

New Data from the Phase II ARCHER Trial Demonstrate CardiolRx(TM) Improves Heart Structure in Patients with Acute Myocarditis, Supporting Expansion Across Inflammatory Cardiac Conditions

- *Phase II ARCHER trial showed a significant reduction in left ventricular (LV) mass ($p=0.0117$) and improvements in multiple key cardiac MRI (CMR) measures of structural heart recovery in patients with acute myocarditis.*
- *Results provide clinical evidence that CardiolRx™ reduces inflammation-driven structural damage in the heart, an important cause of heart failure progression.*
- *The ARCHER data strengthen the scientific and clinical rationale for Cardiol's lead Phase III program in recurrent pericarditis (MAVERIC) and support broader development across inflammatory cardiac conditions.*
- *Chronic inflammation is a central driver of adverse cardiac remodeling and heart failure, yet there are currently no approved therapies that directly target this underlying biology.*
- *Cardiol Therapeutics to host webcast and conference call to discuss positive ARCHER results and next steps for CardiolRx™ today at 8:30 a.m. EST.*

Toronto, Ontario--(Newsfile Corp. - December 1, 2025) - Cardiol Therapeutics Inc. (**NASDAQ: CRDL**) (**TSX: CRDL**) ("**Cardiol**" or the "**Company**"), a clinical-stage life sciences company advancing anti-inflammatory and anti-fibrotic therapies for heart disease, today announced new and comprehensive data from ARCHER, a randomized double-blind, placebo-controlled, multi-center Phase II clinical trial of CardiolRx™ in patients with acute myocarditis. The data show meaningful improvements in cardiac MRI (CMR) measures of myocardial recovery in patients with acute myocarditis, a potentially fatal condition caused by viral infections, autoimmune diseases, immune checkpoint inhibitor therapy to treat cancers, and exposure to cardiotoxic substances.

"The ARCHER results show that CardiolRx™ can drive meaningful structural recovery in the hearts of patients with acute myocarditis," said Dr. Andrew Hamer, Chief Medical Officer and Head of Research & Development of Cardiol Therapeutics. "We are seeing in these patients the same beneficial cardiac changes we previously observed in multiple pre-clinical heart failure models, strengthening our confidence in CardiolRx™ as a potential therapy across multiple inflammatory cardiac conditions."

Key findings from the ARCHER trial presented this past weekend included a marked 9.2-gram reduction in left ventricular (LV) mass ($p=0.0117$), along with reductions in two parameters that directly impact the heart's LV mass: extracellular volume (ECV), a measure that reflects inflammation and fibrosis outside the heart muscle cells and intercellular volume (ICV), a measure of swelling and enlargement of the heart cells. Together, these results indicate a meaningful structural improvement in the heart that is consistent with recovery from inflammation-driven edema.

The magnitude of LV mass reduction observed in ARCHER is similar to that achieved with several commonly prescribed blockbuster drugs for heart failure, obesity, and hypertension-treatments proven to improve long-term survival and reduce major cardiac events. Observing this level of structural cardiac benefit in myocarditis patients who were neither obese nor hypertensive underscores the strong clinical relevance of ARCHER's findings and their potential importance for future treatment options, as it

indicates a meaningful resolution of cardiac inflammation.

The ARCHER data were presented on November 29, 2025, by Dr. Leslie T. Cooper, Jr., Chair of the Department of Cardiovascular Medicine at Mayo Clinic in Florida and Co-Chair of the Steering Committee for the ARCHER trial, at the Annual Meeting of the European Society of Cardiology Working Group on Myocardial & Pericardial Disease in Trieste, Italy.

"ARCHER was an important, well-designed, and well-executed clinical trial. The positive changes in CMR measurements are exciting—most notably the reduction in LV mass, consistent with the numerical reductions in both ECV and ICV," commented Dr. Cooper. "These findings reinforce our original hypothesis that this innovative treatment strategy can attenuate myocardial inflammation and edema. ARCHER's results provide sound rationale for advancing the clinical development of this novel therapy in conditions of the myocardium characterized by edema, fibrosis, and remodeling, including the growing challenge of immune checkpoint inhibitor-induced myocarditis, which can be fatal."

