CARDIOL THERAPEUTICS INC.

Annual Information Form

For the year ended December 31, 2021

March 23, 2022

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GLOSSARY OF TERMS

"**2020 Compensation Warrants**" has the meaning set out under the heading "Business of Cardiol – Corporate History - Year Ended December 31, 2020".

"**2020 Underwriters**" has the meaning set out under the heading "Business of Cardiol – Corporate History - Year Ended December 31, 2020".

"**ACC**" means the American College of Cardiology.

"**ACE**" means Angiotensin Converting Enzyme."

Annual Information Form" or "**AIF**" means this annual information form.

"**ANDA**" means abbreviated new drug application.

"**APIs**" means active pharmaceutical ingredients.

"ARBs" means Angiotensin Receptor Blockers.

"**Audit Committee**" means the Corporation's Audit Committee.

"**BDO**" means the auditors of the Corporation, BDO Canada LLP, Chartered Professional Accountants, of 1000 De La Gauchetière Street West, Suite 200, Montréal, Québec H3B 4W5

"**Bioavailability**" means the proportion of a drug or other substance that enters systemic circulation when introduced into the body.

"**BNP**" means B-type Natriuretic Peptide.

"**Board of Directors**" or "**Board**" means the board of directors of the Corporation and "**Director**" means each director of the Corporation.

"**Cannabis Act**" means *Cannabis Act* (Canada), which came into force on October 17, 2018 and was amended on October 17, 2019 and October 17, 2020.

"**Cannabis Regulations**" means regulations issued pursuant to the Cannabis Act.

"**Cardiol**" or the "**Corporation**" means Cardiol Therapeutics Inc.

"**CARO**" means the Instituto Tecnológico y de Estudios Superiores de Monterrey's Clinical Academic Research Organization, S.A. de C.V.

"**CARO Compensation Warrants**" has the meaning set out under the heading "Business of Cardiol – Commercialization Relationships – TecSalud (CARO Development Agreement)".

"**CARO Compensation Warrant Share**" has the meaning set out under the heading "Business of Cardiol – Commercialization Relationships – TecSalud (CARO Development Agreement)".

"**CARO Development Activities**" has the meaning set out under the heading "Business of Cardiol – Commercialization Relationships – TecSalud (CARO Development Agreement)".

"**CARO Development Agreement**" has the meaning set out under the heading "Business of Cardiol – Commercialization Relationships – TecSalud (CARO Development Agreement)".

"**CARO Development Plan**" has the meaning set out under the heading "Business of Cardiol – Commercialization Relationships – TecSalud (CARO Development Agreement)".

"**CBD**" means cannabidiol.

"**CCA**" has the meaning set out under the heading "Regulatory Overview – Regulatory Framework in Canada for Cannabis – Provincial and Territorial Regulatory Regimes".

"**CCLA**" has the meaning set out under the heading "Regulatory Overview – Regulatory Framework in Canada for Cannabis – Provincial and Territorial Regulatory Regimes".

"**CDN**" means Canadian dollars.

"**CDS**" means CDS Clearing and Depository Services Inc.

"**CDSA**" means the Controlled Drugs and Substances Act, SC 1996, c 19, a Canadian federal act containing restrictions in use of controlled substances.

"**CEC**" means Clinical Endpoint Committee.

"**CEO**" means Chief Executive Officer.

"**CFO**" means Chief Financial Officer.

"**COO**" means Chief Operating Officer

"**CG&C Committee**" means the Corporate Governance and Compensation Committee.

"**cGMP**" means the FDA's Continuing Good Manufacturing Practice regulations.

"**CHMP**" means the Committee for Medicinal Products for Human Use.

"**CIPO**" means the Canadian Intellectual Property Office.

"**CIRT**" means the Cardiovascular Inflammation Reduction Trial.

"**CMOs**" means contract manufacturing organizations.

"**Common Shares**" means the Class A common shares in the capital of the Corporation.

"**Computershare Trust**" means Computershare Trust Company of Canada, the Warrant agent.

"**COVID-19**" means a disease caused by the SARS-CoV-2

"**CRO**" means contract research organizations.

"**CSA**" means the U.S. Controlled Substances Act.

"**CTA**" means clinical trial application.

"CVD" means cardiovascular disease.

"**Dalton**" means Dalton Chemical Laboratories, Inc., operating as Dalton Pharma Services.

"**Dalton Services Agreement**" has the meaning set out under the heading "Business of Cardiol – Commercialization Relationships – Dalton".

"**DSMC**" means the Data Safety Monitoring Committee.

"**DEA**" means the Drug Enforcement Agency.

"**DOX**" means doxorubicin.

"**EMA**" means European Medicines Agency.

"**EPR**" means enhanced permeability and retention.

"**FDA"** means the U.S Food and Drug Administration.

"**FDCA**" means the U.S. Federal Food, Drug, and Cosmetic Act.

"**Founders**" means the founders of Cardiol; namely, David Elsley, Dr. Eldon Smith, and Dr. Anthony Bolton.

"**Free Drug**" means an amount or concentration of a drug that is not encapsulated or delivered by a drug delivery system.

"**GCP**" means Good Clinical Practices.

"**Health Canada**" means the department of the government of Canada with responsibility for national public health.

"**HF**" means heart failure.

"**HFpEF**" means heart failure with preserved ejection fraction.

"**HTN**" means hypertension.

"**ICFR**" means internal controls over financial reporting.

"**IFRS**" means International Financial Reporting Standards.

"**IND**" means an FDA investigational new drug.

"**IPO**" means the initial public offering of the Corporation.

"**IRB**" means Institutional Review Boards.

"**IT**" means information technology.

"***LANCER***" means the Corporation's Phase II/III, double-blind, placebo-controlled clinical trial evaluating the efficacy and safety of its lead product, CardiolRx, in hospitalized COVID-19 patients with a prior history of, or risk factors for, CVD.

"**Legacy Equity Compensation Plan**" means the stock option plan the Board of Directors has adopted whereby options and shares may be granted to the Corporation's Directors, officers, employees, and consultants. This plan was replaced by the Omnibus Equity Incentive Plan.

"**MAA**" means marketing authorization application.

"**Management**" means the management of the Corporation.

"**May 2021 Underwriters**" has the meaning set out under the heading "Business of Cardiol – Corporate History - Year Ended December 31, 2021".

"May 2021 Warrant Indenture" has the meaning set out under the heading "Capital Structure - Share Purchase Warrants".

"**Meros**" means Meros Polymers Inc.

"**Meros Escrow Shares**" has the meaning set out under the heading "Business of Cardiol - Commercialization Relationships – Meros".

"**Meros License Agreement**" has the meaning set out under the heading "Business of Cardiol - Commercialization Relationships – Meros".

"**Meros Milestone**" has the meaning set out under the heading "Business of Cardiol - Commercialization Relationships – Meros".

"Meros Special Warrants" has the meaning set out under the heading "Business of Cardiol - Commercialization Relationships – Meros".

"nanoparticles" means particles of nano-scale – i.e., <100 nanometres in size.

"**nanotherapeutics**" means therapeutic drugs encapsulated within nanoparticles – i.e., particles that are <100 nanometres in diameter.

"**Nasdaq**" means the Nasdaq Stock Market LLC.

"**NDA**" means a new drug application under the FDA.

"**NDS**" means New Drug Submission.

"**NI 52-110**" means National Instrument 52-110 – Audit Committees.

"**NLC**" has the meaning set out under the heading "Regulatory Overview – Regulatory Framework in Canada for Cannabis – Provincial and Territorial Regulatory Regimes".

"**NOC**" means Notice of Compliance.

"**NON**" means Notice of Noncompliance.

"**Noramco**" means Noramco, Inc.

"**November 2021 Underwriters**" has the meaning set out under the heading "Business of Cardiol – Corporate History - Year Ended December 31, 2021".

"November 2021 Warrant Indenture" has the meaning set out under the heading "Capital Structure - Share Purchase Warrants".

"Omnibus Equity Incentive Plan" means the equity compensation plan the Board of Directors has adopted

whereby options, shares, and other share awards may be granted to the Corporation's Directors, officers, employees, and consultants.

"**Option**" means an option under the Legacy Equity Compensation Plan or Omnibus Equity Incentive Plan.

"**Orphan Indication**" means a disease affecting fewer than 200,000 citizens in the U.S. or 5 per 10,000 citizens in Europe. An orphan-designated therapeutic targeting such an indication benefits from 7 years' market exclusivity in the U.S and 10 years' market exclusivity in the EU.

"**PCL**" means polycaprolactone.

"**PEG**" means polyethylene glycol.

"**pharmacokinetics**" or "**PK**" means the fate of a drug once administered, for e.g., concentration and duration retained in circulation.

"**ppm**" means parts-per-million.

"**Purisys**" means Purisys, LLC.

"**Purisys Exclusive Supply Agreement**" has the meaning set out under the heading "Business of Cardiol - Commercialization Relationships – Purisys".

"**Regulations**" has the meaning ascribed thereto under "Regulatory Overview – Regulatory Framework in Canada for Cannabis".

"**SARS-CoV-2**" means severe acute respiratory syndrome coronavirus 2.

"**Share Awards**" means shares, performance share units, restricted share units, and deferred share units.

"**Shareholder**" means a shareholder of the Corporation.

"**SC**" means subcutaneous.

"**Task Force**" means the Task Force on Cannabis Legalization and regulation.

"**TecSalud**" means TecSalud del Tecnológico de Monterrey, Mexico.

"**THC**" means Tetrahydrocannabinol.

"**TMZ**" means temozolomide.

"**TLR**" means Toll Like Receptor.

"**TSX**" means the Toronto Stock Exchange.

"**U.S.**" means the United States of America.

"**USD**" means U.S. dollars.

"**Warrant Indenture**" has the meaning set out under the heading "Capital Structure - Share Purchase Warrants".

MEANINGS OF CERTAIN REFERENCES

In this annual information form ("Annual Information Form" or "AIF"), references to the "Corporation", "Cardiol", "we", "us" or "its" are references to Cardiol Therapeutics Inc. References to "management" in this AIF mean the persons acting in the capacities of Cardiol's President and Chief Executive Officer, Chief Financial Officer, Chief Operating Officer, and Chief Medical Officer. Any statements in this AIF made by or on behalf of management are made in such persons' capacities as officers of Cardiol and not in their personal capacities.

FORWARD-LOOKING INFORMATION

This AIF contains forward-looking information that relates to the Corporation's current expectations and views of future events. In some cases, this forward-looking information can be identified by words or phrases such as "may", "might", "will", "expect", "anticipate", "estimate", "intend", "plan", "indicate", "seek", "believe", "predict", or "likely", or the negative of these terms, or other similar expressions intended to identify forward-looking information. Statements containing forward-looking information are not historical facts. The Corporation has based this forward-looking information on its current expectations and projections about future events and financial trends that it believes might affect its financial condition, results of operations, business strategy, and financial needs. The forward-looking information includes, among other things, statements relating to:

- our anticipated cash needs, and the need for additional financing;
- our development of oral cannabidiol formulations for commercialization;
- our ability to develop new formulations of cannabidiol, including subcutaneous formulations for commercialization;
- the successful development and commercialization of our current product candidates and the addition of future products;
- the ability for our drug delivery technologies to deliver cannabinoids and other anti-inflammatory drugs to inflamed tissue in the heart;
- our intention to build a pharmaceutical brand and cannabidiol products focused on addressing fibrosis and inflammation in heart disease, with a particular focus on acute myocarditis and chronic heart failure;
- the expected medical benefits, viability, safety, efficacy, and dosing of cannabidiol;
- patents and intellectual property, including, but not limited to, our (a) ability to procure, defend, and/or enforce our intellectual property relating to our drugs, drug formulations, drug candidates, and associated uses, methods, and/or processes, and (b) freedom to operate;
- our competitive position and the regulatory environment in which we operate;
- our financial position; our business strategy; our growth strategies; our operations; our financial results; our dividends policy; our plans and objectives; and
- expectations of future results, performance, achievements, prospects, opportunities, or the market in which we operate.

In addition, any statements that refer to expectations, intentions, projections or other characterizations of future events or circumstances contain forward-looking information. Forward-looking information is based on certain assumptions and analyses made by the Corporation in light of the experience and perception of historical trends, current conditions, and expected future developments and other factors it believes are appropriate and are subject to risks and uncertainties. Although we believe that the assumptions underlying these statements are reasonable, they may prove to be incorrect, and we cannot assure that actual results will be consistent with this forward-looking information. Given these risks, uncertainties, and assumptions, prospective purchasers of Securities should not place undue reliance on this forward-looking information. Whether actual results, performance, or achievements will conform to the Corporation's expectations and predictions is subject to a number of known and unknown risks, uncertainties, assumptions, and other factors, including those listed under "*Risk Factors*", which include:

- the inherent uncertainty of product development;

- our requirement for additional financing;
- our negative cash flow from operations;
- our history of losses;
- dependence on success of our early-stage product candidates which may not generate revenue;
- reliance on management, loss of members of management or other key personnel, or an inability to attract new management team members;
- our ability to successfully design, initiate, and complete clinical trials, including the high cost, uncertainty, and delay of clinical trials and additional costs associated with any failed clinical trials;
- potential negative results from clinical trials and their adverse impacts on our future commercialization efforts;
- our ability to receive and maintain regulatory exclusivities, including Orphan Drug Designations, for our drugs and drug candidates;
- delays in achievement of projected development goals;
- management of additional regulatory burdens;
- volatility in the market price for the Securities;
- failure to protect and maintain and the consequential loss of intellectual property rights;
- third-party claims relating to misappropriation by our employees of their intellectual property;
- reliance on third parties to conduct and monitor our pre-clinical studies and clinical trials;
- our product candidates being subject to controlled substance laws which may vary from jurisdiction to jurisdiction;
- changes in laws, regulations, and guidelines relating to our business, including tax and accounting requirements;
- our reliance on current early-stage research regarding the medical benefits, viability, safety, efficacy, and dosing of cannabinoids;
- claims for personal injury or death arising from the use of products and product candidates produced by us;
- uncertainty relating to market acceptance of our product candidates;
- our lack of experience in commercializing any products;
- the level of pricing and reimbursement for our products and product candidates, if approved;
- our dependence on Dalton and other contract manufacturers;
- unsuccessful collaborations with third parties;
- business disruptions affecting third party suppliers and manufacturers;
- lack of control in future prices of our product candidates;
- our lack of experience in selling, marketing, or distributing our products;
- competition in our industry;
- our inability to develop new technologies and products and the obsolescence of existing technologies and products;
- unfavorable publicity or consumer perception towards cannabidiol;

- product liability claims and product recalls;
- expansion of our business to other jurisdictions;
- fraudulent activities of employees, contractors, and consultants;
- our reliance on key inputs and their related costs;
- difficulty associated with forecasting demand for products;
- operating risk and insurance coverage;
- our inability to manage growth;
- conflicts of interest among our officers and directors;
- managing damage to our reputation and third-party reputational risks;
- relationships with customers and third-party payors and consequential exposure to applicable anti kickback, fraud, and abuse and other healthcare laws;
- exposure to information systems security threats;
- no dividends for the foreseeable future;
- future sales of Common Shares and May 2021 Warrants by existing shareholders causing the market price for the Common Shares and May 2021 Warrants to fall;
- the issuance of Common Shares in the future causing dilution; and
- the impact of the recent novel coronavirus (COVID-19) pandemic on our operations, including clinical trials.

If any of these risks or uncertainties materialize, or if assumptions underlying the forward-looking information prove incorrect, actual results may vary materially from those anticipated in the forward-looking information.

Information contained in forward-looking information in this AIF is provided as of the date of this AIF, and the Corporation disclaims any obligation to update any forward-looking information, whether as a result of new information or future events or results, except to the extent required by applicable securities laws. Accordingly, potential investors should not place undue reliance on forward-looking information.

DATE OF INFORMATION

The information in this AIF is presented as of December 31, 2021, unless otherwise indicated.

PRESENTATION OF FINANCIAL INFORMATION

Unless otherwise indicated, all references to "$" or "dollars" are to Canadian dollars, which is Cardiol's functional currency. The fiscal year end of all entities within the corporate structure of Cardiol is December 31. Cardiol's financial statements are prepared in accordance with International Financial Reporting Standards ("IFRS"). References to H1 refer to the six-month period ending June 30 of the relevant fiscal year, and references to H2 refer to the six-month period ending December 31 of the relevant fiscal year.

THIRD-PARTY INFORMATION

Unless otherwise indicated, information contained in this AIF concerning our industry and the markets in which we operate, including our general expectations and market position, market opportunities and market share, is based on information from independent industry organizations, other third-party sources (including industry publications, surveys, and forecasts), and management studies and estimates.

Unless otherwise indicated, our estimates are derived from publicly available information released by independent industry analysts and third-party sources, as well as data from our internal research, and include assumptions made by us which we believe to be reasonable based on our knowledge of our industry and markets. Although

Cardiol believes these sources to be generally reliable, market and industry data are subject to interpretation and cannot be verified with complete certainty due to limits on the availability and reliability of raw data, the voluntary nature of the data gathering process, and other limitations and uncertainties inherent in any statistical survey. Our internal research and assumptions have not been verified by any independent source, and we have not independently verified any third-party information. While we believe the market position, market opportunity, and market share information included in this AIF are generally reliable, such information is inherently imprecise. In addition, projections, assumptions, and estimates of our future performance and the future performance of the industry and markets in which we operate are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described under the heading “Forward-Looking Statements” and “Risk Factors”.

CORPORATE STRUCTURE

The Corporation was incorporated under the *Business Corporations Act* (Ontario) on January 19, 2017. The Corporation has no subsidiaries.

The head and registered office of the Corporation is located at Suite 602 – 2265 Upper Middle Road East, Oakville, Ontario L6H 0G5, Canada.

On August 14, 2018, the Board of Directors of the Corporation approved an amendment and restatement of By-law No. 1 of the Corporation to: (i) amend the by-law to change the number of shares required to be represented at a meeting from a majority of such shares to twenty-five percent (25%) of such shares (the “By-Law Quorum Amendment”); and (ii) adopt by-laws requiring advance notice of director nominees from Shareholders (the “Advance Notice By-Law Amendment” and, together with the By-Law Quorum Amendment, the “By-Law Amendment”). The purpose of the By-law Quorum Amendment is to ensure that if the Corporation’s shares become widely held, a quorum for meetings of Shareholders will be more easily obtained. The purpose of the Advance Notice By-Law Amendment is to ensure that an orderly nomination process is observed, that Shareholders are well-informed about the identity, intentions, and credentials of director nominees, and that Shareholders vote in an informed manner after having been afforded reasonable time for appropriate deliberation. The By-Law Amendment was confirmed by an ordinary resolution of Shareholders of the Corporation on August 28, 2018.The Articles of the Corporation were amended on February 13, 2017 to provide that its authorized capital consists of an unlimited number of Common Shares and make certain amendments of a “housekeeping” nature. The Articles of the Corporation were amended on August 29, 2018 to remove certain share transfer restrictions and to split each issued and outstanding Common Share into two Common Shares. All current and comparative references to the number of shares have been restated to give effect to the stock split, unless otherwise noted.

