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Cardiol Therapeutics Announces FDA Investigational New Drug Application (IND) Authorization for Multicenter Phase II Open-label Pilot Study of CardiolRx™ for Recurrent Pericarditis

- **Third IND authorization for CardiolRx™ in cardiovascular disease**
- **Study to run in parallel with Company's multi-national Phase II acute myocarditis trial, expected to commence imminently**
- **CardiolRx™ is now eligible for orphan drug status in two indications**

Oakville, ON – May 17, 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-fibrotic and anti-inflammatory therapies for the treatment of cardiovascular disease ("CVD"), is pleased to announce the U.S. Food and Drug Administration (FDA) has authorized the Company's Investigational New Drug Application (IND) to commence a Phase II open-label pilot study designed to evaluate the tolerance and safety of CardiolRx™, a pharmaceutically manufactured oral cannabidiol drug formulation, in patients with recurrent pericarditis. The study will also assess the improvement in objective measures of disease, and during an extension period, assess the feasibility of weaning concomitant background therapy including corticosteroids, while taking CardiolRx™. Recurrent pericarditis is an orphan disease in the United States, thereby making CardiolRx™ eligible for orphan drug status under the FDA's Orphan Drug Designation program.

Allan L. Klein, MD, FRCP (C), FACC, FAHA, FASE, FESC, Director Center of Pericardial Diseases and Professor of Medicine, Heart and Vascular Institute, Cleveland Clinic, will serve as study Chair and provide leadership throughout the course of the trial. Dr. Klein commented, "I look forward to investigating the potential of this treatment in patients with recurrent pericarditis, a cardiovascular inflammatory disease and the most common of pericardial diseases. We look forward to evaluating whether this intervention could be a therapeutic option for those who are intolerant to current medical treatment or who require long-term administration of corticosteroids to control their disease."

Cardiol's study is expected to enroll 25 patients at major clinical centers specializing in pericarditis in the United States. The study protocol has been designed in collaboration with thought leaders in pericardial disease. The trial's primary efficacy endpoint is the change, from baseline to 8 weeks, in patient-reported pericarditis pain using an 11-point numeric rating scale (NRS). The NRS is a validated clinical tool used across multiple conditions with acute and

chronic pain, including previous studies of recurrent pericarditis. Secondary endpoints include the pain score after 26 weeks of treatment, and changes in C-reactive protein (CRP).

“We are pleased that Dr. Klein will provide his expertise and leadership to Cardiol’s study, and his contributions thus far with respect to protocol design and facilitating clinical trial site recruitment have been invaluable,” commented Dr. Andrew Hamer, Cardiol’s Chief Medical Officer. “We believe there is a significant opportunity to develop a new oral, well tolerated therapy for treating recurrent pericarditis to prevent multiple recurrences, for colchicine refractory, intolerant, and contraindicated patients, as well as steroid-dependent patients. With IND authorization now in place, we look forward to ramping up initiation of this important study. We also anticipate benefiting from the clinical trial infrastructure already established for our multi-national acute myocarditis study, which is expected to commence patient enrollment imminently.”

Pericarditis refers to inflammation of the pericardium – the membrane, or sac, that surrounds the heart. Symptoms include debilitating chest pain, shortness of breath, and fatigue, which result in physical limitations, reduced quality of life, emergency department visits, and hospitalizations. Causes of pericarditis can include infection (e.g., tuberculosis), systemic disorders such as autoimmune and inflammatory diseases, cancer, and post-cardiac injury syndromes. Based on time of presentation, acute pericarditis is a symptomatic event lasting less than four to six weeks, the diagnosis of which is based on meeting two of four criteria: chest pain; pericardial rub; electrocardiogram changes; and new or worsening pericardial swelling. Elevation of inflammatory markers such as CRP, and evidence of pericardial inflammation by an imaging technique (computed tomography scan or cardiac magnetic resonance) may help the diagnosis and the monitoring of disease activity. Although generally self-limited and not life-threatening, acute pericarditis is diagnosed in 0.2% of all cardiovascular in-hospital admissions and is responsible for 5% of emergency room admissions for chest pain in North America and Western Europe.