"The results of this study are the first that I am aware of to demonstrate improvements in key measures of cardiac structure and remodeling in patients with myocarditis. The results constitute exciting clinical proof of concept that supports advancing the clinical development of this novel therapeutic approach for inflammatory cardiac conditions, including heart failure," said Dr. Dennis M. McNamara, Professor of Medicine at the University of Pittsburgh, Director of the Center for Heart Failure Research at the University of Pittsburgh Medical Center, and Chair of the ARCHER trial. "On behalf of the ARCHER Steering Committee, I would like to extend our sincere gratitude to the patients who participated in the study; to their families and caregivers for their invaluable support; and to the clinical trial site investigators and staff, members of the international Steering Committee, and the Data and Safety Monitoring Committee, whose exemplary efforts in patient recruitment, clinical care, trial execution, monitoring, and oversight were instrumental in achieving the compelling findings of the ARCHER trial."

"The ARCHER results fortify our confidence in our broader pipeline," said David Elsley, President and Chief Executive Officer of Cardiol Therapeutics. "They reinforce the growing recognition that cardiac inflammation is a treatable driver of disease progression, supporting the potential of CardiolRx™, currently being evaluated in the ongoing Pivotal Phase III MAVERIC trial in recurrent pericarditis, and additionally CRD-38, our next-generation small molecule designed to target the same pathway in chronic conditions such as heart failure with preserved ejection fraction. Taken together, these findings strengthen the scientific rationale behind both programs and point to a clear path for developing new therapies for a range of inflammatory heart diseases."

Key Findings from ARCHER

CardiolRx™ improved multiple CMR measures of myocardial recovery, heart size, and function following 12 weeks of treatment.

- LV mass, which represents the weight/thickness of the heart's left ventricle muscle and is increased when the heart works harder, was significantly reduced in the patients receiving CardiolRx™ (the active group) at 121.1 grams (g), compared to those patients receiving placebo at 130.3g, a difference of -9.2g (p=0.0117).
- Extracellular volume, representing the space outside the heart tissue cells that expands with edema or fibrosis, was reduced in the active group at 33.6 milliliters (mL), compared to placebo at 37.3mL, a difference of -3.7mL (p=0.0538).
- Intracellular volume, reflecting the volume of the heart muscle cells themselves that becomes elevated with cellular swelling during inflammation, was reduced in the active group at 85.6mL, compared to placebo at 91.2mL, a difference of -5.6mL (p=0.0928).
- Left atrial end systolic volume (LAESV) was reduced in the active group compared to placebo with a difference of -8.1mL (p=0.0376). LAESV is a measure of atrial size and workload that when elevated reflects dysfunction, higher pressure, or inflammation, but when reduced indicates improved heart relaxation and stress.
- Left ventricular end diastolic volume (LVEDV), which represents the heart's left ventricle size,

compliance, and function, and may become elevated because of inflammation or fibrosis, was reduced in the active group compared to placebo with a difference of -7.4mL (p=0.0981). Reduction of LVEDV reflects improved ventricular function or reverse cardiac remodelling (the process of changes in the heart's size, shape, and function in response to injury or increased stress).

The active and placebo groups were well matched at baseline—patients averaged 39 years of age, were predominantly male (81%), largely reported prior viral-like illness (>70%), showed preserved left-ventricular function, and the vast majority presented with chest pain (95%). Nearly all patients were hospitalized for the index myocarditis event (96.0%), with median hospital stays of five days in both groups and similar ICU durations. All results were adjusted for any baseline differences.

Consistent with prior clinical studies in inflammatory heart disease, CardiolRx™ was shown to be safe and well tolerated, with treatment emergent adverse events leading to discontinuation equal between the groups and balanced serious adverse event rates.

Company Webcast Conference Call Details

Cardiol will host a webcast and conference call today at 8:30 a.m. EST. Management will review ARCHER trial results, discuss implications for future development, and outline next steps for Cardiol's inflammatory heart disease programs. To participate by telephone, please dial 877-346-6112 (Canada and the United States) or +1-848-280-6350 (International). The conference call will also be broadcast live online through a listen-only webcast (with slides), which will be posted under "Events & Presentations" in the Investors section of the Cardiol website (cardiolrx.com/investors/events-presentations/) and archived for approximately 90 days.