See “Capital Structure”.

BUSINESS OF CARDIOL

Corporation’s Overview

The Corporation 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 Corporation’s lead product candidate, CardiolRx, is a pharmaceutically produced oral cannabidiol formulation that is being clinically developed for use in cardiovascular medicine. Extensive pre-clinical investigations in models of CVD have demonstrated anti-fibrotic activity of cannabidiol, as well as anti-inflammatory, anti-ischemic and anti-arrhythmic actions. In experimental models of heart failure and cardiac injury, cannabidiol has also been shown to be cardioprotective by reducing cardiac hypertrophy, fibrosis, and the production markers of cardiac re-modelling.

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. It is now recognized that the impact of SARS-CoV-2 infection that causes COVID-19 is not limited to the pulmonary system. People who have had COVID-19 have an increased risk and burden for adverse cardiovascular outcomes (such as acute myocardial infarction, dysrhythmias, pulmonary

embolism, pericarditis, myocarditis, stroke, and heart failure) up to one year following their COVID-19 diagnosis.

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. This disease remains an important cause of acute and fulminant heart failure and is 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.

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. Heart failure affects 26 million people in the developed world and remains a leading cause of death and hospitalization, with associated annual healthcare costs in the U.S. alone exceeding $30 billion[1].

Corporate History

For over 25 years, the Founders – David Elsley, Dr. Eldon Smith, and Dr. Anthony Bolton – have had an active interest in the role that inflammation plays in a number of serious medical conditions, including heart failure. Prior to the formation of Cardiol, the Founders pursued scientific and clinical research in this area and were successful in securing funding to support the development of a novel therapeutic from concept through to completion of Phase III multi-center and multi-national clinical trials. Based on an extensive review of the scientific literature conducted in late 2014, the Founders identified cannabidiol as a molecule of interest to investigate in heart failure pathology due to its anti-inflammatory, anti-fibrotic, and cardioprotective properties.

Cardiol was incorporated on January 19, 2017 and in June 2017, the Corporation entered into an exclusive manufacturing supply agreement with Dalton to support the Corporation's research programs. Dalton is a Health Canada approved and FDA registered cGMP manufacturer of over 200 Active Pharmaceutical Ingredients (APIs), including pharmaceutical cannabinoids, with manufacturing capability scalable to support all stages of the regulatory process (Phase I, II, III or commercial). During August and September 2018, the Corporation initiated a comprehensive USD $3 million research and development collaboration with TecSalud and Nano4heart, both of the Instituto Tecnológico y de Estudios Superiores de Monterrey, Mexico, combining the significant research capability of TecSalud, with the nanotechnology expertise of Nano4heart and the research and clinical development expertise of Cardiol, for the purpose of working towards a common goal of advancing the treatment of heart failure.

Following is a description of Cardiol's development over its last three completed financial years.

Year Ended December 31, 2019

In January 2019, the remaining outstanding 8% Convertible Debenture, with a face value of $400,000, was converted into 2,700,000 Common Shares.

In January 2019, the Corporation granted 150,000 stock options to a certain officer of the Corporation. Each stock option allows the holder to acquire one Common Shares at an exercise price of $4.30 and expires on January 2, 2026. The options vested on grant.

In January 2019, the Corporation granted 285,000 stock options to certain employees and consultants of the Corporation. Each stock option allows the holder to acquire one Common Shares at an exercise price of $5.34: 125,000 stock options vest 25% every three months from the grant date and expire July 24, 2020. 100,000 stock

1 Cook, C., Cole, G., Asaria, P., Jabbour, R. & Francis, D.P. The annual global economic burden of heart failure. International Journal of Cardiology 171, 368-376 (2014)

options vest 25% every three months from the grant date and expire January 24, 2024. 60,000 stock options vest 1/3 each on the first, second, and third anniversaries of the grant date and expire January 24, 2026.

In January 2019, an additional 374,544 Common Shares at $4.62 per share for gross proceeds of $1,730,393 were granted under the Over-Allotment Option. As a result, an additional 22,472 Compensation Warrants were issued.

In March 2019, the Corporation announced the appointment of Thomas (Tom) Moffatt, BBA, as Chief Commercial Officer.

In March 2019, the Corporation cancelled 40,000 stock options exercisable at $5.00 and originally set to expire August 30, 2025.

In April 2019, the Corporation granted 140,000 stock options to certain officers and consultants of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $5.77 and expires on April 1, 2026. The options vest 1/3 each on the first, second, and third anniversaries of the grant date.

In April 2019, the Corporation granted 60,000 stock options to a certain officer of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $5.42 and expires on April 4, 2026. The options vest 1/3 each on the first, second, and third anniversaries of the grant date.

In June 2019, the Corporation announced it is planning a clinical trial in acute myocarditis utilizing its CardiolRx CBD formulation. See “Business of Cardiol – Overview of Business – Phase II study – Acute myocarditis”.

In October 2019, the Corporation completed the manufacturing scale-up for commercialization of its CBD formulation.

In October 2019, the Corporation granted 160,000 stock options to certain employees of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $3.23 and expires on October 15, 2024. The options vest 1/3 each on the first, second and third anniversaries of the grant date.

In October 2019, the Corporation granted 90,000 stock options to certain consultants of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $3.28 and expires on October 29, 2021. The options vest 25% every three months from the grant date.

In November 2019, the Corporation granted 50,000 stock options to a consultant of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $3.34 and expires on November 24, 2021. The options vest 50% immediately and 50% six months from the grant date.

In December 2019, the Corporation announced the appointment of Mr. Colin Stott to its Board of Directors. Mr. Terry Lynch stepped down from the Board of Directors to accommodate Mr. Stott’s appointment.

In December 2019, the Corporation granted 60,000 stock options to a director of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $4.08 and expires on December 2, 2024. The options vest 1/3 each on the first, second, and third anniversaries of the grant date.

In December 2019, the Corporation announced it had appointed Michael J. Willner, Esq. as a Business Advisor to the Corporation.

In December 2019, the Corporation granted 60,000 stock options to a consultant of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $3.69 and expires on December 5, 2024. The options vest 25% every six months from the grant date.

In December 2019, the Corporation's exclusive manufacturing partner, Dalton, received a three-year renewal and license amendment of its Cannabis Act Processing License from Health Canada. The renewal and amendment permit scaled commercial production of Cardiol's high concentration pharmaceutical cannabidiol formulations and their sale to other license holders.

Year Ended December 31, 2020

In February 2020, the Corporation granted 109,300 stock options to certain employees and consultants of the Corporation. Each stock option allows the holder to acquire one Common Share of the Corporation at an exercise price of $3.54 and expires on February 23, 2025. The options vest 50% on grant and 50% twelve months from the grant date.

In March 2020, the Corporation announced it received a No Objection Letter from Health Canada to conduct a Phase I study of the Corporation's pharmaceutically produced high concentration, pure cannabidiol formulation.

In March 2020, the Corporation announced that it signed a supplier agreement to become a medical cannabidiol supplier to *Shoppers Drug Mart Inc.* ("Shoppers").

In April 2020, the Corporation announced that data submitted by its international research collaborators were accepted for presentation at the ACC's 69th Annual Scientific Session & Expo together with the World Congress of Cardiology, held virtually from March 28 – 30.

The effects of Cardiol's pharmaceutically produced cannabidiol formulation were assessed in a model of non-ischemic heart failure. Heart failure was induced by four weeks of infusion of angiotensin II, a substance that produces hypertension, cardiac enlargement, and subsequent heart failure. Two dosages of Cardiol's cannabidiol formulation (or placebo) were administered by subcutaneous injection every three days for four weeks. In addition, the effects of CBD on angiotensin-induced hypertrophy (cell enlargement) and expression of BNP in a cardiac cell line (H9c2) were assessed. BNP is a substance released from stretched heart cells which is a widely used clinical indicator of the severity of heart failure.

The study found that Cardiol's cannabidiol formulation significantly reduced hypertrophy and produced a dose-dependent reduction of key inflammation markers, decreases in fibrosis, and lower BNP expression. These findings confirm the anti-inflammatory and anti-fibrotic activity of Cardiol's cannabidiol formulation in a model of heart failure. Moreover, the data show that cannabidiol reduced the amount of BNP released, thereby confirming the role of Cardiol's cannabidiol formulation as a cardioprotective therapy.

In April 2020, the Corporation announced that data describing Cardiol's nanotechnology approach to drug delivery were submitted by the Corporation's international research collaborators and accepted for presentation at the ACC's 69th Annual Scientific Session & Expo together with the World Congress of Cardiology, held virtually from March 28 – 30.

Results from this study, conducted at the Houston Methodist DeBakey Heart & Vascular Center, showed that there was a greater than 100-fold increase in uptake of Cardiol's nanoparticles in heart failure hearts compared with control hearts in a pre-clinical model of non-ischemic heart failure. The nanoparticles localized within the diseased hearts, predominantly in areas of fibrosis. Fibrosis is an important component of the pathology of heart failure and is primarily responsible for the stiffening and reduced function of the heart muscle. Moreover, the nanoparticles accumulated within the cytoplasm of the cultured fibroblasts. This evidence of Cardiol's nanoparticles preferentially accumulating intracellularly in fibroblasts shows potential for the successful delivery of anti-fibrotic drugs, such as cannabidiol, to the diseased region of the heart.

Cardiol's proprietary nanotechnology is designed to enable the distribution of water insoluble drugs within the blood (aqueous) circulation, improve pharmacokinetics, and facilitate drug accumulation in the failing heart. Cardiol's nanoparticles are based on a patented family of biocompatible and biodegradable amphiphilic block co-polymers made from PEG and PCL. Both PEG and PCL have a long history of safe use in humans.

In May 2020, the Corporation announced the filing of a new patent application covering the use of CBD to improve the outcome of patients with COVID-19.

In June 2020, the Corporation announced the completion of its short form prospectus offering by issuing 6,900,000 Common Share units at $2.50 per unit for gross proceeds of $17,250,000. Each unit consisted of one Common Share and one-half of one Common Share purchase warrant. Each whole warrant was exercisable into one Common Share at the price of $3.25 per share for a period of two years from closing, subject to accelerated expiry if, at any time, the volume weighted average trading price of the Common Shares is equal to or greater than $4.50 for any ten consecutive trading day period see “Corporate History – Year Ended December 31, 2021”.

The offering was conducted through a syndicate of underwriters (the "2020 Underwriters"). The 2020 Underwriters were paid cash fees of $735,000 and 294,000 compensation warrants (the “2020 Compensation Warrants”). Each 2020 Compensation Warrant entitles the holder to acquire one Common Share unit at a price of $2.50 for a period of 24 months from the date of closing.

In June 2020, the Corporation announced that it appointed Steven Grasso as Business Advisor to the Corporation.

In October 2020, Cardiol announced the commercial introduction of Cortalex.

In December 2020, Cardiol announced the appointment of CRO Worldwide Clinical Trials (“Worldwide”) for its Phase II/III trial in high-risk patients hospitalized with COVID-19. The double-blind, placebo-controlled clinical trial is designed to evaluate the efficacy and safety of CardiolRx 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 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.

In December 2020, the Corporation announced the completion of the Phase I clinical study of CardiolRx. Cardiol’s Phase I double-blind, placebo-controlled, randomized study was designed to assess safety, tolerability, and pharmacokinetics of single, followed by multiple day ascending doses of CardiolRx administered orally to 52 healthy adult subjects, both in the fasting and fed states. The therapy was shown to be generally well tolerated with no serious adverse events reported in the study and 51 subjects completed all requirements of the study protocol. By measuring standard safety parameters and the pharmacokinetics of CardiolRx, including the degree of drug absorption and resulting blood levels at escalating doses, the Phase I study will provide important information to optimize dosing levels.

Year Ended December 31, 2021

In January 2021, the Corporation announced the formation of the DSMC and the CEC for the Corporation’s Phase II/III trial in high-risk patients hospitalized with COVID-19 (See below – “*Phase II/III trial in high-risk patients hospitalized with COVID-19”).*

In February 2021, the Corporation granted 1,146,666 stock options to certain consultants of the Corporation. Each option allows the holder to acquire one common share of the Corporation at an exercise price ranging from $3.16 to $4.80 and expires between January 31, 2023 and February 22, 2023. 696,666 of the options vest immediately, while the remainder vest 25% per quarter from the grant date.

In February 2021, the Corporation received proceeds of $7,879,820 on the exercise of 2,424,560 warrants with an exercise price of $3.25, and $503,068 on the exercise of 201,227 warrants with an exercise price of $2.50. In addition, there were a total of 916,666 stock option exercises, resulting in cumulative proceeds of $2,604,648.

In March 2021, the Corporation announced that it had submitted an application to list the Corporation's common shares on the Nasdaq.

In March 2021, the Corporation announced that Dr. Andrew Hamer joined the Corporation as Chief Medical Officer ("CMO"). Dr. Hamer leads the research and development of the Corporation's clinical-stage products and also guides the development of additional novel therapeutics in the Corporation's pipeline.

Dr. Andrew Hamer brings 30 years of experience in the global life sciences industry, medical affairs, and cardiology practice to the Corporation. Most recently he served as Executive Director, Global Development-Cardiometabolic at California-based Amgen Inc., where he led the Global Development group for Repatha®, the LDL cholesterol lowering PCSK9 inhibitor evolocumab, which generated revenues of almost USD $900 million in 2020. As development lead, Dr. Hamer headed the Repatha® global evidence generation team collaborating with safety, regulatory, health economics, observational research, scientific communications, publications, medical affairs, and clinical operations teams to design and execute several multi-center clinical trials in support of FDA and international regulatory filings. Prior to his five-year tenure with Amgen, Dr. Hamer served for two years as VP Medical Affairs at Capricor Therapeutics Inc., where he was responsible for the development of novel therapeutics for heart disease and for the supervision of the clinical operations of the company, including clinical trial design and execution.

Prior to joining the life sciences industry, Dr. Hamer practiced cardiology and internal medicine in New Zealand for 19 years. His distinguished career in cardiology culminated as Chief Cardiologist at Nelson Hospital, Nelson Marlborough District Health Board, Nelson, while concurrently leading cardiac services nationally in New Zealand. Dr. Hamer graduated with a medical degree (MB, ChB) from the University of Otago, New Zealand, an internationally recognized medical school which recently ranked among the top twenty universities in the world in several medical subject categories. His clinical research training took place at various centres in New Zealand and London, UK, followed by a cardiology fellowship at Deaconess Hospital, Harvard Medical School, Boston. Dr. Hamer has co-authored many high-quality peer-reviewed scientific publications reflecting his considerable experience as a clinical trialist, having served as a principal or co-investigator for 40 multi-centre clinical trials in therapies for acute coronary syndrome, heart failure, hypertension, cholesterol disorders, atrial fibrillation, and diabetes.

In May 2021, the Corporation completed a short form base shelf prospectus offering of units of the Corporation for aggregate gross proceeds of $22,003,200. Under the offering, the Corporation sold a total of 6,112,000 units at a price of $3.60. Each unit is comprised of one common share of the Corporation and one-half purchase warrant of the Corporation (the "May 2021 Warrants"). Each full warrant entitles the holder thereof to acquire one common share at a price of $4.60 for a period of 36 months from issuance. The warrants are listed for trading on the TSX under the symbol "CRDL.WT.A".

The Offering was conducted through a syndicate of underwriters (the "May 2021 Underwriters"). The May 2021 Underwriters were paid cash fees of $1,025,590. Concurrent with the closing, the May 2021 Underwriters purchased an additional 433,400 warrants for gross proceeds $8,668, pursuant to the over-allotment option.

In June 2021, the Corporation adopted an Omnibus Equity Incentive Plan which permits the grant or issuance of stock options, Restricted Share Units, Performance Share Units, and Deferred Share Units, as well as other share-based awards to participants.

In July 2021, the Corporation announced that its Board of Directors appointed Dr. Guillermo Torre-Amione as the new Chairman. Dr. Torre-Amione has been an independent director of Cardiol since August 2018 and has taken over from Dr. Eldon Smith, the founding Chairman of Cardiol and who has now retired from the Board.

In August 2021, the Corporation's common shares commenced trading on the Nasdaq under the symbol "CRDL". Concurrent with the listing on the Nasdaq, the common shares ceased to be quoted on the OTCQX.

In August 2021, the Corporation announced that the FDA provided clearance to proceed with the Corporation's IND application to commence a Phase II, multi-center, 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.

In September 2021, the Corporation announced the appointment of Michael J. Willner, Esq. to its Board of Directors.

Michael J. Willner has practiced as both an Attorney and a Certified Public Accountant. He graduated from Emory University Law School as a member of the Emory Law Review. Subsequently, he practiced real estate and corporate law with New York City-based Milbank, Tweed, Hadley & McCloy, one of the nation's most prominent international law firms. Prior to his legal career, Mr. Willner was employed by the former Arthur Andersen & Company, a national accounting firm, where he practiced in Arthur Andersen's tax department.

Mr. Willner has been a very active and successful opportunistic investor for over forty years and is the founder of Willner Capital, Inc., an investment company specializing in public and private equities, as well as debt instruments. Willner Capital primarily uses fundamental analysis as an evaluation method and event-driven strategies. Over the past ten years, Willner Capital has made significant investments in both the biotechnology and pharmaceutical cannabinoid industries, focusing primarily on clinical-stage companies that seek to address significant unmet medical needs. Mr. Willner has been quoted in the New York Times business section and has served as a moderator and participant on numerous panel discussions and advisory boards regarding his investments in the pharmaceutical side of the cannabinoid industry.

In September 2021, the Corporation announced the acceleration of the expiry date of all outstanding common share purchase warrants of the Corporation that were issued on June 4, 2020, to October 12, 2021, from the original expiry date of June 4, 2022.

In October 2021, the Corporation announced that it is expanding its *LANCER* trial to include several hospital centers in Brazil and Mexico.

In October 2021, the Corporation announced that it is received approval from Health Canada to proceed with the Corporation's Phase II, multi-center, 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.

In November 2021, the Corporation granted 1,200,000 performance share units to certain consultants. Each performance share unit allows the holder to acquire one common share. Vesting of the performance share units is based on specific performance metrics that must be achieved prior to the expiry date of June 30, 2022 (see "Corporate History – Subsequent to Year Ended December 31, 2021").

