Cardiol Therapeutics to Advance CardiolRx™ into a Late-stage Trial in Patients with Recurrent Pericarditis

MAVERIC-2 trial will evaluate the impact of CardiolRx™ following cessation of interleukin-1 blocker therapy (rilonacept or anakinra) and is expected to run concurrently with the Company's planned Phase III program

Toronto, ON – October 22, 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 announced plans to expand the MAVERIC clinical development program and advance CardiolRx™ into a late-stage clinical trial ("MAVERIC-2") to evaluate the impact of CardiolRx™ in recurrent pericarditis patients following cessation of interleukin-1 ("IL-1") blocker therapy. MAVERIC-2 is expected to be initiated during Q4 at major pericardial disease centres in the United States and Europe and to report results ahead of the Company's planned pivotal Phase III study in recurrent pericarditis.

"MAVERIC-2 provides an exciting opportunity to expand the market potential for CardiolRx through the execution of a cost-effective study and potentially provides a path for an accelerated regulatory approval timeline," said David Elsley, President & CEO of Cardiol Therapeutics. "This important new study, designed in collaboration with an international panel of advisors comprised of experts in pericarditis, will also augment data from our planned Phase III MAVERIC-3 trial by exploring the potential for our lead oral drug candidate to assist the growing number of recurrent pericarditis patients who seek alternative options to chronic use of immunosuppressant biologics."

MAVERIC-2 is a randomized, double-blind, placebo-controlled Phase II/III trial in approximately 110 patients. Patients with stable disease who are receiving IL-1 blocker treatment will be randomly assigned to receive either CardiolRx™ or placebo following cessation of the IL-1 blocker. The primary clinical objective of the trial will be to assess the impact of CardiolRx™ versus placebo on freedom from a new episode of recurrent pericarditis. Other clinical endpoints of interest include time to a new episode of pericarditis recurrence and change in patient-reported pericarditis chest pain score and the inflammatory marker C-reactive protein ("CRP").

IL-1 is a key pro-inflammatory cytokine in the pathophysiology of recurrent pericarditis. It is generated downstream following activation of the NLRP3 inflammasome and amplifies the autoinflammatory response characteristic of the disease. IL-1 blockers (rilonacept or anakinra) target and negate the activity of IL-1, but given their expense and immunosuppressant risks, they are generally prescribed as a third-line intervention in difficult-to-treat patients. There is a growing body of evidence indicating pericarditis recurrence rates are as high as seventy-five percent and onset is rapid following cessation of IL-1 blocker therapy. Currently, many patients who discontinue IL-1 blocker therapy and subsequently suffer a recurrence require rescue treatment with further administration of these biologics, potentially leading to IL-1 blocker dependence.

"CardiolRx™ has been shown experimentally to inhibit assembly and activation of the NLRP3 inflammasome and the subsequent generation of IL-1, and following oral administration has led to marked reductions in pericarditis pain in patients suffering from chronic pericardial disease," said Dr. Andrew Hamer, Cardiol Therapeutics' Chief Medical Officer and Head of Research & Development. "In addition to potentially offering a more accessible and non-immunosuppressive therapy to thousands of patients who are non-responsive or intolerant to current therapies, CardiolRx™ may also have therapeutic potential to prevent recurrences following discontinuation of IL-1 blockers, which would address an unmet need in a growing subset of patients dependant on long-term IL-1 blocker therapy."

The Company previously announced positive topline data from MAvERIC-Pilot investigating CardiolRx™ for recurrent pericarditis which showed a substantial reduction in the primary efficacy endpoint of patient-reported pericarditis pain at the end of the 8-week treatment period ("TP"), as well as normalization of inflammation – as measured by CRP – in 80% of the patients with elevated CRP at baseline. Eighty-nine percent of patients (24/27) progressed from the TP into the now completed extension period ("EP") of the study, defined as the additional 18-week period where background therapy was weaned and patients were followed on monotherapy of CardiolRx™. Full clinical data will be reported in an oral presentation November 18th, 2024, at the American Heart Association Scientific Sessions 2024 and will include freedom from pericarditis recurrence during the 18-week EP, 26-week pericarditis pain score and inflammatory marker levels, and safety and tolerability outcomes. The totality of the MAvERIC-Pilot data will support and further inform the Company's plans related to a second late-stage study called MAVERIC-3, a Phase III pivotal trial designed to assess CardiolRx™ for the treatment of the broader population of pericarditis patients to prevent recurrence.

Pericarditis

Pericarditis refers to inflammation of the pericardium (the membrane or sac that surrounds the heart) frequently resulting from a viral infection. Following that initial episode patients may have multiple recurrences, and the primary goal of treatment is recurrence prevention. Symptoms include debilitating chest pain, shortness of breath, and fatigue, resulting in physical limitations, reduced quality of life, emergency department visits, and hospitalizations. Significant accumulation of pericardial fluid and scarring can progress to life-threatening constriction of the heart. The only FDA-approved therapy for recurrent pericarditis, launched in 2021, is costly and is primarily used as a third-line intervention. On an annual basis, the number of patients in the United States having experienced at least one recurrence is estimated at 38,000. Approximately 60% of patients with multiple recurrences (>1) still suffer for longer than two years, and one third are still impacted at five years. Hospitalization due to recurrent pericarditis is often associated with a 6-8-day length of stay and cost per stay is estimated to range between $20,000 and $30,000 in the United States.

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: recurrent pericarditis and acute myocarditis. The MAVERIC Program in recurrent pericarditis, 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, comprises the Phase II MAvERIC-Pilot study (NCT05494788), the Phase II/III MAVERIC-2 trial, and the planned Phase III MAVERIC-3 trial. The ARCHER trial (NCT05180240) is a Phase II study 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 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 regarding the Company's plans to expand the MAVERIC clinical development program and advance CardiolRx™ into a late-stage clinical trial called MAVERIC-2, the Company's expectation to initiate the MAVERIC-2 study during the fourth quarter of 2024 at major pericardial disease centres in the United States and Europe and report results ahead of the Company's planned pivotal Phase III study in recurrent pericarditis, the Company's plans to conduct its Phase III study in recurrent pericarditis concurrently with MAVERIC-2, the Company's intention to report full clinical data from the MAvERIC-Pilot study in an oral presentation at the American Heart Association Scientific Sessions 2024, the Company's expectation that the full clinical data from the MAvERIC-Pilot study presented will include freedom from pericarditis recurrence during the 18-week EP, 26-week pericarditis pain score and inflammatory marker levels and safety and tolerability outcomes, the Company's belief that the MAvERIC-Pilot study data will support and further inform

the Company's plans related to a second late-stage study called MAVERIC-3 which the Company intends to be a Phase III pivotal trial designed to assess CardiolRx™ for the treatment of the broader population of pericarditis patients to prevent recurrence, 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 the Company's plan to complete the Phase III study in recurrent pericarditis with CardiolRx, and the Company's plan to advance the development of CRD-38, a novel subcutaneous formulation of cannabidiol intended 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 Report on Form 20-F filed with the U.S. Securities and Exchange Commission and Canadian securities regulators on 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. Investors are cautioned not to rely on these forward-looking statements and are encouraged to read the Supplement, the accompanying Base Prospectus and the documents incorporated by reference therein.

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