About Acute Myocarditis

Acute myocarditis is an inflammatory disease of the myocardium with a highly variable clinical presentation, ranging from mild flu-like symptoms or chest pain to severe heart failure, life-threatening arrhythmias, or sudden cardiac death. Although this condition is most commonly caused by viral infections, it can also result from autoimmune diseases, hypersensitivity reactions, or exposure to cardiotoxic substances. Patients hospitalized with the condition experience an average seven-day length of stay and a 4 - 6% risk of in-hospital mortality, with average hospital charge per stay estimated at \$110,000 in the United States.

About the Phase II ARCHER Study

ARCHER enrolled 109 patients from leading cardiovascular research centers in the United States, France, Brazil, and Israel, and investigated the safety, tolerability, and impact of CardiolRx™ on myocardial recovery in patients presenting with acute myocarditis. The design and rationale for ARCHER were published on June 27, 2024, in the journal, *ESC Heart Failure* (pubmed.ncbi.nlm.nih.gov/38937900/).

About Cardiol Therapeutics

Cardiol Therapeutics Inc. (**NASDAQ: CRDL**) (**TSX: CRDL**) is a clinical-stage life sciences company advancing late-stage, anti-inflammatory, and anti-fibrotic therapies for heart disease. The Company's lead small-molecule drug candidate, CardiolRx™, modulates inflammasome pathway activation, an intracellular process known to play an important role in the development and progression of inflammation and fibrosis associated with pericarditis, myocarditis, and heart failure.

The MAVERIC Program is evaluating CardiolRx™ for the treatment of recurrent pericarditis, an inflammatory disease of the pericardium associated with symptoms including debilitating chest pain, shortness of breath, and fatigue, which can lead to physical limitations, reduced quality of life, emergency department visits, and hospitalizations. The program comprises the completed Phase II MAVERIC-Pilot

study (NCT05494788) and the ongoing pivotal Phase III MAVERIC trial (NCT06708299). The U.S. FDA has granted Orphan Drug Designation to CardiolRx™ for the treatment of pericarditis, including recurrent pericarditis.

The ARCHER Program is also studying CardiolRx™, specifically in acute myocarditis—an important cause of acute and fulminant heart failure in young adults and a leading cause of sudden cardiac death in individuals under 35 years of age. The program comprises the completed Phase II ARCHER study (NCT05180240), which evaluated the safety, tolerability, and efficacy of CardiolRx™ in this patient population.

The Company is also developing CRD-38, a novel, subcutaneously administered drug formulation intended for the treatment of inflammatory heart disease, including heart failure—a leading cause of death and hospitalization in the developed world, with associated healthcare costs in the United States exceeding US\$30 billion per year.

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 regarding the Company's focus on developing anti-inflammatory and anti-fibrotic therapies for the treatment of heart disease, the Company's intended clinical studies and trial activities and timelines associated with such activities, including the Company's plan to complete the Phase III study in recurrent pericarditis with CardiolRx™, the Company's plan to advance the development of CRD-38, a novel subcutaneous formulation intended for use in heart failure, including through the initiation of the first-in-human clinical evaluation, the potential implications of the results of the ARCHER trial including the possibility that CardiolRx™ can drive meaningful structural recovery in the hearts of patients with acute myocarditis, the Company's belief that results from the ARCHER trial provide compelling clinical proof of concept for CardiolRx™, strengthen the scientific and clinical rationale for Cardiol's lead Phase III program in recurrent pericarditis, and strongly support advancing the clinical development of CardiolRx™ and CRD-38 for the treatment of inflammatory cardiac disorders including cardiomyopathies, heart failure, and myocarditis, and the intention of the Company to review the ARCHER trial data, discuss implications for future development, and outline next steps regarding the Company's inflammatory heart disease programs. 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 filed with the Canadian securities administrators and U.S. Securities and Exchange Commission on March 31, 2025, available on SEDAR+ at sedarplus.ca and EDGAR at sec.gov, 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. Investors are cautioned not to rely on these forward-looking statements.

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