In November 2021, the Corporation completed a short form base shelf prospectus offering of units of the Corporation for aggregate gross proceeds of USD$50,194,500. Under the offering, the Corporation sold a total of 16,350,000 units at a price of USD$3.07. Each unit is comprised of one common share of the Corporation and one-half purchase warrant of the Corporation (the "November 2021 Warrants"). Each full warrant entitles the holder thereof to acquire one common share at a price of USD$3.75 for a period of 36 months from issuance.

The Offering was conducted through a syndicate of underwriters (the "November 2021 Underwriters"). The November 2021 Underwriters were paid cash fees of USD$3,011,670.

Subsequent to Year Ended December 31, 2021

Subsequent to December 31, 2021, the Corporation granted 220,000 stock options to certain consultants of the Corporation. Each option allows the holder to acquire one common share of the Corporation at an exercise price of $2.18 and expires on January 11, 2027. These options vest 1/3 on each anniversary date.

Subsequent to December 31, 2021, the Corporation announced the appointment of the Scientific Advisory Board ("SAB"). For biographies of members, see "Scientific Advisory Board".

Subsequent to December 31, 2021, the Corporation extended the life of 1,200,000 performance share units issued in November 2021 to expire on June 30, 2022.

Subsequent to December 31, 2021, the Corporation announced the appointment of Jennifer M. Chao to its Board of Directors. Ms. Chao has also been appointed Chair of the Corporate Governance and Compensation Committee. Iain Chalmers has stepped down from the Board of Directors to accommodate Ms. Chao's appointment.

Phase II/III study – COVID-19 (*LANCER)*

In September 2020, the FDA issued clearance for the Corporation's Investigational New Drug application to commence a Phase II/III, double-blind, placebo-controlled clinical trial investigating the efficacy and safety of CardiolRx, an oral cannabidiol formulation that is pharmaceutically manufactured under cGMP, in 422 hospitalized COVID-19 patients with a prior history of, or risk factors for CVD.

In December 2020, Cardiol announced the appointment of contract research organization (the "CRO"), Worldwide Clinical Trials ("Worldwide"), for its Phase II/III trial in high-risk patients hospitalized with COVID-19. Worldwide has been the CRO for multiple international COVID-19 clinical programs and has extensive experience in conducting clinical research focused on cardiovascular disease. With a global footprint, Worldwide provides 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.

Cardiol's Phase II/III trial has been designed to evaluate the efficacy and safety, of CardiolRx as a cardioprotective therapy to reduce major cardiovascular and respiratory events in patients hospitalized within the previous 48 hours, with a confirmed diagnosis of COVID-19, and who have pre-existing CVD and/or significant risk factors for CVD, and to investigate the influence CardiolRx has on key biomarkers associated with heart disease. 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 twenty-eight days following randomization and first dose of study medication, one or more of several common outcomes in this patient population, including all-cause mortality, requirement for ICU admission and/or ventilatory support, as well as cardiovascular complications, including the development of heart failure, acute myocardial infarction, myocarditis, stroke, or new sustained or symptomatic arrhythmia.

Patients with COVID-19 primarily present with respiratory symptoms which can progress to bilateral pneumonia and serious pulmonary complications. It is now recognized that the impact of COVID-19 is not limited to the pulmonary system. Individuals with pre-existing CVD or who have risk factors for CVD (such as diabetes, hypertension, obesity, abnormal serum lipids, or age greater than 64) are at significantly greater risk of developing serious disease from COVID-19 and experience greater morbidity. Moreover, such COVID-19 patients are at significant risk of developing cardiovascular complications (such as acute myocardial infarction, cardiac arrhythmias, myocarditis, stroke, and heart failure) during the course of their illness. Cardiol believes a therapeutic strategy that limits the number or severity of both pulmonary and cardiovascular complications will improve the socioeconomic burden of this disease.

In March 2022, the Corporation announced it received clearance from the FDA and regulatory agencies in Brazil and Mexico to modify the inclusion criteria for the *LANCER* trial to allow the eligible patient pool to include the following: (i) vaccinated patients; (ii) use of therapies approved for treatment of COVID-19 under emergency use authorization label; and (iii) a prior history of smoking or obesity, both CVD risk factors prevalent in younger patients. Corporation also announced plans to expand the clinical trial infrastructure to include up to an additional 20 clinical research centers.

The rationale for using cannabidiol to treat patients with COVID-19 is based on pre-clinical investigations conducted by Cardiol and others in models of cardiovascular disease which have demonstrated anti-fibrotic

activity of cannabidiol, as well as anti-inflammatory, anti-ischemic and anti-arrhythmic actions. In experimental models of heart failure and cardiac injury, cannabidiol has also been shown to be cardioprotective by reducing cardiac hypertrophy, fibrosis, and the production markers of cardiac re-modelling.

The *LANCER* study was designed and will be overseen by an independent Steering Committee, consisting of international thought leaders in cardiovascular disease. Members of the Steering Committee include:

Dennis M. McNamara, MD (Chair)

Dr. Dennis McNamara is a Professor of Medicine at the University of Pittsburgh. He is also the Director of the Center for Heart Failure Research at the University of Pittsburgh Medical Center. Dr. McNamara received his undergraduate/graduate education at Yale University, New Haven, Connecticut, and Harvard Medical School, Boston, Massachusetts, respectively. He completed his internship, residency, and cardiology fellowship at Massachusetts General Hospital in Boston. McNamara's current research interests include etiology and pathogenesis of dilated cardiomyopathies; inflammatory syndromes of cardiovascular disease; myocardial recovery in recent onset non- ischemic primary cardiomyopathy; etiology and management of peripartum cardiomyopathy; and genetic modulation of outcomes in cardiovascular disease.

Leslie T. Cooper, Jr., MD (Co-Chair)

Dr. Leslie T. Cooper, Jr., is a general cardiologist and the chair of the Mayo Clinic Enterprise Department of Cardiovascular Medicine, as well as chair of the Department of Cardiovascular Medicine at the Mayo Clinic in Florida. Dr. Cooper's clinical interests and research focus on clinical and translational studies of rare and undiagnosed cardiomyopathies, myocarditis, and inflammatory cardiac and vascular diseases, such as giant cell myocarditis, cardiac sarcoidosis, eosinophilic myocarditis, and Takayasu's arteritis. He has published over 130 original peer- reviewed papers, as well as contributing to and editing books on myocarditis. In addition to his clinical and research work, Dr. Cooper is a fellow of the American College of Cardiology, the American Heart Association, the European Society of Cardiology Heart Failure Association, the International Society for Heart and Lung Transplantation, and the Society for Vascular Medicine and Biology. He is also the founder and former president of the Myocarditis Foundation and continues to serve on its Board of Directors.

Arvind Bhimaraj, MD

Dr. Arvind Bhimaraj is a specialist in Heart Failure and Transplantation Cardiology and is Assistant Professor of Cardiology, Institute for Academic Medicine, at Houston Methodist and at Weill Cornell Medical College, NYC. He has been Co-Director of the Heart Failure Research Laboratory at Houston Methodist since 2016. His area of focus is anti- fibrotic mechanisms and how to promote recovery of a damaged heart. Dr. Bhimaraj was a Heart Failure Fellow at the Cleveland Clinic from July 2010 to September 2011. Dr. Bhimaraj also specializes in Interventional Cardiology, is board certified in cardiovascular disease, and the author of numerous cardiovascular publications.

Barry Trachtenberg, MD

Dr. Barry H. Trachtenberg is a cardiologist specializing in heart failure and cardiac transplantation. He is also the director of the Michael DeBakey Cardiology Associates Cardio-Oncology program, an evolving field devoted to prevention and management of cardiovascular complications of cancer therapies such as chemotherapy and radiation. His clinical experience includes heart failure and heart transplantation, mechanical support pumps, and cardio- oncology. He has contributed to multiple publications related to advanced heart failure, cardiac transplantation, regenerative therapies, and ventricular assist devices. Dr. Trachtenberg is a member of the American Heart Association, the International Society for Heart and Lung Transplantation, the Heart Failure Society of America, and the International CardiOncology Society of North America.

Wai Hong Wilson Tang, MD

Dr. Wai Hong Wilson Tang is the Advanced Heart Failure and Transplant Cardiology specialist at the Cleveland

Clinic in Cleveland, Ohio. Dr. Tang is also the Director of the Cleveland Clinic's Center for Clinical Genomics; Research Director, and staff cardiologist in the Section of Heart Failure and Cardiac Transplantation Medicine in the Sydell and Arnold Miller Family Heart & Vascular Institute at the Cleveland Clinic. He attended and graduated from Harvard Medical School in 1996, having over 23 years of diverse experience, especially in Advanced Heart Failure and Transplant Cardiology. Dr. Tang is affiliated with many hospitals including the Cleveland Clinic and cooperates with other doctors and physicians in medical groups including The Cleveland Clinic Foundation.

Peter Liu, MD

Dr. Peter Liu is the Chief Scientific Officer and Vice President, Research, of the University of Ottawa Heart Institute, and Professor of Medicine and Physiology at the University of Toronto and University of Ottawa. He was the former Scientific Director of the Institute of Circulatory and Respiratory Health at the Canadian Institutes of Health Research, the major federal funding agency for health research in Canada. Prior to that role, he was the inaugural Director of the Heart & Stroke/Lewar Centre of Excellence in Cardiovascular Research at University of Toronto. Dr. Liu received his MD from the University of Toronto, and postgraduate training at Harvard University. His laboratory investigates the causes and treatments of heart failure, the role of inflammation, and the identification of novel biomarkers and interventions in cardiovascular disease. Dr. Liu has published over 300 peer-reviewed articles in high impact journals and received numerous awards in recognition of his research and scientific accomplishments.

Carsten Tschöpe, MD

Dr. Carsten Tschöpe is Professor of Medicine and Cardiology. Vice Director of the Department of Internal Medicine and Cardiology, Charité Hospital, Freie Universität Berlin. He received his doctorate in medicine in 1993 and has over 140 peer - reviewed publications, including overview and book articles, and 120 international original articles. His research interests include inflammatory cardiomyopathy, diabetic cardiopathy, and ischemic cardiopathy. He also includes diastolic dysfunction, endothelial dysfunction, peptide systems, and experimental and clinical studies in cardiology and stem cells in his research studies. For his outstanding research work, Dr. Tschöpe was awarded the prestigious Arthur Weber Prize by the German Cardiac Society – Cardiovascular Research.

Matthias Friedrich, MD

Dr. Matthias Friedrich is Full Professor with the Departments of Medicine and Diagnostic Radiology at the McGill University in Montreal and Chief, Cardiovascular Imaging at the McGill University Health Centre. He is also Professor of Medicine at Heidelberg University in Germany. Dr. Friedrich earned his MD at the Friedrich-Alexander-University Erlangen-Nürnberg, Germany. He completed his training as an internist and cardiologist at the Charité University Medicine Center, Humboldt University in Berlin. Dr. Friedrich founded one of the first large Cardiovascular Magnetic Resonance centers in Germany at the Charité Hospital in Berlin. After his move to Canada, from 2004 to 2011, he was Director of the Stephenson Cardiovascular MR Centre at the Libin Cardiovascular Institute of Alberta and Professor of Medicine within the Departments of Cardiac Sciences and Radiology at the University of Calgary, Canada. From 2011 to 2015, he directed the Philippa and Marvin Carsley Cardiovascular MR Centre at the Montreal Heart Institute and was Michel and Renata Hornstein Chair in Cardiac Imaging at the Université de Montréal.

Guilherme Oliveira, MD, MBA

Dr. Guilherme Oliveira is a Professor of Medicine and Chairman of Cardiovascular Sciences at the University of South Florida Health Morsani College of Medicine. He is also the Executive Director of the Tampa General Hospital Heart and Vascular Institute, located in Tampa, Florida. Dr. Oliveira received his Doctor of Medicine from Universidade Federal do Rio De Janeiro, Rio De Janeiro, Brazil and completed the Internal Medicine Residency Program at the Mayo Graduate School, Rochester, Minnesota. He served a Fellowship at the Baylor College of Medicine, Houston, Texas, and earned an MBA at the Massachusetts Institute of Technology, Cambridge, Massachusetts. Dr. Oliveira's areas of expertise include advanced heart failure; left ventricular assist devices; onco-cardiology; heart transplantation; and mechanical circulatory support. For his outstanding work, Dr. Oliveira was granted admission into the Fellowship of the American College of Cardiology.

Paolo Caramori, MD, PhD, FSCAI

Dr. Paolo Caramori is currently head of the Division of Cardiovascular Medicine and the Center for Diagnosis and Interventional Treatment at Hospital São Lucas at PUCRS and coordinator of Cardiarte. He also works at Hospital Mãe de Deus and Hospital Moinhos de Vento, in Porto Alegre (RS). He has intense scientific activity, publishing several articles that, to date, have received more than 3,100 international citations. He has supervised nine doctoral theses and 12 master's dissertations. Dr. Caramori graduated in Medicine from the Federal University of Rio Grande do Sul (UFRGS) in 1988. He completed his residency in Internal Medicine and then in Cardiology at Hospital de Clínicas de Porto Alegre, linked to UFRGS, from 1989 to 1992. He obtained his Master's degree in Cardiology from UFRGS in 1995. Afterwards, he resided for three years in Toronto (Canada), where he held a Clinical Fellowship in Interventional Cardiology at the Toronto General Hospital, at the University of Toronto. In 1999, he received the title of Doctor of Cardiology and Cardiovascular Sciences.

In January 2021, the Corporation announced the formation of the Data Safety Monitoring Committee (the "DSMC") and the Clinical Endpoint Committee (the "CEC"). The DSMC comprises independent experts who will assess the patient safety data, and, if needed, critical efficacy endpoints of the trial. In order to do so, the DSMC may review unblinded study information (on a patient level or treatment group level) during the conduct of the trial. After each data review, the DSMC will advise the study Steering Committee with recommendations for protocol modifications, if concerns over safety have developed, or that the study should continue according to the protocol if no concerns are identified. The DSMC will also perform an interim analysis after 200 patients have completed the study, to be certain that the investigational drug is not exposing trial patients to undo risk. Study management will also perform a blinded analysis at this time to determine if the expected number of endpoints have occurred or if the sample size for the study needs to be adjusted so that enough patients will be enrolled to achieve statistical significance.

The DSMC currently consists of three members:

- **Chair: Dr. Jean Lucien Rouleau** – Professor and Former Dean, University of Montreal and Cardiologist, Montreal Heart Institute. Dr. Rouleau has an international reputation in cardiovascular research, particularly in basic mechanisms and improving the clinical care of patients with heart failure. His publication list includes more than 475 articles and seven book chapters;
- **Statistician: Dr. George Wells** – Professor, School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa and Director, Cardiovascular Research Methods Centre, University of Ottawa Heart Institute. Dr. Wells has worked extensively with governments and non-government research organizations, as well asprivate pharmaceutical and biotechnology companies. He has been an Investigator in over 240 research projects with research funding exceeding $120 million. Dr. Wells is the author or co-author of over 400 published articles; and
- **Dr. John Teerlink** – Professor of Medicine, University of California, San Francisco and Director of Heart Failure and the Echocardiographic Laboratory at the San Francisco Veterans Affairs Center. Dr. Teerlink is actively involved in many acute and chronic heart failure clinical trials, serving on endpoint, data safety monitoring and steering committees for numerous international cardiovascular studies. He currently serves on the Acute Heart Failure Committee of the European Society of Cardiology Heart Failure Association and has served on theNational Committee on Heart Failure and Transplantation of the American Heart Association. Dr. Teerlink was profiled in *The Lancet* as an internationally recognized leader in heart failure.

The CEC comprises clinical experts in cardiology and Intensive Care and has been established to ensure accurate and consistent assessment of the trial endpoints and/or serious adverse events. In order to ensure an unbiased endpoint assessment, members of the CEC are blinded to treatment assignment. The goal of the CEC is to standardize endpoints and optimize data quality.

The CEC currently consists of three members:

- **Chair: Dr. Brent Mitchell** – Professor of Cardiac Sciences and Former Director of the Libin Cardiovascular Institute, University of Calgary. Dr. Mitchell completed a Fellowship in Clinical Cardiology at Dalhousie University inHalifax, and a Fellowship in clinical electrophysiology at Stanford University Medical Centre, California. Dr. Mitchell's clinical practice and research interests are in the area of cardiac electrophysiology, particularly in the diagnosis and management of tachyarrhythmias. Dr. Mitchell has published several sentinel papers in the diagnosis and management of serious cardiac arrhythmias;
- **Dr. Maria Rosa Costanzo** – Professor, Rush Medical College and Cardiologist, Advocate Health, Naperville, IL. Dr. Costanzo is Board Certified in Advanced Heart Failure and Cardiac Transplantation. Dr. Costanzo is currently the Medical Director of the Midwest Heart Specialists – Advocate Medical Group Heart Failure and Pulmonary Arterial Hypertension Programs, and Medical Director of the Edward Hospital Center for Advanced Heart Failure. Dr. Costanzo has published nearly 200 peer-reviewed manuscripts and is the author of numerous review papers, monographs, and book chapters; and
- **Dr. Courtney Bennett** – Cardiologist and Intensive Care Physician, Director of Quality Improvement in the Cardiac Intensive Care Unit, Mayo Clinic, Rochester, MN. Dr. Bennett is a board-certified cardiologist and is board-eligiblein critical care medicine. Her clinical interests include cardiac critical care and contrast echocardiography. Dr. Bennett is Mayo Quality Academy gold-certified and serves as the Director of Quality Improvement in the Cardiac Intensive Care Unit.

In April 2021, Cardiol announced first patient enrolled in the Phase II/III study. Subject to how the pandemic evolves, the Corporation expects to complete patient enrollment during H2, 2022. Top-line data from the study is expected during H1, 2023. Cardiol has budgeted additional costs of approximately USD $11.3 million for study execution and $1.3 million for potential post study analysis.

Subject to study outcomes, management intends to review the findings from the *LANCER* study with the FDA to determine what additional studies may be required to support an NDA for CardiolRx. Cardiol may also review study outcomes with prospective development and commercialization partners from the pharmaceutical industry.

Phase I study

In April 2021, the Corporation announced results from a Phase I single and multiple ascending dose clinical trial of CardiolRx.

The Phase I trial was a randomized, placebo-controlled, double-blind study designed to evaluate the safety, tolerability, and pharmacokinetic (PK) profile of CardiolRx at various dose levels. The study randomized 52 subjects (age range 25 to 60 years) to one of two groups. In Group A, there were three sub-groups, each involving 12 subjects (nine active and three placebo), with each subject receiving a single dose of 5 mg/kg or 15 mg/kg of CardiolRx, in either the fed or fasted state. In Group B, there were two sub-groups, each involving eight subjects (six active and two placebo) with each subject receiving 5 mg/kg or 15 mg/kg twice daily for six days. Serial blood samples were taken to measure the level of cannabidiol and its two main metabolites.

