteristics towards a mesenchymal cell, such as a myofibroblast, which are the primary cells during wound healing and fibrosis. Mounting evidence indicates the transition to mesenchymal cells is involved in adult cardiovascular diseases, such as heart failure. Pericarditis leads to pericardial effusion and thickening that may evolve to fibrosis, and by limiting MMT and the ensuing fibrosis, CardiolRx™ may also represent a novel strategy to prevent pericarditis complications.

About Cardiol Therapeutics

Cardiol 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 heart disease. The Company's lead small molecule drug candidate, CardiolRx™ (cannabidiol) oral solution, is pharmaceutically manufactured and in clinical development for use in the treatment of heart disease. It is recognized that cannabidiol inhibits activation of the inflammasome pathway, an intracellular process known to play an important role in the development and progression of inflammation and fibrosis associated with myocarditis, pericarditis, and heart failure.

Cardiol has received Investigational New Drug Application authorization from the United States Food and Drug Administration ("US FDA") to conduct clinical studies to evaluate the efficacy and safety of CardiolRx™ in two diseases affecting the heart: (i) a Phase II multi-center open-label pilot study in recurrent pericarditis (the MAvERIC-Pilot study; NCT05494788), an inflammatory disease 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; and (ii) a Phase II multi-national, randomized, double-blind, placebo-controlled trial (the ARCHER trial; NCT05180240) 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. The US FDA has granted Orphan Drug Designation to CardiolRx™ for the treatment of pericarditis, which includes recurrent pericarditis.

Cardiol is also developing CRD-38, a novel subcutaneously administered drug formulation of cannabidiol intended for use in heart failure – a leading cause of death and hospitalization in the developed world, with associated healthcare costs in the United States exceeding $30 billion annually.

For more information about Cardiol 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 heart disease, the molecular targets and mechanism of action of the Company's product candidates, the Company's intended clinical studies and trial activities and timelines associated with such activities, including for primary efficacy endpoint and secondary endpoints, the Company's plan to advance the development of a novel subcutaneous formulation of CardiolRx™ for use in heart failure, and the Company's expectation to report topline results from MAvERIC-Pilot in the second quarter of 2024 and that these results will inform the design of a pivotal Phase III clinical trial in recurrent pericarditis to underpin the potential regulatory approval of CardiolRx™, the Company's plan to complete full enrollment of approximately 100 patients at major cardiac centers in North America, Europe, Latin America, and Israel in the ARCHER trial during the third quarter of 2024, the Company's belief that its product candidates may be eligible for orphan drug designation in the United States and the European Union as a therapy for acute myocarditis, the Company's expectation that operations will be funded into 2026 and the Company's expectation that it will achieve significant corporate milestones during 2024. 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 Report on Form 20-F dated April 1, 2024, 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, and such information may not be appropriate for other purposes. Any forward-looking information speaks only as of the date of this press release 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