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Cardiol Therapeutics Announces Year-End 2022 Update on Operations

- ***Initiated patient enrollment in a Phase II open-label clinical trial investigating the safety, tolerability, and efficacy of CardiolRx™ in patients with recurrent pericarditis – a debilitating heart disease associated with chest pain, shortness of breath and fatigue, resulting in markedly reduced quality of life, emergency department visits, and hospitalizations***

- ***Initiated patient enrollment in the ARCHER Trial – a Phase II multi-national, randomized, placebo-controlled clinical trial evaluating the safety and efficacy of CardiolRx™ in patients with acute myocarditis, an important cause of acute and sudden heart failure in young adults and a leading cause of sudden cardiac death in people less than 35 years of age***

- ***Data presented at the late-breaking scientific sessions of The American Heart Association 2022 demonstrating the cardioprotective effects of CardiolRx™ in a model of acute pericarditis***

- ***Pre-clinical study results presented at The Annual Scientific Meeting of the Heart Failure Society of America demonstrating CardiolRx™ inhibits and promotes reversal mechanisms leading to cardiac fibrosis***

- ***Made key appointments to the Board of Directors, adding extensive and diversified experience to provide additional independent guidance and stewardship to oversee the Company´s continued growth and development***

- ***Appointed thought leaders in cardiovascular medicine to its Scientific Advisory Board***

- ***Cash and cash equivalents of $59.5 million as of December 31, 2022, providing capital to achieve corporate milestones and fund operations into 2026***

Oakville, ON – March 29, 2023 – 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 2022 update on operations following the filing of its audited Financial Statements and Management's Discussion and Analysis for the year ended

December 31, 2022. Both are available under the Company's profile on SEDAR at sedar.com and on the Company's website at cardiolrx.com.

"In 2022, Cardiol made important progress with the development of CardiolRx, our lead drug candidate for the treatment of inflammation and fibrosis in heart disease. We initiated the ARCHER trial, a multi-national clinical study in acute myocarditis, that is one of the largest company-sponsored clinical trials to be undertaken in this underserved condition in over 30 years. Our research collaborators presented compelling evidence at The American Heart Association demonstrating the ability of CardiolRx to confer cardioprotective effects in a model of recurrent pericarditis. This presentation was followed by the initiation of our U.S. Phase II open-label pilot study in patients with recurrent pericarditis at the renowned Cleveland Clinic and Mayo Clinic sites," said David Elsley, President and Chief Executive Officer of Cardiol Therapeutics. "These clinical advancements have been complemented with important basic science initiatives that have furthered our understanding of CardiolRx's mode of action in inflammatory heart disease. In conjunction with our strong financial position, with cash to achieve our corporate milestones and fund operations into 2026, we are well-positioned to pursue our objective of developing new treatment options to improve the health and quality of life for patients living with debilitating forms of heart disease."

Key Highlights during the 2022 Fiscal Period:

Clinical Developments

- In May, the Company received Investigational New Drug Application authorization from the United States ("U.S.") Food and Drug Administration ("FDA") to conduct a multi-center Phase II open-label pilot study of CardiolRx™ for recurrent pericarditis, extending orphan drug eligibility for CardiolRx™ to a second heart disease, alongside acute myocarditis.

- In August, Cardiol announced the first patient had been enrolled in ARCHER, the Company's Phase II multi-national, 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 100 patients at major cardiac centers in North America, Europe, Latin America, and Israel.

- In December, the Company commenced a Phase II open-label pilot study, to investigate the safety, tolerability, 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™. The Cleveland Clinic and the Mayo Clinic study sites were initiated and are eligible to recruit participants. The first patient was enrolled in January 2023.

Pre-clinical Developments

- In October, the Company announced study results demonstrating 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 cardiac fibrosis. The data were presented by Cardiol's 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 Program. The authors concluded that the API in CardiolRx™ protects cardiac function and exhibits an antifibrotic effect, possibly mediated by endothelial-to-mesenchymal transition.

- In November, Cardiol announced study results demonstrating that pharmaceutically manufactured cannabidiol, the API in CardiolRx™, significantly reduces pericardial effusion and thickening in a pre-clinical model of acute pericarditis and significantly suppresses the secretion of key inflammatory markers interleukin-1β ("IL-1β") and interleukin-6 ("IL-6") *in vitro*. The release of these cytokines IL-1β and IL-6 is responsible for the cycle of inflammation in recurrent pericarditis leading to the pericardial effusion and thickening characteristic of the disease. The data were presented by the Corporation's research collaborators from Virginia Commonwealth University at The American Heart Association Scientific Sessions 2022 ("AHA2022").

  The poster entitled "Protective Effects of Pharmaceutically Manufactured Cannabidiol in a Mouse Model of Acute Pericarditis" was presented on November 5, 2022, within the "Late-Breaking Basic Science Posters" session of AHA2022. The authors concluded that the pharmaceutically manufactured cannabidiol administered in the study may represent a novel therapy for treating pericarditis and preventing its complications and recurrence. Data presented also demonstrated a dose-response effect on IL-1β *in vitro*. In addition, cannabidiol was shown *in vitro* to significantly inhibit the transcription of IL-1β and NLRP3, as measured by mRNA expression. NLRP3 is a sensor protein that comprises a part of the NLRP3 inflammasome, a large multiprotein complex that regulates inflammatory responses of the innate immune system. Cardiol has filed comprehensive patent applications with the U.S. patent office in connection with these new findings.