Results indicated that CardiolRx was safe and generally well tolerated at all dose levels, with no serious adverse events reported in the study. Fifty-one of the 52 enrolled subjects completed all requirements of the protocol. Each subject had repeated standard measures of safety including physical examination (with vital signs), electrocardiogram (ECG) to monitor cardiac time intervals (particularly, the QTc interval, which is an important measure of the risk for abnormal heart rhythms), as well as biochemical and coagulation laboratory tests. Despite the relatively high doses of CardiolRx administered during the study, there were no ECG or abnormal laboratory findings after six days of dosing and no elevation of liver enzymes or QTc changes were detected. The recorded adverse events were all mild or moderate in severity and were primarily related to the gastro-intestinal tract.

The results of the study formed an integral part of the Corporation's IND application with the FDA for an international Phase II clinical trial in acute myocarditis.

Phase II study – Acute myocarditis

In August 2021, Cardiol received clearance from the FDA for its IND application for a Phase II clinical trial of

CardiolRx in acute myocarditis. Cardiol's acute myocarditis program has been designed by an independent Steering Committee comprised of thought leaders in cardiology from North America and Europe. The study is expected to commence in H1 2022, with patient recruitment estimated to take 12 to 18 months. Cardiol has budgeted additional costs to complete this study to be approximately $13.4 million.

If Cardiol determines that the Phase II study meets its objectives, it currently expects to undertake the next steps of its clinical development program, which would consist of a larger clinical study, the details of which will be determined in conjunction with discussions with regulatory agencies. The Corporation expects the completion of this clinical development program, if undertaken, to take at least until 2025 and may involve a commercial partner from the pharmaceutical industry, with research, development, and commercialization costs potentially being shared with its commercial partner. Cardiol relies on CROs, clinical data management organizations, and consultants to assist with the design, conduct, supervision, and monitoring of pre-clinical and clinical studies. The total costs to complete the clinical development program cannot be determined at this stage as they will depend on a variety of factors.

Acute myocarditis is characterized by inflammation in the heart muscle (myocardium). It has many causes but the most common is a viral infection. In a proportion of patients, the inflammation in the heart persists and causes decreased heart function with symptoms and signs of heart failure. In some cases, this becomes progressive and leads to a chronic dilated cardiomyopathy, which is the most common reason for heart transplantation.

Since people with acute myocarditis have heart failure, its treatment is based on standard-of-care recommendations for heart failure. This includes diuretics, ACE inhibitors, angiotensin receptors blockers, beta blockers, and aldosterone inhibitors. For those with a fulminant presentation, intensive care is often required, with the use of inotropic medications (to increase the force of the heart muscle contraction) and, occasionally, heart-lung bypass or ventricular assist devices. There is otherwise no specific treatment for acute myocarditis. Although some patients have responded to therapy with immuno-suppressive therapy (azathioprine) added to steroids, the data are not conclusive enough to be the recommended therapy. Immune-modulation therapy with immune globulin has been trialed but without clear success.

A number of published studies have shown that cannabidiol has anti-inflammatory activities in a range of experimental inflammatory pathologies. In particular, cannabidiol has been shown to reduce vascular inflammation and inflammation in the heart in a model of myocarditis. The Corporation’s studies in an experimental model of heart failure have shown anti-inflammatory activity, as well as a prominent anti-fibrotic action of cannabidiol. Increasing fibrosis leads to progression of the heart dysfunction. Based upon this evidence, cannabidiol has the potential to offer therapeutic benefits in the treatment for myocarditis.

Acute myocarditis is a rare disease but is still a significant cause of acute heart failure in younger individuals and remains the most common cause of sudden cardiac death in people under 35 years of age. The most recent data from the ‘Global Burden of Disease Study’ suggests that the prevalence of myocarditis is approximately 22/100,000 persons (estimated U.S. patient population of 73,000), qualifying the condition as an orphan disease in the U.S. and in Europe. Cardiol believes that there is a significant opportunity to develop a therapy for acute myocarditis that may be eligible for designation as an Orphan Drug.

The Phase II myocarditis study was designed and will be overseen by an independent Steering Committee, consisting of international thought leaders in heart disease. The following members biographies can be seen under “Phase II/III study – COVID-19 (*LANCER*)”: Dennis McNamara, Leslie Cooper, Barry Trachtenberg, Matthias Friedrich, Carsten Tschöpe, Arvind Bhimaraj, Peter Liu and Wai Hong (Wilson) Tang. Other members of the Steering Committee include:

Yaron Arbel, MD

Dr. Yaron Arbel is an attending interventional cardiologist and the director of the CardioVascular Research Center (CVRC) at the Tel Aviv Medical Center. Prof. Arbel has been involved in entrepreneurship for the past 15 years. He has been working as a researcher/advisor/medical director in various fields of medicine: Heart failure (Corassist- diastolic heart failure), interventional cardiology (Angioslide- preventing distal embolization),

myocardial infarction (LBT-low level laser activation of bone marrow), medical informatics and wearables (CUBX-contactless hemodynamic assessment). Dr. Arbel graduated from the Faculty of Medicine in Sackler School of Medicine at the Tel Aviv University. He completed his training in Internal Medicine and Cardiology at the Tel Aviv medical center. He also completed a fellowship in interventional and structural cardiology at Sunnybrook Medical Centre in Toronto, Canada. He has published over 130 articles and has initiated local, national and international studies. He is a reviewer/board member in over 40 journals.

Edimar Bocchi, MD

Dr. Edimar Alcides Bocchi trained as a cardiologist at the Heart Institute (InCor) Of São Paulo University Medical School and obtained his PhD at the São Paulo University Medical School. Currently, he serves as the Head of Heart Failure Clinics and Heart Failure Team at Heart Institute (Incor) of Hospital das Clinicas of São Paulo University Medical School. His areas of clinical and research interest include heart failure, Chagas heart disease, cardio-oncology, heart transplantation, and exercise in heart failure. He is one of the founders of the Department of Heart Failure of the Brazilian Society of Cardiology. It is a pioneer in the development of heart transplantation in Chagasic cardiomyopathy; nitric oxide and phosphodiesterase type 5 inhibitors in heart failure. Dr. Bocchi is an author of more than 500 publications in peer-reviewed journals, contributed to 70 book chapters, and serves as the national coordinator for several randomized clinical trials, including the BELIEF, COMMANDER, SHIFT, RAD 2401, VICTORIA, DETERMINE, and EMPEROR Trials. Main investigator of the REMADHE trial and group leader of the trial CECCY.

Heart Failure

Market Overview

Heart failure is a chronic condition that affects more than 26 million people globally[2]. Over six million adults in Canada and the United States suffer from heart failure[3] and it remains a leading cause of death and hospitalization, with associated healthcare costs exceeding $30 billion annually[4] in the U.S. alone. According to the American Heart Association, one in five Americans over the age of 40 will develop heart failure in their lifetime. Heart failure contributes to one in nine deaths in America, and every minute at least one person is diagnosed with heart failure. People with heart failure suffer from shortness of breath, rapid heart rate, edema, reduced exercise capacity, often struggle with simple daily activities, and are frequently hospitalized. For many, these symptoms significantly reduce their quality of life. Concerning life expectancy after being diagnosed with heart failure, 30% of patients with heart failure die within one year[5], 50% within five years[6], and up to 90% within ten years of diagnosis[7].

Normal Heart Function

In a healthy heart, the left ventricle (lower left chamber) relaxes to fill with blood from the atrium (upper left chamber). Once filled, the left ventricle pumps the blood to the body.

Types of Heart Failure

Heart failure is a condition in which the heart fails to pump enough blood to supply sufficient oxygen to the tissues of the body.

There are two major types of heart failure:

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2 Savarese, G. *et al.* Global Public Health Burden of Heart Failure. *Cardiac Failure Review* 03, 7 (2017).

3 Blair, J. E. A., Huffman, M. & Shah, S. J. Heart Failure in North America. *Current Cardiology Reviews* 9, 128–146 (2013).

4 Cook, C., Cole, G., Asaria, P., Jabbour, R. & Francis, D. P. The annual global economic burden of heart failure. *International Journal of Cardiology* 171, 368–376 (2014).

5 Cowie, M. *et al.* Survival of patients with a new diagnosis of heart failure: a population based study. *Heart* 83, 505–510 (2000).

6 Levy, D. *et al.* Long-Term Trends in the Incidence of and Survival with Heart Failure. *New England Journal of Medicine* 347, 1397–1402 (2002).

7 Taylor, C. J., Roalfe, A. K., Iles, R. & Hobbs, F. D. R. Ten-year prognosis of heart failure in the community: follow-up data from the Echocardiographic Heart of England Screening (ECHOES) study. *European Journal of Heart Failure* 14, 176–184 (2012).

- Systolic heart failure
- Diastolic heart failure (Cardiol's primary focus)

Systolic heart failure, also known as heart failure with reduced ejection fraction, results from reduced contraction of the left ventricle such that not enough blood is pumped into the circulation. An estimated 50% of heart failure patients have poor systolic heart function.

In diastolic heart failure, also known as heart failure with preserved ejection fraction ("HFpEF"), the left ventricle becomes stiff and does not relax normally. As a result, it cannot fill properly, and pressure begins to increase in the left heart chambers and in the lungs. The increased pressure in the lungs is the cause for shortness of breath. Approximately 50% of heart failure patients have diastolic dysfunction[8].

Diastolic heart failure is commonly associated with several co-existing conditions including obesity, hypertension, diabetes, and older age. Diastolic heart failure is almost always associated with thickened LV muscle and increased fibrosis – both of which contribute to the increased stiffness of the ventricle and impairment to diastolic filling. There is also associated inflammation in the heart muscle; inflammation leads to progressive death of cardiac cells, increased fibrosis (scarring) and decreased contraction of the heart cells. As the amount of fibrosis increases, the ability of the heart to contract is diminished, leading to progressive loss of cardiac function.

Treatment of Heart Failure

Heart failure is a chronic disease, usually needing lifelong management. In some patients, doctors can correct heart failure by treating the underlying cause. For example, repairing a heart valve or controlling a fast heart rhythm may reverse heart failure. But for most patients, the current treatment of heart failure involves a balance of the right medications and, in some cases, use of medical devices that help the heart beat and contract more normally.

The goal of treatment for patients with heart failure is to improve their clinical status, functional capacity, and quality of life, prevent hospital admissions, and ultimately reduce mortality.

Existing Treatments of diastolic heart failure (as described by 2021 European Society of Cardiology Guidelines)

No treatment has yet been convincingly shown to reduce morbidity or mortality in patients with purely diastolic heart failure with completely normal systolic function (left ventricular ejection fraction > 55%). However, since patients with diastolic heart failure are often elderly, highly symptomatic, and have a poor quality of life, an important aim of therapy may be to help alleviate symptoms as best as possible to improve general well-being.

Effect of treatment on symptoms in heart failure with preserved ejection fraction

Fluid retention is a consistent finding in chronic heart failure patients. Fluid retention is the abnormal accumulation of fluid in the legs, feet, abdomen, and lungs – where it causes a chronic cough and shortness of breath. Diuretics, which increase the excretion of salts in the kidney and decrease fluid retention, can improve symptoms and signs of heart failure. The evidence that diuretics improve symptoms is similar across systolic and diastolic heart failure. Evidence that beta-blockers and Mineralocorticoid Receptor Antagonists improve symptoms in diastolic heart failure patients is lacking. There is also inconsistent evidence for an improvement in symptoms in those treated with ARBs and ACE Inhibitors. Nonetheless, patients with HFpEF often receive one or more of these medications in an attempt to improve quality of life.

Cardiol's Approach to the Treatment of Cardiovascular Disease

Cardiol is investigating the potential of using CardiolRx, a pharmaceutically produced oral cannabidiol (CBD) formulation for the treatment of acute myocarditis, COVID-19 with CVD, and other cardiovascular diseases. Cardiol

8 Hogg, K., Swedberg, K. & McMurray, J. Heart failure with preserved left ventricular systolic function: epidemiology, clinical characteristics, and prognosis. *Journal of the American College of Cardiology* 43, 317–327 (2004).

is developing a subcutaneous formulation of CardiolRx for the potential treatment of fibrosis and inflammation in the heart that is associated with the development and progression of heart failure with preserved ejection fraction (HFpEF).

Published third-party research has shown that there is an experimental basis for investigating the efficacy of CBD in cardiovascular disease. CBD has been shown in pre-clinical models to improve endothelial function by reducing inflammatory activation of the endothelial lining of blood vessels thus improving endothelial vasorelaxation and blood flow. In COVID-19, viral infection of endothelial cells can be accompanied by diffuse endothelial inflammation, suggesting that there may be a benefit of CBD in ameliorating some aspects of the pathology of this viral disease. CBD has also been shown to attenuate a number of other measures of potential importance in the treatment of cardiovascular disease, including cardiac dysfunction, oxidative stress, fibrosis, and inflammatory and cell death signalling pathways, in models of diabetes, a common co-morbidity in cardiovascular disease and heart failure patients. Cardiol is currently investigating the effect of CBD on heart failure induced by hypertension in pre-clinical models.

The rationale for the clinical program of CBD as a therapeutic approach to the treatment of COVID-19 is based upon the reported anti-inflammatory effect of CBD, specifically by inhibiting the activation of the NLRP3 inflammasome and attenuating TLR activation. In addition, CBD has been shown to have a cardio-protective effect pre-clinical models and, therefore, it is anticipated that this cannabinoid may prevent COVID-19 related cardiovascular complications thereby reducing morbidity and mortality. Cardiovascular complications such as myocardial injury as reflected by elevated serum troponin levels are common in patients with COVID-19, and it has been demonstrated that patients with myocardial injury suffer a higher rate of mortality. CBD has been shown to reduce elevated serum troponin T and reduce pro-inflammatory responses in the heart in pre-clinical models. CBD has also been shown to attenuate a number of measures of potential importance in the treatment of HF, including cardiac dysfunction, oxidative stress, fibrosis, and inflammatory and cell death signaling pathways in pre-clinical models of diabetes, a common co-morbidity in cardiovascular disease and COVID-19 patients.

The rationale for using cannabidiol to treat patients with cardiovascular disease is based on pre-clinical investigations by Cardiol and others in models of cardiovascular disease which have demonstrated that CBD has anti-fibrotic and anti-inflammatory activity, as well as anti-ischemic, and anti-arrhythmic action. In pre-clinical models of cardiac injury, cannabidiol was shown to be cardio-protective by reducing cardiac hypertrophy, fibrosis, and the production of certain re-modelling markers, such as cardiac BNP, which is typically elevated in patients with heart failure. Data generated with our collaborators at TecSalud del Tecnológico de Monterrey were accepted for presentation at the American College of Cardiology's 69th Annual Scientific Session held virtually on March 28 – 30, 2020.

Development of a subcutaneous (SC) CBD formulation

Almost all CBD formulations are administered orally; however, this route poses a number of limitations with respect the treatment of disease. The challenges of achieving a precise and reproduceable dose via an oral route of administration should be overcome by SC delivery of CBD. Cardiol has shown pre-clinically that CBD is effective when administered via the SC route in a heart failure model. The SC approach is practical and widely used in human medicine although the formulation requires specific characteristics. Currently, Cardiol has investigated a number of preparations, and development is ongoing into a formulation with the appropriate characteristics.

If Cardiol determines that the formulation development work meets its objectives, it currently expects to undertake additional pre-clinical studies in a variety of cardiovascular models, and investigate the safety characteristics of the formulation using pharmacokinetic and toxicity testing. Due to the early stage of development, the total costs and timing of the development program cannot be determined at this stage as they will depend on a variety of factors. Cardiol relies on CROs, clinical data management organizations, and consultants to assist with the design, conduct, supervision, and monitoring of pre-clinical studies of Cardiol's product candidates.

Nanotechnology for Drug Encapsulation and Delivery

Cardiol's nanotechnology is based on a patented family of biocompatible and biodegradable polymers made from PEG and PCL (See "Business of Cardiol - Commercialization Relationships – Meros"). Both PEG and PCL have a history of safe use in humans and are non-immunogenic when tested *in vitro*. PCL lies at the core of the nanoparticles and is lipophilic, allowing the solubilization and encapsulation of lipophilic drugs such as CBD. PEG forms the surface layer of the nanoparticles and is compatible with water, allowing the nanoparticles with their encapsulated drug to circulate in the aqueous environment of the blood. Cardiol's nanoparticles also accumulate within inflamed and fibrotic tissue and are therefore particularly appropriate for the delivery of anti-fibrotic, as well as anti-inflammatory drugs – fibrotic stiffening of the heart muscle is a feature of HF pathology. Cardiol's lead drug delivery technologies have also been shown to prolong the drug circulation time of lipophilic drugs and comprise a versatile system that supports drug delivery via parenteral injection routes.

Due to the early stage of development, the total costs and timing of the development program cannot be determined at this stage as they will depend on a variety of factors. Cardiol relies on CROs, clinical data management organizations, and consultants to assist with the design, conduct, supervision, and monitoring of pre-clinical studies of Cardiol's product candidates.

Research Programs

Cardiol has assembled an international network of experts in the synthesis, formulation, pharmacology and testing of drugs. Currently Cardiol has four research programs underway or completed with the following organizations:

- University of Alberta
- TecSalud del Tecnológico de Monterrey & Nano4Heart
- The Houston Methodist DeBakey Heart & Vascular Center
- School of Medicine at Trinity College

Due to the early stage of these research programs, the total costs and timing of these programs beyond the costs previously funded cannot be determined at this stage as they will depend on a variety of factors. Cardiol relies on CROs, clinical data management organizations, and consultants to assist with the design, conduct, supervision, and monitoring of these research programs.

University of Alberta

Cardiol's research program at the University of Alberta, the current phase of which has recently been completed, was focused on the development of proprietary nanoformulations of anti-inflammatory drugs designed to enhance the solubility of lipophilic drugs, improve PK, and increase drug concentration at the site of disease. The Corporation's research program was being conducted under the direction of Dr. Afsaneh Lavasanifar, Professor in Pharmaceutical Sciences at the University of Alberta, and a recognized expert in pharmacology, nanomedicines, and drug formulation. In 2001, the University of Alberta, the National Research Council of Canada, and the Government of Alberta collaborated to create the National Institute for Nanotechnology, the mission of which is to transform nanoscience ideas into novel, sustainable nanotechnology solutions.

In collaboration with Dr. Lavasanifar and the Faculty of Pharmaceutical Sciences at the University of Alberta, Cardiol developed and optimized proprietary nanoformulations of drugs for the treatment of heart failure, including pharmaceutical cannabidiol. CBD nanoformulations developed from this project are currently being tested *in vivo* in a model of heart failure at the Houston Methodist DeBakey Heart & Vascular Center as described below. The research was completed at the end of 2021 showing encouraging results. Based upon these data, further optimization and development work is expected to support future investigations at Houston Methodist DeBakey Heart & Vascular Center.

