



2265 Upper Middle Road East, Suite 602
Oakville, ON L6H 0G5, Canada

Cardiol Therapeutics Appoints *Worldwide Clinical Trials* as CRO for the Company’s Phase II/III Outcomes Trial in High-risk Patients Hospitalized with COVID-19

Trial designed to investigate the cardioprotective properties of CardiolRx™ in patients hospitalized with COVID-19 who have a prior history of, or risk factors for, cardiovascular disease now being initiated at clinical centers in the United States

Oakville, ON – December 15, 2020 – Cardiol Therapeutics Inc. (TSX: CRDL)(OTCQX: CRTPF) (“Cardiol” or the “Company”), a clinical-stage biotechnology company focused on the research and clinical development of anti-inflammatory therapies for the treatment of cardiovascular disease (“CVD”), announces that it has appointed contract research organization (“CRO”) Worldwide Clinical Trials (“Worldwide”), as the Company initiates its Phase II/III trial in high-risk patients hospitalized with COVID-19 at clinical centers throughout the United States. The double-blind, placebo-controlled clinical trial is designed to investigate the efficacy and safety of CardiolRx™, a pharmaceutically produced extra strength cannabidiol formulation, in 422 hospitalized COVID-19 patients with a prior history of, or risk factors for, cardiovascular disease. This patient population is at significant risk of developing cardiovascular complications, which are frequently fatal, during their illness.

Worldwide has been the CRO for several international COVID-19 clinical programs and has extensive experience in conducting clinical research focused on cardiovascular disease. With a global footprint, *Worldwide* provides unparalleled drug development expertise from early phase to late-stage clinical development, post-approval, and real-world evidence studies; delivering high quality clinical programs designed to support regulatory approvals in multiple jurisdictions. Employing more than 1,900 professionals, *Worldwide* provides drug development support services in over 60 countries with offices in North and South America, Europe, and Asia.

“We are pleased to be collaborating with *Worldwide Clinical Trials* as we initiate our Phase II/III trial in high-risk patients hospitalized with COVID-19 at clinical centers throughout the U.S.,” stated David Elsley, President and CEO of Cardiol Therapeutics. “While this potentially registrational trial is designed primarily to evaluate the impact of CardiolRx on reducing mortality and major cardiovascular outcomes in COVID-19 patients who have a prior history of, or risk factors for, cardiovascular disease, this important study will also investigate the therapy’s influence on key markers of inflammatory heart disease. These findings are expected to provide invaluable data with respect to the therapeutic potential of CardiolRx in the treatment of inflammatory heart disease, including heart failure which remains a leading cause of death and disability and a major economic burden in developed nations.”

The composite primary efficacy endpoint will be the difference between the active and placebo groups in the percentage of patients who develop, during the first 28 days following first dose of study medication, one or more of the following outcomes: i) all-cause mortality, ii) requirement for ICU admission and/or ventilatory support, and iii) cardiovascular complications, including the development of heart failure, acute myocardial infarction, myocarditis, stroke, or new sustained or symptomatic arrhythmia. The study was designed by and will be overseen by an independent Steering Committee, consisting of international thought leaders in inflammatory heart disease. The Steering Committee is chaired by Dr. Dennis McNamara, Professor of Medicine and Director of the Center for Heart Failure Research, University of Pittsburgh and co-chaired by Dr. Leslie Cooper, Chair of the Mayo Clinic Enterprise Department of Cardiovascular Medicine and Chair of the Department of Cardiovascular Medicine, Mayo Clinic.

The rationale for using cannabidiol to treat patients with COVID-19 is based on its reported anti-inflammatory and cardioprotective effects which are anticipated to prevent COVID-19-related cardiovascular complications, thereby reducing morbidity and mortality. Cardiovascular complications such as myocardial injury (demonstrated by elevated blood troponin levels) are common in COVID-19 patients and are linked to a higher rate of mortality. Cannabidiol has been shown to reduce elevated troponin and reduce pro-inflammatory responses in models of cardiotoxicity. In pre-clinical models of cardiac injury, cannabidiol has been shown to be cardioprotective by reducing cardiac hypertrophy, fibrosis, and the production of certain remodelling markers, such as cardiac B-type Natriuretic Peptide (BNP), which is elevated in patients with COVID-19, cardiac damage, and/or heart failure.

About Cardiol Therapeutics

Cardiol Therapeutics Inc. (**TSX: CRDL**)(**OTCQX: CRTPF**) is a clinical-stage biotechnology company focused on the research and clinical development of anti-inflammatory therapies for the treatment of cardiovascular disease (CVD). The Company's lead product, CardiolRx™, is a pharmaceutically produced oral cannabidiol formulation that is currently entering a Phase II/III outcomes study in hospitalized patients testing positive for the COVID-19 virus. This potentially registrational trial is designed to evaluate the efficacy and safety of CardiolRx as a cardioprotective therapy to reduce mortality and major cardiovascular events in COVID-19 patients who have a prior history of, or risk factors for, CVD, and to investigate the influence CardiolRx has on key markers of inflammatory heart disease.

Cardiol is also planning to file an IND for a Phase II international trial that will investigate the anti-inflammatory and anti-fibrotic properties of CardiolRx in patients with acute myocarditis, which remains the most common cause of sudden cardiac death in people under 35 years of age. In addition, Cardiol is developing a subcutaneous formulation of CardiolRx and other anti-inflammatory therapies for the treatment of chronic heart failure – a leading cause of death and hospitalization in North America, with associated annual healthcare costs in the U.S. alone exceeding \$30 billion.

Cardiol recently commercialized Cortalex™ (cortalex.com) in the Canadian market. Cortalex is a pharmaceutically produced cannabidiol formulation, developed for patients who wish to avoid

THC or for whom THC exposure is not recommended. For more information about Cardiol Therapeutics, please visit cardiolrx.com.

For further information, please contact:

David Elsley, President & CEO +1-289-910-0850
david.elsley@cardiolrx.com

Trevor Burns, Investor Relations +1-289-910-0855
trevor.burns@cardiolrx.com

Cautionary statement regarding forward-looking information:

This news release contains “forward-looking information” within the meaning of applicable Canadian securities laws. All statements, other than statements of historical fact, that address activities, events, or developments that Cardiol Therapeutics Inc. (“Cardiol” or the “Company”) 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 with respect to that, our Phase II/III study is potentially a registrational trial and is expected to provide invaluable data with respect to the therapeutic potential of CardiolRx in the treatment of inflammatory heart disease, including heart failure and the Company’s plans for a Phase II international trial of CardiolRx™ in acute myocarditis and developing a subcutaneous formulation of CardiolRx and other anti-inflammatory therapies for the treatment of chronic heart failure. Forward-looking information contained herein reflects the current expectations or beliefs of Cardiol based on information currently available to it and is 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. These risks and uncertainties and other factors include the risks and uncertainties referred to in the Company’s Annual Information Form dated March 30, 2020, including the risks and uncertainties associated with product commercialization and clinical studies, and uncertainties in predicting treatment outcomes. These 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. Although Cardiol believes that the expectations reflected in the forward-looking information are reasonable, they do involve certain assumptions, risks, and uncertainties and are not (and should not be considered to be) guarantees of future performance. It is important that each person reviewing this news release understands the significant risks attendant to the operations of Cardiol.