Corporate Updates

- In January, Cardiol announced the appointment of Paul M. Ridker, MD, MPH, Bruce McManus, PhD, MD, and Joseph A. Hill, MD, PhD to its Scientific Advisory Board.

  Dr. Ridker is director of the Center for Cardiovascular Disease Prevention, a translational research unit at Brigham and Women's Hospital, Boston. A cardiovascular medicine specialist, he is also the Eugene Braunwald Professor of Medicine at Harvard School of Medicine. Dr. Ridker is the author of over 900 peer-reviewed publications and reviews, 64 book chapters, and six textbooks related to cardiovascular medicine.

  Dr. McManus is Professor Emeritus, Department of Pathology and Laboratory Medicine, the University of British Columbia. Dr. McManus' investigative passion relates to mechanisms, consequences, detection and prevention of injury and aberrant repair in inflammatory diseases of the heart and blood vessels.

  Dr. Hill is Professor of Internal Medicine and Molecular Biology, Chief of Cardiology at UT Southwestern Medical Center, Dallas, TX, and Director of the Harry S. Moss Heart Center. For the past six years, Dr. Hill has been the Editor-in-Chief of the prestigious American Heart Association journal *Circulation*.

- In March, the Board of Directors appointed Jennifer M. Chao to serve as a director. She has also been appointed Chair of the Corporate Governance and Compensation Committee. Ms. Chao is Managing Partner of CoreStrategies Management, LLC, a company she founded in 2008 to provide corporate and financial strategies to biotech/life science companies for maximizing core valuation.

- In May, the Board of Directors appointed Teri Loxam and Chris Waddick to serve as directors.

  Ms. Loxam has over 25 years of experience in biotech, life sciences, and entertainment industries with diverse roles spanning strategy, investor relations, finance, and communications. She currently serves as Chief Operating Officer and Chief Financial Officer of Kira Pharmaceuticals.

  Mr. Waddick has served as Chief Financial Officer and Corporate Secretary of Cardiol since August 16, 2018. He has over thirty years of experience in financial and executive roles in the biotechnology and energy industries, with substantial knowledge of public company management and corporate governance, and expertise in designing, building, and managing financial processes, procedures, and infrastructure.

Outlook

During the next 12-24 months, the Company expects the following key corporate milestones to be achieved:

- Completion of patient enrollment in the Company-sponsored Phase II open-label pilot study (NCT05494788) 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™. Recurrent pericarditis refers to inflammation of the pericardium (the membrane or sac that surrounds the heart) that follows an initial episode (frequently resulting from a viral infection). Patients may have multiple recurrences. 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. The number of patients seeking and receiving treatment for recurrent pericarditis annually in the U.S. is estimated at 38,000. 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.

- Completion of patient enrollment into the ARCHER, the Company's Phase II multi-national, double-blind, randomized, placebo-controlled trial (NCT05180240) designed to study the safety and tolerability of CardiolRx™, as well as its impact on myocardial recovery, in patients presenting with acute myocarditis, an important cause of acute and sudden heart failure in young adults and a leading cause of sudden cardiac death in people less than 35 years of age. Although viral causes of myocarditis are the most common, myocarditis can result from a broad range of infections and can be caused by certain drugs, including chemo-therapeutic agents used to treat several common cancers. Myocarditis can also manifest as post-acute sequelae of SARS-CoV-2 infection and, more recently, has been reported as a rare

complication associated with certain vaccines for COVID-19. Cardiol believes there is a significant opportunity to develop CardiolRx™ as an orphan drug for the treatment of acute myocarditis, for which there is currently no accepted standard of care.

- Advance our novel subcutaneously administered drug formulation of cannabidiol as a potential anti-fibrotic and anti-inflammatory therapy for use in heart failure. Heart failure is a leading cause of death in the developed world, with associated annual healthcare costs in the United States exceeding $30 billion annually.

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 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 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 (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; and (ii) 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.

Cardiol is also developing 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 Company having enough capital to achieve its corporate milestones and fund operations into 2026, the molecular targets and mechanism of action of the Company's product candidates, Cardiol being well positioned to pursue its objective of developing new treatment options to improve health and quality of life for patients with heart disease, the Company's Phase II open-label pilot study being designed to evaluate improvement in objective measures of disease, the Company's ARCHER study being designed to study the safety and tolerability of CardiolRx, as well as its impact on myocardial recovery, the Company's expectation that the ARCHER study will enroll 100 patients,

the authors of a clinical study concluding that manufactured cannabidiol may represent a novel therapy for treating pericarditis, the Company's expectations that its corporate milestones will be key drivers of shareholder value over the next 12-24 months, the completion of patient enrollment in the Company-sponsored Phase II open-label pilot study investigating the tolerance, safety, and efficacy of CardiolRx™ in patients with recurrent pericarditis, the completion of patient enrollment into the ARCHER, the Company's Phase II multi-national, double-blind, randomized, placebo-controlled trial designed to study the safety and tolerability of CardiolRx™, the Company's intended clinical study and trial activities and timelines associated with such activities, the Company's plan to advance its novel subcutaneously administered drug formulation of cannabidiol as a potential anti-fibrotic and anti-inflammatory therapy for use in heart failure 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 Report dated March 28, 2023, 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.

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