TecSalud & Nano4Heart

Cardiol established a USD $3 million research and development collaboration (See "Commercialization Relationships") with TecSalud and Nano4Heart, both of the Instituto Tecnológico y de Estudios Superiores de Monterrey, Mexico, to collaborate on the research and development of proprietary therapeutics for the treatment of heart failure. This research collaboration combines the significant research capability of TecSalud and Nano4heart's extensive experience in preclinical cardiovascular research with Cardiol's scientific, clinical, and business expertise. By combining these intellectual resources, Cardiol expects to accelerate the necessary research towards the mutual goal of developing a breakthrough heart failure treatment.

Nano4heart is an early-stage association specializing in medicine targeted for cardiovascular diseases, such as heart failure, that has emerged from TecSalud's Biomedical Research Center to focus on developing breakthrough medicines to improve the quality of life of patients with heart failure. In collaboration with leading cardiologists, Nano4Heart is developing formulations designed to treat heart diseases with a goal of improving the efficacy and safety profile of important medicines.

TecSalud is committed to delivering outstanding patient care with four state-of-the-art academic medical centers that combine innovative research, clinical services, and education. TecSalud has collaborative relationships with the Houston Methodist DeBakey Heart & Vascular Center and has established a formal agreement with the Massachusetts Institute of Technology to promote research and development in Mexico.

The primary objective of this collaboration is to develop the experimental evidence necessary to support advancing breakthrough medicines for heart failure into clinical development. Research is currently underway to investigate the therapeutic potential of cannabidiol formulations that target inflammation in a model of hypertension-induced heart failure. Initial research was completed in 2021 showing encouraging results. Building on these data, we expect to expand this research program into additional cardiovascular models with the aim of researching the effect of cannabidiol in a broader range of cardiovascular areas.

Further work is being undertaken to investigate the anti-inflammatory properties of a new phospholipid nanoparticle formulation, to assess the potential of the formulation as a systemic anti-inflammatory treatment for inflammatory cardiovascular conditions. Work is underway is a series of *in vitro* systems to determine the formulations' anti-inflammatory activity, and is expected to be expanded into *in vivo* cardiovascular models.

Houston Methodist DeBakey Heart & Vascular Center

The Houston Methodist DeBakey Heart & Vascular Center is recognized internationally as a center of excellence for the treatment of heart failure. The center was the birthplace of cardiovascular bypass surgery in 1964 and currently is ranked the 14th best hospital for care in cardiology and heart surgery out of 5,028 hospitals in the United States by US News.

In January 2018, Cardiol announced that experimental research performed at the Houston Methodist DeBakey Heart & Vascular Center showed new functionality of the Corporation's in-licensed patented nanotherapeutics. Designed to act as a vehicle to target anti-inflammatory drugs to inflamed heart tissue, these data demonstrated the accumulation of nanoparticles at regions of inflammation and fibrosis in diseased hearts, showing potential for Cardiol's proprietary nanotechnology to be used to target drugs directly to areas of inflammation and fibrosis to treat heart failure.

In August 2018, Cardiol entered into a research contract with the Houston Methodist DeBakey Heart & Vascular Center to build upon the initial research in an experimental model of heart failure. Encouraging results generated in 2021 showed significant advantages of nanoformulations developed at the University of Alberta and has laid the foundation for further work to be initiated in 2022. Further work is expected to include detailed investigation into the behaviour of the nanoformulation, and important experiments into the method of action of cannabidiol in *in vitro* and *in vivo* models to better understand how CBD works.

School of Medicine at Trinity College

Cardiol is investigating ageing and its effects on inflammation, particularly neuroinflammation, with collaborators at the School of Medicine at Trinity College, Dublin. These investigations have indicated that increased levels of endocannabinoids in the brain exerts a beneficial effect on synaptic function in animals. CBD is known to have anti-inflammatory activities, and to enter the brain compartment. Further investigations are being performed into these CBD related effects.

The research is expected to be completed in 2022 and is not expected to have material expenditures.

Commercialization Relationships

Dalton

Cardiol entered into an exclusive master services agreement (the "Dalton Services Agreement") dated April 17, 2018 and effective as of June 12, 2017 for pharmaceutical cannabidiol and has subcontracted the manufacturing of its drug product candidates to Dalton. Dalton has the manufacturing capability for Cardiol's clinical trial materials, scalable to support all stages of the drug development process (Phase I, II, III, and commercial). As consideration under the Dalton Services Agreement, Cardiol issued 400,000 Common Shares to Dalton. Cardiol also agreed to issue to Dalton an additional 400,000 Common Shares if Dalton meets certain performance objectives. The Dalton Services Agreement may be terminated by Cardiol upon provision of thirty days' notice of termination.

The services provided by Dalton under the Dalton Services Agreement are undertaken on a project and product basis. With respect to each project or product, Cardiol and Dalton agree in writing upon objectives, scope, price, and fees payable, specifications, deliverables, milestones, and timelines in a work order.

Purisys

Cardiol entered into an exclusive supply agreement (the "Purisys Exclusive Supply Agreement") with Noramco (Purisys) dated September 28, 2018, as amended on December 7, 2018, December 11, 2018, July 2, 2019, September 11, 2019, and November 12, 2019 pursuant to which Purisys will be the exclusive supplier of pharmaceutical cannabidiol for Cardiol, provided Purisys is able to meet Cardiol's supply requirements.

In 2020, the agreement was assigned to Purisys, an affiliate of Noramco headquartered in Athens, Georgia. This assignment had no impact on Cardiol's rights under the original agreement.

Pursuant to the terms of the Purisys Agreement, Cardiol paid a non-refundable payment of US$3,000,000 (the "Exclusivity Payment"). The Exclusivity Payment represents a prepayment for inventory and is being credited towards purchases.

Effective upon entering into a supply agreement with Shoppers on March 16, 2020 (see "Business of Cardiol – Corporate History –Year Ended December 31, 2020), Purisys shall not sell pharmaceutical cannabidiol to any third party for use in the production of products sold to retail pharmacies in Canada and Mexico, such as Shoppers. Notwithstanding this restriction, Purisys shall have the right to sell pharmaceutical cannabidiol to third parties outside Canada for use in products that are approved as prescription medicines by the Therapeutic Products Directorate of Health Canada for delivery into Canada.

The initial term of the Purisys Exclusive Supply Agreement expires on December 31, 2038, and thereafter automatically renews for successive periods of two calendar years each, unless written notice of termination is given by either party at least 18 months before the expiration of the initial term or completion of the then-current renewal term.

TecSalud (CARO Development Agreement)

Cardiol entered into a development agreement (the "CARO Development Agreement") with CARO dated August 29, 2018, for research and development of proprietary drug formulations for the treatment of heart failure. CARO is a Mexican corporation dedicated to providing clinical and scientific experimentation and consulting, as well as performing its own development activities or through third-party providers. TecSalud and Nano4heart are third parties through which CARO will provide its consulting and development activities for Cardiol.

Pursuant to the terms of the CARO Development Agreement, CARO will provide scientific experimentation, research activities, drug development activities, access to intellectual property, and drug formulation and discovery activities to Cardiol (the "CARO Development Activities"), as set out in a development plan (the "CARO Development Plan") through TecSalud and Nano4heart. CARO and Cardiol value the CARO Development Activities, provided through research, at USD $3,000,000. Under the CARO Development Agreement, CARO may also engage third-party providers for development activities in support of the CARO Development Plan, which is anticipated to be limited to third-party vendors of materials.

As consideration under the CARO Development Agreement, Cardiol issued 824,000 Common Share purchase warrants (the "CARO Compensation Warrants") to CARO, with each CARO Compensation Warrant entitling CARO to purchase one Common Share (a "CARO Compensation Warrant Share") at an exercise price of CDN $4.00 per CARO Compensation Warrant Share until August 31, 2022. Cardiol also paid CARO USD $400,000 in cash.

The CARO Compensation Warrants and the issuance of the CARO Compensation Warrant Shares on the exercise thereof are to constitute full payment for the CARO Development Activities, both past and future, under the CARO Development Plan. CARO is not to issue invoices for any of the CARO Development Activities under the CARO Development Plan until such time as CARO, in its discretion, wishes to exercise any of its CARO Compensation Warrants. If CARO wishes to exercise any of the CARO Compensation Warrants, CARO is to provide Cardiol with one or more invoices, tied to milestones in the CARO Development Plan, and the aggregate amount of the invoices shall constitute payment in full of the aggregate exercise prices of the CARO Compensation Warrants being exercised.

Both Cardiol and CARO may terminate the CARO Development Agreement if the other party commits a material breach of the CARO Development Agreement and the breaching party fails to remedy the material breach within 60 days following receipt of written notice of the breach. In addition, either party may terminate the CARO Development Agreement by giving 30 days' written notice to the other party if, acting reasonably and in good faith, it determines that the continued performance of the CARO Development Activities would (i) constitute a potential or actual violation of applicable law or any policy of the terminating party adopted to ensure compliance with applicable law; (ii) constitute a potential or actual violation of any regulatory, medical or scientific standard of integrity or ethics; or (iii) potentially jeopardize patient safety, provided that during such 30-day period, the parties discuss in good faith possible changes to the CARO Development Activities.

However, if CARO terminates the CARO Development Agreement for any reason except breach of contract by Cardiol, or terminates the CARO Development Activities prior to achievement of all milestones in the CARO Development Plan, then any unexercised CARO Compensation Warrants that are not related to CARO Development Activities and milestones in the CARO Development Plan that have been attained up to the time of termination of the CARO Development Agreement shall be deemed terminated as of the time of termination of the CARO Development Agreement.

If Cardiol terminates the CARO Development Agreement for any reason (including breach of contract by CARO), or requires CARO to terminate the CARO Development Activities prior to achievement of all milestones in the CARO Development Plan, then the CARO Compensation Warrants issued to CARO that can be invoiced for the CARO Development Activities completed up to the time of termination shall be considered to have been earned notwithstanding such termination. The CARO Compensation Warrants that cannot be exercised (because invoices for CARO Development Activities not completed cannot be issued) will be deemed terminated, null and void as of termination.

Meros

Meros is a privately-held Alberta corporation formed in 2009 to commercialize advanced drug delivery technologies developed within the Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta.

Cardiol entered into a license agreement (the "Meros License Agreement") with Meros dated January 20, 2017, granting Cardiol the sole, exclusive, irrevocable, royalty-bearing license, including the right to sublicense, certain patented nanotechnologies for use with any drugs or classes of drugs currently used or developed in the future to diagnose or treat heart failure and/or any cardiovascular disease and/or cardiopulmonary disease and/or cardiac arrhythmias. The term of the Meros License Agreement is 20 years or for the life of the patents of the licensed technologies.

Under the Meros License Agreement, Cardiol agreed to certain milestones and milestone payments, including the following:(i) payment of $100,000 upon enrolling the first patient in a Phase IIB clinical trial designed to investigate the safety and indications of efficacy of one of the licensed technologies; (ii) payment of $500,000 upon enrolling the first patient in a Pivotal Phase III clinical trial designed to investigate the safety and efficacy of one of the licensed technologies; (iii) $1,000,000 upon receiving regulatory approval from the FDA on any therapeutic and/or prophylactic treatment incorporating the licensed technologies. Cardiol also agreed to pay Meros the following royalties: (i) 5% of worldwide proceeds of net sales of the licensed technologies containing cannabinoids that Cardiol receives from human and animal disease indications and derivatives as outlined in the Meros License Agreement; (ii) 7% of any non-royalty sub license income that Cardiol receives from human and animal disease indications and derivatives for licensed technologies containing cannabinoids as outlined in the Meros License Agreement; (iii) 3.7% of worldwide proceeds of net sales that Cardiol receives from the licensed technology in relation to human and animal cardiovascular and/or cardiopulmonary disease, heart failure, and/or cardiac arrhythmia diagnosis and/or treatments using the drugs outlined in the Meros License Agreement; and (iv) 5% of any non-royalty sub license income that Cardiol receives in relation to any human and animal heart disease, heart failure and/or arrhythmias indications as outlined in the Meros License Agreement.

In addition, as part of the consideration under the Meros License Agreement, Cardiol: (i) issued to Meros 1,020,000 Common Shares; (ii) issued to Meros an additional 1,020,000 Common Shares to be held in escrow (the "Meros Escrow Shares") and to be released upon the first patient being enrolled in a Phase I clinical trial as described in the Meros License Agreement (the "Meros Milestone"). The 1,020,000 Meros Escrow Shares were subsequently cancelled and replaced with 1,020,000 special warrants (the "Meros Special Warrants") convertible automatically into Common Shares for no additional consideration upon the Corporation achieving the Meros Milestone.

The Meros License Agreement may be terminated by Meros, if Cardiol breaches any payment provisions, if Cardiol ceases to develop and/or commercialize the licensed technologies, or if Cardiol ceases any and all attempts to raise capital to support developing and or commercializing the licensed technologies. Cardiol may terminate the Meros License Agreement if Cardiol determines in its sole discretion that the licensed technologies are not worthy of development based on research outcomes or commercial viability.

Competitive Conditions

Cardiol's competitors include multinational pharmaceutical companies and specialized biotechnology companies, other medical cannabis licensees, universities, and other research institutions that are conducting research in cannabinoid products, as well as those focusing on therapies for heart failure.

More established companies may have a competitive advantage over Cardiol due to their greater size, capital resources, cash flows, and institutional experience. Compared to Cardiol, many competitors may have significantly greater financial, technical, and human resources at their disposal. Due to these factors, competitors may have an advantage in marketing their approved products and may obtain regulatory approval of their product candidates before Cardiol can, which may limit Cardiol's ability to develop or commercialize its product candidates. Competitors may also develop drugs that are safer, more effective, more widely used, and less expensive, and may also be more successful in manufacturing and marketing their products.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of Cardiol's competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties also compete with Cardiol in recruiting and retaining qualified scientists, management, and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, Cardiol's programs.

Employees

As of December 31, 2021, Cardiol had 11 employees and 8 management consultants providing management services to Cardiol.

Intellectual Property Rights

Cardiol strives to obtain and protect intellectual property that is important to its business. Such intellectual property includes, or may in future include, patents, patent applications, regulatory dossiers, manufacturing and process know-how, proprietary unpatented information including trade secrets, contractual arrangements, and trademarks. Patents and patent applications owned by or licensed to Cardiol cover compositions of matter, their methods of use, related technology, and other applicable inventions.

Cardiol's intellectual property portfolio has been built from in-house technology and product research and development, as well as strategic relationships with partners, including Dalton, the University of Alberta, the Houston Methodist DeBakey Heart and Vascular Centre, and TecSalud Instituto Tecnológico y de Estudios Superiores de Monterrey.

Cardiol has an exclusive in-licensing arrangement with Meros under which Cardiol licenses territorial rights to certain technologies, patents, and related know-how.

The Corporation has filed for and/or licensed patents and patent applications in major pharmaceutical markets, including Canada, the U.S., Japan, major European countries, Australia, Brazil, and Mexico. Cardiol also relies on proprietary unpatented information, including trade secrets. Cardiol has entered into contractual arrangements to protect its technology and enhance its competitive position. Furthermore, Cardiol has registered and applied for trademarks in many, if not all, of the same jurisdictions.

Patent Portfolio

Cardiol owns or licenses the following patents and applications:

Patent Family 1 – Poly (Ethylene Oxide)-Block-Poly (Ester) Block Copolymers (the "Block Copolymer Family")

Cardiol currently has a sole, exclusive, worldwide, irrevocable, royalty-bearing license to exploit the Block Copolymer Family for the following fields of use:

(a) the delivery of any cannabinoids for any and all human or animal disease indications and any derivatives thereof; and

(b) the delivery of any drugs or classes of drugs currently used or developed in the future to diagnose or treat cardiovascular and/or cardiopulmonary disease, heart failure and/or cardiac arrhythmias in humans and animals, including Sildenafil, Pirfenidone, Rapamycin, Methotrexate, Amiodarone, Cannabinoids, blockers of HSP60 activity or inhibitors of production and/or transport of HSP60 and any derivatives of any of them.

The Block Copolymer Family consists of the following patents:

Country	Publication Number	Application Date	Status
Canada	CA2857023C	21Mar2007	Granted
Canada	CA2646425C	21Mar2007	Granted
France	FR2730604B1	21Mar2007	Granted
France	FR1994081B1	21Mar2007	Granted
Switzerland	CH2730604B1	21Mar2007	Granted
Switzerland	CH1994081B1	21Mar2007	Granted
United Kingdom	GB2730604B1	21Mar2007	Granted
United Kingdom	GB1994081B1	21Mar2007	Granted
Germany	DE602007056634.7.	21Mar2007	Granted
Germany	DE602007036834.0.	21Mar2007	Granted
Japan	JP5933889B2	21Mar2007	Granted
United States	US9139553B2	26Sep2012	Granted
United States	US8309515B2	21Mar2007	Granted

These patents cover, broadly, micelle-forming poly (ethylene oxide)-block-poly (ester) block copolymers having reactive groups on the polyester block therein. The block copolymer compounds are considered to be biodegradable and are effective carriers of a large number of bioactive agents such as DNA, RNA, oligonucleotides, proteins, peptides, and drugs. Example drugs that can be delivered using this technology include methotrexate, Cyclosporine A, cannabinoids, and a wide range of other drugs, such as vaccines, DOX, amphotericin B, cisplatin, paclitaxel, etoposide, PSC833, amiodarone, rapamycine, camptothecin, cholesterol and ergoesterol, dexamethasone, prednisone, cortisol, testosterone, estrogens, progestins, dromostanolone, testolactone, diethelstilbestrol, ethinyl estradiol, budesonide, beclomethasone, and vitamin D.

Thus, the Block Copolymer Family is relevant to many product candidates in our product pipeline for delivering drugs to the heart.

Patent Family 2 – Amphiphilic Block Copolymers, Micelles, And Methods for Treating and/or Preventing Heart Failure

Cardiol has filed the following patent applications of which the Australian application has matured to patent.

Country	Application Number	Application Date	Status
United States	62/597740	12 December 2017	Completed
United States	16/772113	10 December 2018 [national phase entry date is 11 June 2020]	Pending
WIPO	PCT/CA2018/051573	10 December 2018	Completed
Canada	3076248	10 December 2018	Pending
Europe	18889068.5	10 December 2018	Pending
Australia	2018384096	10 December 2018	Granted

Country	Application Number	Application Date	Status
New Zealand	762418	10 December 2018	Pending
Mexico	MX/a/2020/006005	10 December 2018	Pending
Brazil	112020006191-3	10 December 2018	Pending

These applications are directed towards micelles comprising a cardioactive agent (e.g. cannabidiol) and amphiphilic block copolymer. The micelles are for use in treating and/or preventing heart failure and, when administered systemically, localize in fibrotic heart tissue. The application also covers related compositions, methods, and uses for treating or preventing heart failure.