Recurrent pericarditis is the reappearance of symptoms after a symptom-free period of at least 4–6 weeks following an episode of acute pericarditis. These recurrences appear in 15% to 30% of acute cases and usually within 18 months. Further, up to 50% of patients with a recurrent episode of pericarditis experience more recurrences. Standard first-line medical therapy consists of non-steroidal anti-inflammatory drugs or aspirin with or without colchicine. Corticosteroids such as prednisone are second-line therapy in patients with continued recurrence and inadequate response to conventional therapy. Recently a potent subcutaneously injected interleukin-1 inhibitor has been approved by the FDA for patients with recurrent pericarditis; however, this immunosuppressant is primarily used in patients with a third or fourth recurrence.

The U.S. Orphan Drug Designation program was created to provide the sponsor of a drug significant incentives, including seven-year marketing exclusivity and exemptions from certain FDA fees, to develop treatments for diseases that affect fewer than 200,000 people in the U.S. Products with Orphan Drug Designation also frequently qualify for accelerated regulatory review. The prevalence of recurrent pericarditis in the U.S. is estimated at 38,000. The program was successfully utilized to support the first FDA approval of cannabidiol for the treatment of rare pediatric epilepsy syndromes. Cardiol believes there is a similar opportunity to develop its oral CardiolRx™ formulation as an orphan drug for the treatment of recurrent pericarditis.

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 cannabidiol as an anti-fibrotic and anti-inflammatory therapy for the treatment of cardiovascular disease ("CVD"). The Company's lead product candidate, CardiolRx™, is a pharmaceutically produced oral cannabidiol formulation that is being clinically developed for use in cardiovascular medicine. CardiolRx™ is currently 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 CardiolRx™ 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 CardiolRx™ has on key biomarkers associated with heart disease. Cardiol has also received IND authorization from the FDA to conduct a Phase II multi-national, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of CardiolRx™ in acute myocarditis (also an orphan indication), which remains an important cause of acute and fulminant heart failure in young adults and is a leading cause of sudden cardiac death in people less than 35 years of age. In addition, Cardiol is developing a subcutaneous formulation of CardiolRx™ for the treatment of fibrosis and inflammation in the heart that is 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 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 intention that the pericarditis study run in parallel with the Company's myocarditis trial, which is expected to commence imminently; the fact that the pericarditis study is designed to evaluate the tolerance and safety of CardiolRx™; the point that the pericarditis study will also assess the improvement in objective measures of disease, and assess the feasibility of weaning concomitant background therapy including corticosteroids, while taking CardiolRx™; the fact that Allan L. Klein, MD, will serve as study Chair and provide leadership throughout the course of the trial; the possibility that CardiolRx™ may offer a therapeutic option in the patient population who are intolerant to current medical treatment or who require long-term administration of corticosteroids to control their disease; the expectation that the study will enroll 25 patients at major clinical centers specializing in pericarditis in the United States; the expectation that Cardiol will now ramp up for initiation of the study; the belief that the study will benefit from the infrastructure synergies, including streamlining of site contracting and activation; the belief there is a significant opportunity to develop a new oral, well tolerated, and safe therapy for treating recurrent pericarditis to prevent multiple recurrences, for colchicine refractory, intolerant, and contraindicated patients, as well as steroid dependent patient; the belief that there is a similar opportunity to develop the Company's oral CardiolRx™ formulation as an orphan drug for the treatment of recurrent pericarditis; the focus on developing innovative anti-inflammatory therapies for the treatment of cardiovascular disease; the completion of patient enrollment into the LANCER Phase II/III trial; the initiation of patient enrollment into the Phase II trial; and advancing the subcutaneous formulation of CardiolRx™ as a potential anti-fibrotic and anti-inflammatory therapy. Forward-looking information contained herein reflects the

current expectations or beliefs of Cardiol based on information currently available to it, including Cardiol's ability to successfully initiate and complete patient enrollment in trials and to advance the subcutaneous formulation of CardiolRx™. This forward-looking information 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.

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