This patent family is relevant to micellar formulations for treating or preventing heart failure (e.g. micellar CBD formulations), and related methods

Patent Family 3 – Stable Medicinal Cannabidiol Compositions

The Corporation filed International application number PCT/CA2019/051259 on September 9, 2019 which has been nationalized in Canada, U.S., Mexico, Brazil, Europe, Japan, Australia and South Africa.

The International Search Report and Written Opinion found all claims to be patentable. The applications are directed towards a stable, oral CBD oil formulation employing synthetic CBD and beta-caryophyllene (BCP) as active ingredients.

Patent Family 4 – Parenteral Cannabidiol Compositions for Treating Heart Conditions

Cardiol filed International application number PCT/CA2020/051405 on October 20, 2020, which claims the benefit of U.S. provisional application 62/926,066 filed on October 25, 2019. This application designated all member states of the Patent Cooperation Treaty (over 150 countries including all major industrialized nations) and relates to parenteral, e.g. injectable, CBD formulations for use in treating or preventing heart failure or precursor conditions thereof, e.g. cardiac inflammation, cardiac fibrosis, and cardiac hypertrophy.

Patent Family 5 – Stable Oral Cannabidiol Compositions

The Corporation filed International application number PCT/CA2020/051680 on December 7, 2020 designating all member states of the Patent Cooperation Treaty (over 150 countries including all major industrialized nations).

The International Search Report and Written Opinion found all claims to be patentable. The application is directed towards a stable, oral CBD oil formulation employing synthetic and/or botanical CBD and beta-caryophyllene (BCP) as active ingredients.

Patent Family 6 - Injectable Cannabinoid Formulations

The Corporation filed International application number PCT/CA2022/050239 on February 18, 2022, which claims the benefit of U.S. provisional patent application 63/151903 on February 22, 2021. This application covers an injectable CBD composition.

Patent Family 7 - Cannabidiol For Use In Improving Outcomes In Subjects With Covid-19

Cardiol filed U.S. provisional application number 63/233,365 on August 16, 2021. This application covers the use of CBD in improving outcomes in Covid-19 patients who suffer from or are at risk of developing cardiovascular problems.

Future Filings

Cardiol plans to file additional patent applications to protect ongoing research and development.

Domain Names

Cardiol has registered the domain cardiolrx.com.

Trademarks

Trademark	**Current Statement(s) of Goods and/or Services for Canada [foreign applications / registrations have broader statements, in general**]**	**Status and Country Coverage**	**Representative Application Details**
CARDIOL (standard character mark)	Class 5: Pharmaceutical preparations containing cannabidiol (CBD); CBD oil for medicinal and/or nutritional purposes, for use by humans and/or animals Class 35: Sale of pharmaceuticals and supplements	Pending in Canada.	Canadian application 1917764 filed August 31, 2018
CARDIOLRX (standard character mark)	Class 5: Pharmaceutical preparations containing cannabidiol (CBD); CBD oil for medicinal and/or nutritional purposes, for use by humans and/or animals	Pending in Canada and Brazil. Registered in Australia, Mexico and New Zealand.	Canadian Application 1917765 filed August 31, 2018
CARDIOL THERAPEUTICS (standard character mark)	Class 5: Pharmaceutical preparations containing cannabidiol (CBD); CBD oil for medicinal and/or nutritional purposes, for use by humans and/or animals Class 35: Sale of pharmaceuticals and supplements	Pending in Canada.	Canadian application 1917766 filed August 31, 2018
CARDIOL THERAPEUTICS (design mark)	Class 5: Pharmaceutical preparations containing cannabidiol (CBD); CBD oil for medicinal and/or nutritional purposes, for use by humans and/or animals Class 35: Sale of pharmaceuticals and supplements	Pending in Canada.	Canadian application 1917767 filed August 31, 2018
CORTALEX (standard character mark)	Class 5: Therapeutic products, namely, pharmaceutical preparations and natural	Pending in Canada, Brazil and U.S.	Canadian application 2014492 filed February 27, 2020

Trademark	Current Statement(s) of Goods and/or Services for Canada [foreign applications / registrations have broader statements, in general**]	Status and Country Coverage	Representative Application Details
	health products, whether sold-over-the-counter or by prescription, and including therapeutic products containing cannabinoids.	Registered in Australia, European Union, Iceland, Mexico, New Zealand, Switzerland, and United Kingdom.	
CORTALEX (design mark)	Class 5: Therapeutic products, namely, pharmaceutical preparations and natural health products, whether sold-over-the-counter or by prescription, and including therapeutic products containing cannabinoids.	Pending in Canada.	Canadian application 2019187 filed March 25, 2020

Most, if not all, of the foreign registrations are for goods, namely, “therapeutic products, namely, pharmaceutical preparations and natural health products, whether sold-over-the-counter or by prescription, and including therapeutic products containing cannabinoids.”

Cardiol’s Intellectual Property Practices

Cardiol’s intellectual property practices include striving to keep all information relating to proprietary compounds, inventions, improvements, trade secrets, know-how, and continuing technological innovation confidential.

Cardiol also will, where it deems practicable and commercially reasonable:

- perform surveillance of third-party patents and patent applications in order to identify any third-party patent or third-party patent application which, if granted, could be infringed by our activities or could infringe our patents;
- file patent applications for any new and patentable invention, development, or improvement in the United States and in other countries;
- prosecute all pending patent applications in conformity with applicable patent laws and in a manner that efficiently covers our activities;
- identify and protect confidentiality of trade secrets;
- file trademark applications in countries of interest for our trademarks;
- register domain names whose addresses include our trademark names; and
- maintain our intellectual property rights by paying government fees as may be necessary to ensure such rights remain in force.

Regulatory Exclusivity

The regulatory regimes of certain countries, such as the United States, European Union members and Canada, provide market exclusivity for a pharmaceutical product once approved. Data protection provides a person or entity with protection against third parties who may wish to commercialize a product similar to an approved product bridging to the data developed for the approved product.

In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, awards, in certain circumstances, non-patent marketing exclusivities to pioneer drug manufacturers. The Hatch-Waxman Act provides five years of non-patent marketing exclusivity within the United States to an applicant who gains approval of a new drug application under the FDA for a “new chemical entity,” a drug with the same active moiety which the FDA has not previously approved. This marketing exclusivity generally prevents the FDA from approving, in certain circumstances, any abbreviated new drug application (“ANDA”), for a generic drug or any 505(b)(2) NDA that references data from the pioneer drug product.

In Canada, the Food and Drug Regulations provide an 8-year market exclusivity period to a Notice of Compliance holder who markets an innovative drug in Canada. The Patented Medicines (Notice of Compliance) Regulations provide freedom from generic competition for patented drugs under certain conditions.

In Europe, when a marketing authorization for a product is issued by the European Medicines Agency (the “EMA”), the approved product (including a biological product) benefits from ten years of market exclusivity.

Scientific Advisory Board

To provide guidance and oversight to the Corporation’s ongoing research programs, Cardiol has constituted a world-class Scientific Advisory Board comprising thought leaders in cardiovascular medicine. Their combined knowledge and insight will prove to be invaluable as Cardiol pursues the commercial development of breakthrough therapies for heart failure.

Cardiol’s Scientific Advisory Board includes:

Paul M. Ridker, MD, MPH

Dr. Ridker is director of the Center for Cardiovascular Disease Prevention, a translational research unit at Brigham and Women’s Hospital (BWH), Boston. A cardiovascular medicine specialist, he is also the Eugene Braunwald Professor of Medicine at Harvard School of Medicine (HMS). Dr. Ridker received his medical degree from HMS and then completed an internal medicine residency and a cardiology fellowship at BWH. Dr. Ridker is board certified in internal medicine. His clinical interests include coronary artery disease and the underlying causes and prevention of atherosclerotic disease. Dr. Ridker is the author of over 900 peer-reviewed publications and reviews, 64 book chapters, and six textbooks related to cardiovascular medicine. His primary research focus has involved inflammatory mediators of heart disease and the molecular and genetic epidemiology of hemostasis and thrombosis, with particular interests in biomarkers for coronary disease, “predictive” medicine, and the underlying causes and prevention of atherosclerotic disease. Notably, Dr. Ridker has been the Principal Investigator or Study Chairman of several large international trials that have demonstrated the role of inflammation in the genesis and management of coronary artery disease. He was included in TIME magazine’s list of 100 most influential people of 2004, and between the years 2000 and 2010, Dr. Ridker was among the ten most often cited researchers in cardiovascular medicine worldwide. Amongst many other honors, he received the American Heart Association Distinguished Scientist Award in 2013, gave the Braunwald Lecture of the American College of Cardiology in 2019, was awarded the Gotto Prize for Atherosclerosis Research from the International Atherosclerosis Society in 2021, and is an elected Member of the National Academy of Medicine (USA).

Bruce McManus, PhD, MD

Dr. McManus is Professor Emeritus, Department of Pathology and Laboratory Medicine, the University of British Columbia. He has served as CEO, Centre of Excellence for Prevention of Organ Failure (PROOF Centre), Director, UBC Centre for Heart Lung Innovation, and Scientific Director, Institute of Circulatory and Respiratory Health, CIHR. Dr. McManus received BA and MD degrees (University of Saskatchewan), an MSc (Pennsylvania State University), and a PhD (University of Toledo). He pursued post-doctoral fellowships at the University of California, Santa Barbara (Environmental Physiology) and at the National Heart, Lung, and Blood Institute, Bethesda, MD (Cardiovascular & Pulmonary Pathology), and residency training at the Peter Bent Brigham Hospital, Harvard University (Internal Medicine and Pathology). 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. He has had a longstanding interest in the diagnosis and management of acute viral myocarditis.

His life's scholarship is reflected in more than 400 original peer-reviewed publications, over 60 chapters, and several books. He is an extraordinary mentor. Dr. McManus has been widely appreciated for his research, mentoring, and leadership contributions to the health sciences. Amongst many awards and honors, Dr. McManus received the prestigious Max Planck Research Award in 1991, was elected a Fellow of the Royal Society of Canada in 2002, was appointed a Member of the Order of Canada in 2018, and to the Order of British Columbia the following year.

Joseph A. Hill, MD, PhD

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. Dr. Hill holds both the James T. Willerson, MD, Distinguished Chair in Cardiovascular Diseases, and the Frank M. Ryburn Jr. Chair in Heart Research. He graduated from Duke University with MD and PhD degrees in 1987. His PhD dissertation research was in the field of cardiac ion channel biophysics. Dr. Hill then worked for five years as a postdoctoral fellow at the Institut Pasteur in Paris studying central and peripheral nicotinic receptors. He next completed an internal medicine internship and residency, as well as a clinical cardiology fellowship, at the Brigham and Women's Hospital, Harvard Medical School. He served on faculty at the University of Iowa for five years before moving in 2002 to the UT Southwestern. Dr. Hill's research examines molecular mechanisms of structural, functional, metabolic, and electrophysiological remodeling in cardiac hypertrophy and heart failure. He has served on many NIH panels and committees and delivered numerous invited lectures in the U.S. and around the world. Dr. Hill has received many recognitions and awards, including election to the Association of American Professors and the 2018 Research Achievement Award from the International Society for Heart Research. For the past six years, Dr. Hill has been the Editor-in-Chief of the prestigious American Heart Association journal Circulation.

REGULATORY OVERVIEW

Drugs are evaluated for safety, efficacy, and manufacturing quality as a condition of market access, and promotional messages must adhere to approved product labelling. Drug prices also are regulated in most countries with national health insurance systems. Regulation of market access and promotion derives from uncertainty about the real-life value of drugs. Real-life product characteristics can only be determined from accumulated experience over large numbers of patients in carefully designed epidemiological trials or observational studies.

Government Regulation and Product Approval

As a biopharmaceutical company that intends to test, register, and commercialize products in Canada and the United States and other jurisdictions, we are subject to extensive regulation by various regulatory authorities. The primary regulatory agency in the United States is the FDA, in Canada it is Health Canada, and in Europe it is the EMA. Together with these three, there are other federal, state, and local regulatory agencies. In the United States, the Federal Food, Drug, and Cosmetic Act (the "FDCA"), and its implementing regulations set forth, among other things, requirements for the research, testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, and advertising and promotion of our products. Although the discussion below focuses on regulation in the United States, we anticipate seeking approval for, and marketing of, our products in other countries.

Generally, our activities outside the United States will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Approval in the United States, Canada, or Europe does not assure approval by other regulatory agencies, although often test results from one country may be used in applications for regulatory approval in another country. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way through the EMA, but country-specific regulation remains essential in many respects. The April 2015 publication titled "Medicinal Products in the European Union, the legal framework for medicines for human use"[9] from the European Parliamentary Research Service gives a general overview of several aspects of European Union legislation on human medicines. A major

9 https://www.europarl.europa.eu/RegData/etudes/IDAN/2015/554174/EPRS_IDA(2015)554174_EN.pdf

difference in Europe, when compared to Canada and the United States, is with the approval process. In Europe, there are different procedures that can be used to gain marketing authorization. The first procedure is referred to as the centralized procedure and requires that a single application be submitted to the EMA and, if approved, allows marketing in all countries of the European Union. The centralized procedure is mandatory for certain types of medicines and optional for others. The second procedure is the decentralized procedure which requires one member state to act as the reference member state conducting the review of the application which is simultaneously filed to the reference member state and to selected other member states. The third procedure is a state by state application.

The process of obtaining regulatory marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources and may not be successful. See “Risk Factors”.

The Corporation does not engage in any U.S. marijuana-related activities as defined in Canadian Securities Administrators Staff Notice 51-352 - Issuers with U.S. Marijuana-Related Activities. The Corporation has research and/or business relationships with Purisys and the Houston Methodist DeBakey Heart & Vascular Center, both of which are based in the U.S. and/or are U.S. based companies. The Houston Methodist DeBakey Heart & Vascular Center provides contract research services investigating the Corporation’s nanotechnology in experimental models of heart failure. Purisys is a manufacturer of controlled drug substance APIs and is registered with the DEA to manufacture pharmaceutically produced cannabidiol.

New Drug Submissions (NDS) – Health Canada

To obtain approval to market a drug in Canada, a sponsor usually requests a pre-submission meeting with the review division of Health Canada responsible for the therapeutic field. If the meeting is granted, the sponsor must submit a Pre-Submission Information package to Health Canada to meet with the review division. This process occurs prior to submitting the NDS application. The purpose of the pre-submission meeting is to review the evidence (non-clinical and clinical research, quality information, indication) that will be submitted in the NDS application.

During the drug development process, the sponsor prepares study reports. Once the sponsor releases the last study required for the submission, the sponsor completes the NDS application and submits it to Health Canada. Prior to submitting the NDS and if applicable based on the intended use of the product in the identified patient population, the sponsor may submit in advance a request for priority review status.

After submitting the NDS application, the file undergoes a screening process prior to being accepted for review. TPD has 45 calendar days from receipt to complete the screening review process. If granted a priority review, the screening period is reduced to 25 calendar days.

After a comprehensive review of an NDS application, Health Canada will issue a NOC if the product is approved or a NON if further questions remain. If a NOC is issued, a Drug Identification Number (DIN) is also issued that is required to be printed on each label of the product, as well as the final version of the Product Monograph that has been agreed to between Health Canada and the sponsor.

The average target time for reaching a first decision on an NDS is 300 calendar days, unless the submission has received a priority review in which case the time is 180 calendar days.

Fees are levied for a review of an NDS application.

U.S. Government Regulation

The FDA is the main regulatory body that controls pharmaceuticals in the United States, and its regulatory authority is based in the FDCA. Pharmaceutical products are also subject to other federal, state, and local statutes. A failure to comply explicitly with any requirements during the product development, approval, or post-approval periods, may lead to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an Institutional Review Board (“IRB”) of a hold on clinical trials, refusal to approve pending marketing applications or

supplements, withdrawal of approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, or criminal prosecution. As presented on the section of the FDA's website titled "Drug Review Process: Ensuring Drugs are Safe and Effective[10]", the steps required before a new drug may be marketed in the United States generally include:

- completion of nonclinical studies, animal studies, and formulation studies in compliance with the FDA's Good Laboratory Practice (GLP), regulations;
- submission to the FDA of an Investigational New Drug ("IND") application to support human clinical testing in the United States;
- approval by an IRB at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with federal regulations and with Good Clinical Practices ("GCP"), and regulations to establish the safety and efficacy of the investigational product candidate for each target indication;
- submission of an NDA to the FDA;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the investigational product candidate is produced to assess compliance with cGMP regulations, and to assure that the facilities, methods, and controls are adequate; and
- FDA review and approval of the NDA.

Clinical Trials

An IND is a request for authorization from the FDA to administer an investigational product candidate to humans. This authorization is required before interstate shipping and administration of any new drug product to humans in the United States that is not the subject of an approved NDA. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease under study, under the supervision of qualified investigators following GCPs, an international standard meant to protect the rights and health of patients with the disease under study and to define the roles of clinical trial sponsors, administrators, and monitors. Clinical trials are conducted under protocols that detail the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. Each protocol involving testing on patients in the United States and subsequent protocol amendments must be submitted to the FDA as part of the IND. Cardiol has submitted two INDs on CardiolRx, and have received two "Study May Proceed" letters from the FDA. The first IND was to study CardiolRx in the prevention of cardiovascular complications due to COVID-19 infections. The second was to study CardiolRx in the treatment of myocarditis.

As set out in the October 8, 2021 publication "ICH E8(R1) Guideline – General Considerations for Clinical Trials[11]", published by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, the three phases of clinical investigation are as follows:

- Phase I. Phase I includes the initial introduction of an investigational product candidate into humans. Phase I clinical trials may be conducted in patients with the target disease or condition, or in healthy volunteers. These studies are designed to evaluate the safety, metabolism, PK, and pharmacologic actions of the investigational product candidate in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase I clinical trials, sufficient information about the investigational product's PK and pharmacological effects may be obtained to inform the design of Phase II clinical trials. The total number of participants included in Phase I clinical trials varies but is generally in the range of 20 to 80.

10 https://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143534.htm

11 https://database.ich.org/sites/default/files/E8_Guideline.pdf

- Phase II. Phase II includes the controlled clinical trials conducted to evaluate the effectiveness of the investigational product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the product candidate. Phase II clinical trials are typically well-controlled, closely monitored, conducted in a limited subject population, and usually involve no more than several hundred participants
- Phase III. Phase III clinical trials are controlled clinical trials conducted in an expanded subject population at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the investigational product has been obtained, are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the product candidate, and to provide an adequate basis for drug approval. Phase III clinical trials usually involve several hundred to several thousand participants. In most cases, the FDA requires two adequate and well-controlled Phase III clinical trials to demonstrate the efficacy of the drug.

The decision to terminate development of an investigational product may be made by either a health authority body, such as the FDA or IRB/ethics committees, or by a company for various reasons. The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor or the clinical monitoring board. This group provides authorization for whether or not a trial may move forward at designated check points. These decisions are based on the limited access to data from the ongoing trial. The suspension or termination of development can occur during any phase of clinical trials if it is determined that the participants or patients are being exposed to an unacceptable health risk. In addition, there are requirements for the registration of ongoing clinical trials of products on public registries and the disclosure of certain information pertaining to the trials, as well as clinical trial results after completion.

New Drug Applications (NDA) – FDA

In order to obtain approval to market a drug in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the product candidate for the proposed indication. The application includes all relevant data available from pertinent nonclinical studies and clinical trials, including negative or ambiguous results, as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational product candidate to the satisfaction of the FDA. In most cases, the NDA must be accompanied by a substantial user fee; there may be some instances in which the user fee is waived. The FDA will initially review the NDA for completeness before it accepts it for filing. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. After the NDA is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review products are reviewed within ten to twelve months. The FDA can extend this review by three months to consider certain late submitted information or information intended to clarify data already provided in the submission. The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP. The FDA may refer applications for novel products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required

specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. Product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs, are required to register and disclose certain clinical trial information (though not specifically required for Phase I trials) on a public website maintained by the U.S. National Institutes of Health ("NIH"). Information related to the product, patient population, phase of investigation, study sites and investigator, and other aspects of the clinical trial is made public as part of the registration. Sponsors are also obligated to disclose the results of these trials after completion. Disclosure of the results of these trials can be delayed until the product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the design and progress of our development programs.

Advertising and Promotion

As set out in the FDA`s website discussion[12] on the "The Prescription Drug Marketing Act of 1987", the FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. A product cannot be commercially promoted before it is approved. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling (package insert) approved by the FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses – that is, uses not approved by the FDA and, therefore, not described in the drug's labeling – because the FDA does not regulate the practice of medicine. However, FDA regulations impose stringent restrictions on manufacturers' communications regarding off-label uses.

Post-Approval Regulations

As set out in the FDA`s website discussion[13] on "Post Marketing Requirements and Commitments", after regulatory approval of a drug is obtained, a company is required to comply with a number of post-approval requirements. For example, as a condition of approval of an NDA, the FDA may require post-marketing testing, including Phase IV clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. In addition, as a holder of an approved NDA, a company would be required to report adverse drug reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling for any of its products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval to assure and preserve the long-term stability of the drug or biological product. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural and substantive record keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon a company

12 https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/prescription-drug-marketing-act-1987

13 https://www.fda.gov/drugs/guidance-compliance-regulatory-information/postmarket-requirements-and-commitments

and any third-party manufacturers that a company may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Controlled Substances

As described in Brian T. Yeh's 2012 publication[14] "The Controlled Substances Act: Regulatory Requirements", the United States federal Controlled Substances Act of 1970 ("CSA"), and its implementing regulations establish a "closed system" of regulations for controlled substances. The CSA imposes registration, security, recordkeeping and reporting, storage, manufacturing, distribution, importation, and other requirements under the oversight of the DEA. The DEA is the federal agency responsible for regulating controlled substances, and requires those individuals or entities that manufacture, import, export, distribute, research, or dispense controlled substances to comply with the regulatory requirements in order to prevent the diversion of controlled substances to illicit channels of commerce.

Facilities that research, manufacture, distribute, import, or export any controlled substance must register annually with the DEA. The DEA registration is specific to the particular location, activity(ies), and controlled substance schedule(s). For example, separate registrations are required for importation and manufacturing activities, and each registration authorizes which schedules of controlled substances the registrant may handle. However, certain coincident activities are permitted without obtaining a separate DEA registration, such as distribution of controlled substances by the manufacturer that produces them.

The DEA categorizes controlled substances into one of five schedules – Schedule I, II, III, IV, or V – with varying qualifications for listing in each schedule. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in treatment in the United States, and lack accepted safety for use under medical supervision. They may be used only in federally-approved research programs and may not be marketed or sold for dispensing to patients in the United States. Pharmaceutical products having a currently accepted medical use that are otherwise approved for marketing may be listed as Schedule II, III, IV, or V substances, with Schedule II substances presenting the highest potential for abuse and physical or psychological dependence, and Schedule V substances presenting the lowest relative potential for abuse and dependence. The regulatory requirements are more restrictive for Schedule II substances than for Schedule III substances. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist in most situations, and cannot be refilled.

The DEA inspects all manufacturing facilities to review security, record keeping, reporting, and handling prior to issuing a controlled substance registration. The specific security requirements vary by the type of business activity and the schedule and quantity of controlled substances handled. The most stringent requirements apply to manufacturers of Schedule I and Schedule II substances. Required security measures commonly include background checks on employees and physical control of controlled substances through storage in approved vaults, safes, and cages, and through use of alarm systems and surveillance cameras. Manufacturing facilities must maintain records documenting the manufacture, receipt, and distribution of all controlled substances. Manufacturers must submit periodic reports to the DEA of the distribution of Schedule I and II controlled substances, Schedule III narcotic substances, and other designated substances. In addition to an importer or exporter registration, importers and exporters must obtain a permit for every import or export of a Schedule I and II substance or Schedule III, IV, and V narcotic, and submit import or export declarations for Schedule III, IV, and V non-narcotics.

For drugs manufactured in the United States, the DEA establishes annually an aggregate quota for the amount of substances within Schedules I and II that may be manufactured or produced in the United States based on the

14 Yeh, BT. The Controlled Substances Act: Regulatory Requirements. https://www.amazon.com/Controlled-Substances-Act-Regulatory-Requirements-ebook/dp/B00BUBS8FC

DEA's estimate of the quantity needed to meet legitimate medical, scientific, research, and industrial needs. The quotas apply equally to the manufacturing of the API, and production of dosage forms.

The states also maintain separate controlled substance laws and regulations, including licensing, record keeping, security, distribution, and dispensing requirements. State Authorities, including Boards of Pharmacy, regulate use of controlled substances in each state. Failure to maintain compliance with applicable requirements, particularly as manifested in the loss or diversion of controlled substances, can result in enforcement action that could have a material adverse effect on our business, operations, and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal prosecution.

Potential sources of API for our cannabinoid products are in the United States, Canada, and certain European countries. We may choose to conduct clinical trials for any of our drug candidates outside the United States subject to regulatory approval. We may decide to develop, manufacture, or commercialize our product candidates in additional countries. As a result, we may also be subject to controlled substance laws and regulations from the various other regulatory agencies in other countries where we develop, manufacture, or commercialize our cannabinoid products in the future.

Marketing Exclusivity

As discussed in the May 19, 2015 issue[15] of the "FDA/CDER SBIA Chronicles" published by the FDA, upon NDA approval of a new chemical entity, which for this purpose is defined as a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot approve any abbreviated new drug application seeking approval of a generic version of that drug. Certain changes to the scope of an approval for a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA for a generic drug that includes the change. A Section 505(b)(2) NDA may be eligible for three-year marketing exclusivity, assuming the NDA includes reports of new clinical studies (other than bioequivalence studies) essential to the approval of the NDA.

An ANDA may be submitted one year before marketing exclusivity expires if a Paragraph IV certification is filed. In this case, the 30 months stay, if applicable, runs from the end of the five-year marketing exclusivity period. If there is no listed patent in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Additionally, six months of marketing exclusivity in the United States is available under Section 505A of the FDCA if, in response to a written request from the FDA, a sponsor submits and the agency accepts requested information relating to the use of the approved drug in the pediatric population. This six-month pediatric exclusivity period is not a stand-alone exclusivity period, but rather is added to any existing patent or non-patent exclusivity period for which the drug product is eligible.

Patent Term Extension

As set out in the FDA`s website discussion[16] "Small Business Assistance: Frequently Asked Questions on the Patent Term Restoration Program", the term of a patent that covers an FDA-approved drug may be eligible for patent-term extension, which provides patent-term restoration as compensation- for the patent term lost during the FDA regulatory review process. The United States Federal Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent-term extension of up to five years beyond the expiration of the patent. The length of the patent-term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and

15 SBIA Chronicles. Patents and Exclusivity. May 19, 2015. https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM447307.pdf

16 https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/small-business-assistance-frequently-asked-questions-patent-term-restoration-program

only one patent applicable to an approved drug may be extended. Similar provisions are available in Canada, Europe, and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

European and Other International Government Regulation

In addition to regulations in the United States and Canada, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Some countries outside of the United States have a similar process that requires the submission of a clinical trial application ("CTA") much like the IND prior to the commencement of human clinical trials. In Europe, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

To obtain regulatory approval to commercialize a new drug under European Union regulatory systems, we must submit a marketing authorization application ("MAA"). The MAA is similar to the NDA, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Latin America, or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary from country to country. Internationally, clinical trials are generally required to be conducted in accordance with GCP, applicable regulatory requirements of each jurisdiction, and the medical ethics principles that have their origin in the Declaration of Helsinki.

Compliance

During all phases of development (pre- and post-marketing), failure to comply with applicable regulatory requirements may result in administrative or judicial sanctions. These sanctions could include the FDA's imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, product detention, or refusal to permit the import or export of products, injunctions, fines, civil penalties, or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect.

Other Special Regulatory Procedures

Fast Track Designation

According to the discussion[17] on the FDA's website on "Fast Track", under the Fast Track program, the sponsor of an IND may request the FDA to designate the drug candidate as a Fast Track drug if it is intended to treat a serious condition and fulfill an unmet medical need. The FDA must determine if the drug candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. Once the FDA designates a drug as a Fast Track candidate, it is required to facilitate the development and expedite the review of that drug by providing more frequent communication with and guidance to the sponsor.

In addition to other benefits such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's review period for filing and reviewing an application does not begin until the last section of the NDA has been submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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17 https://www.fda.gov/ForPatients/Approvals/Fast/ucm405399.htm

Breakthrough Therapy Designation

According to discussion[18] on the FDA's website on "Breakthrough Therapy", the FDA may provide the Breakthrough Therapy designation to drugs to expedite the development and review of a candidate that is planned for use to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A Breakthrough Therapy designation includes all of the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program. The FDA also has an organizational commitment to involve senior management in such guidance.

Orphan Drug Designation

As set out in the FDA website discussion[19] on "Designating an Orphan Product: Drugs and Biological Products", the FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or, if the disease or condition affects more than 200,000 individuals in the United States, if there is no reasonable expectation that the cost of developing and making the drug would be recovered from sales in the United States. As set out in the EMA's website discussion[20] on "Orphan Designation", in the European Union, the EMA's Committee for Orphan Medicinal Products grants Orphan Drug Designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union community. Additionally, the Orphan Drug Designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug.

In the United States, Orphan Drug Designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax credits for certain research, and user fee waivers under certain circumstances. In addition, if a product receives the first FDA approval for the indication for which it has Orphan Drug Designation, the product is entitled to seven years of market exclusivity, which means the FDA may not approve any other application for the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. In the European Union, Orphan Drug Designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug approval. This period may be reduced to six years if the Orphan Drug Designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan Drug Designation must be requested before submission of an application for marketing approval. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Priority Review (United States) and Accelerated Assessment (European Union)

Based on results of the Phase III clinical trial(s) submitted in an NDA, upon the request of an applicant, a priority review designation may be granted to a product by the FDA, which sets the target date for FDA action on the application at six months from the FDA's decision on priority review application, or eight months from the NDA filing. According to the FDA website discussion[21] on "Priority Review", this status is given where preliminary estimates indicate that a product, if approved, has the potential to provide a safe and effective therapy where no satisfactory alternative therapy exists, or a significant improvement compared to marketed products is possible. If criteria are not met for priority review, the standard FDA review period is ten months from the FDA's decision on

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18 https://www.fda.gov/ForPatients/Approvals/Fast/ucm405397.htm

19 https://www.fda.gov/industry/developing-products-rare-diseases-conditions/designating-orphan-product-drugs-and-biological-products

20 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&mid=WC0b01ac0580b18a41

21 https://www.fda.gov/forpatients/approvals/fast/default.htm

priority review application, or 12 months from the NDA filing. The priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

According to the EMA website discussion[22] on "Accelerated Assessment", under the Centralised Procedure in the European Union, the maximum timeframe for the evaluation of a MAA is 210 days (excluding "clock stops," when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use ("CHMP"). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, which takes into consideration: the seriousness of the disease (e.g., heavy-disabling or life-threatening diseases) to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days.

Accelerated Approval

As set out in the FDA website discussion[23] on "Accelerated Approval", under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. This approval mechanism is provided for under 21CRF314 Subpart H and Subpart E. In this case, clinical trials are conducted in which a surrogate endpoint is used as the primary outcome for approval. A surrogate endpoint is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. This surrogate endpoint substitutes for a direct measurement of how a patient feels, functions, or survives and is considered reasonably likely to predict clinical benefit. Such surrogate endpoints may be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. When the Phase 4 commitment is successfully completed, the biomarker is deemed to be a surrogate endpoint. Failure to conduct required post-approval studies or confirm a clinical benefit during post-marketing studies, could lead the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Regulatory Framework in Canada for Cannabis

The production, processing, and sale of the Corporation's CardiolRx and Cortalex products are subject to regulation under Canada's regulatory framework for cannabis.

Cannabis Act and Cannabis Regulations

On December 13, 2016, the Task Force on Cannabis Legalization and Regulation (the "Task Force"), which was established by the Canadian Federal Government to seek input on the design of a new system to legalize, regulate and restrict access to cannabis, published its report outlining its recommendations. On April 13, 2017, the Canadian Federal Government released Bill C 45, an Act respecting cannabis and to amend the Controlled Drugs and Substances Act, the Criminal Code and other Acts (the "Cannabis Act"), which proposed the enactment of the Cannabis Act (Canada) to regulate the production, distribution, and sale of cannabis for unqualified adult use. On November 27, 2017, the House of Commons passed Bill C 45. On June 20, 2018, the Senate approved Bill C 45 and the Act received Royal Assent on June 21, 2018. The Cannabis Act came into force on October 17, 2018.

On November 22, 2017, Health Canada released for public consultation its proposed approach to the regulation of cannabis (the "Cannabis Regulations"). The purpose of the consultation paper was to solicit public feedback on an initial set of regulatory proposals that Health Canada was considering and was focused on the regulations that would facilitate the coming into force of the proposed Cannabis Act. Health Canada's consultation addressed

22 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000955.jsp&mid=WC0b01ac05809f843a

23 https://www.fda.gov/ForPatients/Approvals/Fast/ucm405447.htm

licensing, security requirements for producers and their facilities, product standards, labelling and packaging, and the proposed cannabis tracking system. It also addressed cannabis for medical purposes and health products containing cannabis. Health Canada proposed a risk-based approach to regulation, balancing the protection of health and safety of Canadians while enabling a competitive legal industry made up of large and small enterprises in all regions of Canada producing quality-controlled cannabis. On July 11, 2018, Health Canada released the regulations of cannabis in Canada Gazette, Part II, Volume 152, Number 14 – SOR/2018 144.

In June 2019, amended Cannabis Regulations were published outlining changes to the Cannabis Act that came into force October 17, 2019. As of October 17, 2019, The Cannabis Act grants authorization to licenced organization, to produce and sell “edibles containing cannabis”, “topical cannabis” and “cannabis concentrates” no earlier than December 17, 2019. The regulations provide for the addition of three product classes: edibles, extracts and topicals.

The Regulations are divided into the following seven major categories:

1. Licenses, Permits and Authorizations;
2. Security Clearances;
3. Reporting and Disclosure;
4. Cannabis Products;
5. Packaging and Labelling;
6. Access to Cannabis for Medical Purposes; and
7. Drugs Containing Cannabis.

On October 17, 2020, amendments were made to the Cannabis Act and Regulations including the removal of cannabis oil as a separate product class under Schedule 4 of the Cannabis Act. Oil products have been reclassified either as cannabis extracts, edibles, or topical products, depending on the intended use. Label requirements under the Regulations were amended during this period.

On June 19, 2019, Health Canada opened a consultation on a potential new market classification for cannabis health products (“CHP”) that would not require practitioner oversight. The contemplated regulatory pathway would allow for specific health claims that would need to be supported by scientific evidence. Provinces and territories would continue to have the flexibility to authorize CHP sellers operating at any physical location. This could allow for CHPs for human and veterinary uses to be sold at pharmacies, veterinary clinics, pet stores, or livestock medicine outlets under strict conditions that respect federal requirements. Strictly controlled online sales would also remain possible. This consultation closed on September 3, 2019.

On February 27, 2020, the Government of Canada announced a call for nomination of a new Science Advisory Committee for Health Products Containing Cannabis which will provide independent scientific and clinical advice to support the Department’s consideration of appropriate safety, efficacy, and quality standards for health products containing cannabis, including the conditions under which these products would be suitable to be used without practitioner oversight. Nominations for the Science Advisory Committee were to be made by April 9, 2020. On November 18, 2020, Health Canada released the membership list and biographies of the science advisory committee on health products containing cannabis. The science advisory committee met on November 2 and 3, 2020 to review the current regulatory framework for cannabis and potential alternative available regulatory pathways for prescription drugs, non-prescription drugs, natural health products and veterinary drugs. On November 30, 2020 and December 2, 2020 the committee met to discuss the evidence for cannabis use in humans, adverse reactions of cannabis, potential products for human use (non-prescription) and veterinary use. Health Canada updated their disclosed Science Advisory Committee meetings on January 28th, 2022 to include the discussions held January 19, 2021 , March 3, 2021 and June 17, 2021. The discussions focused on current state of evidence in animals, a review of the Prescription Drug List and how cannabis products currently sit within Health Canada’s current regulatory framework, the proposed amendments to the Cannabis regulations to regulate non-therapeutic cannabis research and on defining CBD-containing products on which to focus initial evidence review

efforts included purified CBD, CBD isolates, CBD-rich cannabis extracts and synthetic CBD, which meet certain criteria.

The Cannabis Act, which came into force on October 17, 2018, requires that the Minister of Health initiate a review of the Act by October 17, 2021, three years following the legalization of recreational cannabis for adult use. As of March 22, 2022, no legislative review has occurred. Health Canada has commented that preparations are underway for the launch of the legislative review.

The impact of any regulatory changes on the Corporation's business is unknown. See "Risk Factors – Changes in laws and regulations".

Licenses, Permits and Authorizations

The Regulations establish different types of authorizations based on the activity being undertaken and, in some cases, the scale of the activity. Rules and requirements for different categories of authorized activities are intended to be proportional to the public health and safety risks posed by each category of activity. The types of authorizations include: (i) cultivation; (ii) processing; (iii) sale to the public for medical purposes and non-medical purposes in provinces and territories that have not enacted a retail framework; (iv) analytical testing; (v) import/export; and (vi) research.

Security Clearances

Select personnel (including individuals occupying a "key position", such as directors, officers, large shareholders, and individuals identified by the Minister of Health) associated with certain licenses issued under the Cannabis Act are obliged to hold a valid security clearance issued by the Minister of Health. The Regulations enable the Minister of Health to refuse to grant security clearances to individuals with associations to organized crime or with past convictions for, or an association with, drug trafficking, corruption, or violent offences.

Reporting and Disclosure

Under the Cannabis Act, the Minister of Health is authorized to establish and maintain a national cannabis tracking system. The purpose of this system is to track cannabis throughout the supply chain to help prevent diversion of cannabis into, and out of, the legal market. The Regulations provide the Minister of Health with the authority to make a ministerial order that would require certain persons named in such order to report specific information about their authorized activities with cannabis, in the form and manner specified by the Minister.

Cannabis Products

The Regulations permit the sale to the public by licensed entities of dried cannabis, cannabis oil, fresh cannabis, cannabis plants, cannabis seeds, edibles containing cannabis, topical cannabis and cannabis concentrates (extracts). The Regulations acknowledge that a range of product forms should be enabled to help the legal industry displace the illegal market.

A solution containing 100% pharmaceutically manufactured cannabidiol (CBD) and no tetrahydrocannabinol (THC) is classified as "Cannabis" under the Cannabis Act. Specifically, Schedule 1 of the Cannabis Act defines "Cannabis" to include "any substance that is identical to any phytocannabinoid produced by, or found in, such a plant [cannabis], regardless of how the substance was obtained." Cannabidiol, pharmaceutically manufactured, is identical to cannabidiol found in the cannabis plant.

Packaging and Labeling

The Regulations set out requirements pertaining to the packaging and labelling of cannabis products. Such requirements promote informed consumer choice and allow for the safe handling and transportation of cannabis. The Regulations require all cannabis products to be packaged in a manner that is tamper-evident and child-resistant.

While minor allowances for branding are permitted, Health Canada has mandated strict limits on the use of colours, graphics, and other special characteristics of packaging, and products are required to be labelled with specific information about the product, contain mandatory health warnings similar to tobacco products, and be marked with a clearly recognizable standardized cannabis symbol. All packaging is required to contain a standardized cannabis symbol for those products containing greater than 10 ppm of THC.

Drugs Containing Cannabis

Health Canada is following a scientific, evidenced-based approach for the oversight of health products with cannabis that are approved with health claims, including prescription and non-prescription drugs, natural health products, veterinary drugs and veterinary health products, and medical devices. Health products can only be sold if they have been approved by Health Canada following a scientific review.

Provincial and Territorial Regulatory Regimes

While the Cannabis Act provides for the regulation of the commercial production of cannabis for recreational purposes and related matters by the federal government, the Cannabis Act states that the provinces and territories of Canada have authority to regulate other aspects of recreational cannabis (similar to what is currently the case for liquor and tobacco products), such as sale and distribution, minimum age requirements, pricing and promotion, places where cannabis can be consumed, and a range of other matters.

The government of each Canadian province and territory has in place regulatory regimes for the distribution and sale of cannabis for consumer purposes within those jurisdictions.

RISK FACTORS

Investing in our Common Shares involves significant risks. You should carefully consider the risks described below, which are qualified in their entirety by reference to, and must be read in conjunction with, the detailed information appearing elsewhere in this AIF. The risks and uncertainties described below are those we currently believe to be material, but they are not the only ones we face. If any of the following risks, or any other risks and uncertainties that we have not yet identified or that we currently consider not to be material, actually occur, or become material risks, our business, prospects, financial condition, results of operations, and cash flows could be materially and adversely affected.

The Corporation's prospects depend on the success of our acute myocarditis and subcutaneous product candidates which are at early stages of development, and the success of our Phase II/III trial in high-risk patients hospitalized with COVID-19. We do not expect to generate revenue for several years, if at all, from the acute myocarditis and subcutaneous product candidates.

Given the early stage of development of our acute myocarditis and subcutaneous product candidates, and the uncertainty inherent in clinical trials, we can make no assurance that our research and development programs will result in regulatory approval or commercially viable products. To achieve profitable operations, we, alone or with others, must successfully develop, gain regulatory approval, and market our future product candidates, if approved. We currently have no products that have been approved by the FDA, Health Canada, or any similar regulatory authority. To obtain regulatoryapprovals for our product candidates being developed and to achieve commercial success, if approved, clinical trials must demonstrate that the product candidates are safe for human use and that they demonstrate efficacy, as determined by the appropriate regulatory agency.

Many product candidates never reach the stage of clinical testing and even those that do have only a small chance of successfully completing clinical development and gaining regulatory approval. Product candidates may fail for a number of reasons, including, but not limited to, being unsafe for human use or due to the failure to provide therapeuticbenefits equal to or better than the standard of treatment at the time of testing. Positive results of early pre-clinical research may not be indicative of the results that will be obtained in later stages of pre-clinical or clinical research. Interim results of a clinical trial do not necessarily predict final results. Similarly, positive results from early-stage clinical trials may not be indicative of favorable outcomes in later-stage clinical trials. We can make no assurance that any future studies, if undertaken, will yield favorable results. The early stage of our acute

myocarditis and subcutaneous product development makes it particularly uncertain whether any of these product development efforts will prove to be successful and meet applicable regulatory requirements, and whether any of our product candidates will receive the requisite regulatory approvals, be capable of being manufactured at a reasonable cost, or be successfully marketed, if approved. If we are successful in developing our current and future product candidates into approved products, we will still experience many potential obstacles such as the need to develop or obtain manufacturing, marketing, and distribution capabilities. If we are unable to successfully commercialize any of our product candidates, our financial condition and results of operations may be materially and adversely affected.

The Continued Development of the Corporation will Require Additional Financing. If we fail to raise such capital, it could result in the delay or indefinite postponement of our current business strategy, or we could cease to carry on business.

There is no guarantee that the Corporation will be able to execute on its strategy. The continued development of the Corporation will require additional financing. The failure to raise needed capital could result in the delay or indefinite postponement of current business strategy or the Corporation ceasing to carry on business. There can be no assurance that additional capital or other types of financing will be available if needed or that, if available, the terms of such financing will be favourable to the Corporation. If additional funds are raised through issuances of equity or convertible debt securities, existing shareholders could suffer significant dilution, and any new equity securities issued could have rights, preferences, and privileges superior to those of holders of common shares. In addition, from time to time, the Corporation may enter into transactions to acquire assets or the shares of other Companies. These transactions may be financed wholly or partially with debt, which may temporarily increase the Corporation's debt levels above industry standards. Any debt financing secured in the future could involve restrictive covenants relating to capital raising activities and other financial and operational matters, which may make it more difficult for the Corporation to obtain additional capital and to pursue business opportunities, including potential acquisitions. Debt financings may contain provisions, which, if breached, may entitle lenders to accelerate repayment of loans and there is no assurance that the Corporation would be able to repay such loans in such an event or prevent the enforcement of security granted pursuant to such debt financing. The Corporation may require additional financing to fund its operations to the point where it is generating positive cash flows. Negative cash flow may restrict the Corporation's ability to pursue its business objectives.

In the event of bankruptcy, liquidation, or reorganization of Cardiol, holders of its debt and its trade creditors will generally be entitled to payment of their claims from the assets of Cardiol before any assets are made available for distribution to Cardiol or its shareholders. The common shares are effectively subordinated to the debt and other obligations of Cardiol.

We intend to expend our limited resources to pursue our current product candidates, and may fail to capitalize on other product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are focusing on research programs relating to our current product candidates, which concentrates the risk of product failure in the event that our current product candidates prove to be unsafe or ineffective or inadequate for clinical development or commercialization. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on proprietary research and development programs relating to our current product candidates may not yield any commercially viable products.

We have a history of operating losses and may never achieve or maintain profitability in the future.

Cardiol's net loss for the year ended December 31, 2021 was $31,638,244 and for the year ended December 31, 2020 was $20,640,935. It is possible that we will never have sufficient product sales revenue to achieve profitability. We expect to continue to incur losses for at least the next several years as we or our collaborators and licensees pursue clinical trials and research and development efforts. To become profitable, we, either alone or with our collaborators and licensees, must successfully market our pharmaceutical cannabidiol and develop, manufacture, and market our current product candidates, as well as continue to identify, develop, manufacture, and market new product candidates. It is possible that we will never have significant product sales revenue or receive royalties on

our licensed product candidates. If funding is insufficient at any time in the future, we may not be able to develop or commercialize our products, take advantage of business opportunities, or respond to competitive pressures.

We currently do not earn any revenues from our drug candidates and are therefore considered to be in the development stage. The continuation of our research and development activities and the commercialization of the targeted therapeutic products are dependent upon our ability to successfully finance and complete our research and development programs through a combination of equity financing and payments from strategic partners. We have no current sources of significant payments from strategic partners.

We rely on Management and need additional key personnel to grow our business, and the loss of key employees or inability to hire key personnel could harm our business.

The loss of David Elsley, our President and CEO, or other key members of our staff, could harm us. We also depend on our scientific and clinical collaborators and advisors, all of whom have outside commitments that may limit their availability to us. In addition, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled scientific, managerial, medical, clinical, and regulatory personnel, particularly as we expand our activities and seek regulatory approvals for clinical trials. We routinely enter into consulting agreements with our scientific and clinical collaborators and advisors, key opinion leaders, and academic partners in the ordinary course of our business. We also enter into contractual agreements with physicians and institutions who will recruit patients into our clinical trials on our behalf in the ordinary course of our business. Notwithstanding these arrangements, we face significant competition for these types of personnel from other companies, research and academic institutions, government entities, and other organizations. We cannot predict our success in hiring or retaining the personnel we require for continued growth. The loss of the services of any of our executive officers or other key personnel could potentially harm our business operating results, or financial condition.

Clinical trials for our product candidates are expensive, time consuming, uncertain, and susceptible to change, delay or termination.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we mustconduct pre-clinical studies in animals and extensive clinical trials in humans to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive and difficult to design and implement, can take many years to complete, and has uncertain outcomes. The outcome of pre-clinical studies and early clinical trials may not predict the success of later clinical trials and interim results of a clinical trial do not necessarily predict final results.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials. We do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any of our product candidates in any jurisdiction. A product candidate may failfor safety or efficacy reasons at any stage of the testing process. A major risk we face is the possibility that none of our product candidates under development will successfully gain market approval from the FDA, Health Canada, or other regulatory authorities, resulting in us being unable to derive any commercial revenue from them after investing significant amounts of capital in multiple stages of pre-clinical and clinical testing.

Even if the results of our clinical trials are favourable, the clinical trials for a number of our product candidates are expected to continue for several years and may take significantly longer to complete. In addition, we, the FDA, Health Canada or other regulatory authorities, including state and local authorities may suspend, delay, or terminate our clinical trials at any time, require us to conduct additional clinical trials, require a particular clinical trial to continue for a longer duration than originally planned, require a change to our development plans such that we conduct clinical trials or a product candidate in a different order, e.g., in a step-wise fashion rather than running two trials of the same product candidate in parallel. Any of the foregoing could have a material adverse effect on our business, results of operations, and financial condition.

If we experience delays in clinical testing, we will be delayed in commercializing our product candidates, if approved, and our business may be substantially harmed.

We cannot predict whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before us, which would impair our ability to successfully commercialize our product candidates and may harm our financial condition, results of operations, and prospects. The commencement and completion of clinical trials for our products may be delayed for a number of reasons, including delays related, but not limited, to:

- failure by regulatory authorities to grant permission to proceed or placing the clinical trial on hold;
- difficulties obtaining institutional review board ("IRB") or ethics committee approval to conduct a clinical trial at aprospective site;
- import/export and research restrictions for cannabinoid-based pharmaceuticals delaying or preventing clinical trialsin various geographical jurisdictions;
- patients failing to enroll or remain in our trials at the rate we expect;
- suspension or termination of clinical trials by regulators for many reasons, including concerns about patient safetyor failure of our contract manufacturers to comply with cGMP requirements;
- delays or failure to obtain clinical supply from contract manufacturers of our product candidates necessary to conduct clinicaltrials;
- product candidates demonstrating a lack of safety or efficacy during clinical trials;
- patients choosing an alternative treatment for the indications for which we are developing any of our productcandidates or participating in competing clinical trials and/or scheduling conflicts with participating clinicians;
- patients failing to complete clinical trials due to dissatisfaction with the treatment, side effects or other reasons;
- reports of clinical testing on similar technologies and products raising safety and/or efficacy concerns;
- clinical investigators not performing our clinical trials on their anticipated schedule, dropping out of a trial, or employing methods not consistent with the clinical trial protocol, and regulatory requirements, or other third parties not performing data collection and analysis in a timely or accurate manner;
- failure of our CROs to satisfy their contractual duties or meet expected deadlines;
- inspections of clinical trial sites by regulatory authorities or IRBs, or ethics committees finding regulatory violations that require us to undertake corrective action, resulting in suspension or termination of one or more sites or the imposition of a clinical hold on the entire study;
- one or more IRBs or ethics committees rejecting, suspending, or terminating the study at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial; or
- failure to reach agreement on acceptable terms with prospective clinical trial sites.

In addition, a clinical trial may be suspended or terminated by us, the FDA, IRBs, ethics committees, data safety monitoring boards, or other foreign regulatory authorities overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols;
- inspection of the clinical trial operations or clinical trial sites by the FDA, the European Medicines Agency, or other foreign regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, including any safety issues that could be identified in our ongoing pre-clinical studies;
- adverse side effects or lack of effectiveness; and
- changes in government regulations or administrative actions.

Our product development costs will increase if we experience delays in testing or approval or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend study protocols to reflect these changes. Amendments may require us to resubmit our study protocols to regulatory authorities, IRBs, or ethics committees for re-examination, which may impact the cost, timing, or successful completion of that trial. Delays or increased product development costs may have a material adverse effect on our business, financial condition, and prospects.

Negative results from clinical trials or studies of others and adverse safety events involving the targets of our product candidates may have an adverse impact on our future commercialization efforts.

From time to time, studies or clinical trials on various aspects of biopharmaceutical products are conducted by academic researchers, competitors, or others. The results of these studies or trials, when published, may have a significant effect on the market for the biopharmaceutical product that is the subject of the study. The publication of negative results of studies or clinical trials or adverse safety events related to our product candidates, or the therapeutic areas in which our product candidates compete, could adversely affect the price of the securities and our ability to finance future development of our product candidates, and our business and financial results could be materially and adversely affected.

Our activities are subject to comprehensive regulation, including under healthcare laws and compliance requirements.

In the United States, our activities are potentially subject to additional regulation by various federal, state, and local authorities in addition to the FDA, including, among others, the Centers for Medicare and Medicaid Services, other divisions of Health and Human Services, or HHS, (for example, the Office of Inspector General), the Department of Justice, and individual United States Attorney offices within the Department of Justice, and state and local governments.

In Canada, our activities are potentially subject to additional regulation by various federal and provincial authorities in addition to Health Canada, including among others, and publicly-mandated organizations given a provincial sales license under the Cannabis Act.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private “qui tam” actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into supply contracts, including government contracts, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

We may not achieve our projected development goals in the time frames and cost estimates we announce and expect.

We set goals for, and make public statements regarding, the expected timing and costs of the accomplishment of objectives material to our success, the commencement and completion of clinical trials and the expected costs to develop our product candidates. The actual timing and costs of these events can vary dramatically due to factors within and beyond our control, such as delays or failures in our clinical trials, issues related to the manufacturing of drug supply, uncertainties inherent in the regulatory approval process, market conditions, and interest by partners in our product candidates among other things. We may not make regulatory submissions or receive regulatory approvals as planned; our clinical trials may not be completed; or we may not secure partnerships for any of our product candidates. Any failure to achieve one or more of these milestones as planned would have a material adverse effect on our business, financial condition, and results of operations.

Unpredictable and volatile market price for common shares

The market price for common shares may be volatile and subject to wide fluctuations in response to numerous factors, many of which are beyond our control, including the following:

- actual or anticipated fluctuations in our quarterly results of operations;
- recommendations by securities research analysts;
- changes in the economic performance or market valuations of companies in the industry in which we operate;
- addition or departure of our executive officers and other key personnel;
- sales or perceived sales of additional common shares;
- significant acquisitions or business combinations, strategic partnerships, joint ventures, or capital commitments byor involving us or our competitors;
- operating and share price performance of other companies that investors deem comparable to us
- fluctuations to the costs of vital production materials and services;
- changes in global financial markets and global economies and general market conditions, such as interest ratesand pharmaceutical product price volatility;
- operating and share price performance of other companies that investors deem comparable to the Corporation orfrom a lack of market comparable companies; and
- news reports relating to trends, concerns, technological or competitive developments, regulatory changes, andother related issues in our industry or target markets.

Financial markets have recently experienced significant price and volume fluctuations that have particularly affected the market prices of equity securities of companies and that have often been unrelated to the operating performance, underlying asset values, or prospects of such companies. Accordingly, the market price of the common shares may decline even if our operating results, underlying asset values or prospects have not changed. Additionally, these factors, as well as other related factors, may cause decreases in asset values that are deemed to be other than temporary, which might result in impairment losses. There can be no assurance that continuing fluctuations in price and volume will not occur. If such increased levels of volatility and market turmoil continue, our operations could be adversely affected, and the trading price of the common shares might be materially adversely affected.

Securities or industry analysts may publish inaccurate or unfavorable research reports, stock price and trading volume could decline.

The trading market for our common shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, our share price would likely decline. If one or more of these analysts cease coverage of our Corporation or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our share price and trading volume to decline.

If we fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of our intellectual property rights would diminish.

Our success, competitive position, and future revenues will depend in part on our ability and the abilities of our licensors to obtain and maintain patent protection for our products, methods, processes, and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights, and to operate without infringing the proprietary rights of third parties.

To date, we have exclusive rights to certain Canadian, United States, and other foreign intellectual property. We anticipate filing additional patent applications in Canada, the United States, and in other countries, as appropriate. However, we cannot predict:

- the degree and range of protection any patents will afford us against competitors, including whether third partieswill find ways to invalidate or otherwise circumvent our patents;
- if and when patents will issue;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings which may be costly whether we win or lose.

Our success also depends upon the skills, knowledge, and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents may be unobtainable or difficult to obtain, we rely on trade-secret protection and confidentiality agreements. To this end, it is our policy generally to require our employees, consultants, advisors, and contractors to enter into agreements which prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries, and inventions important to our business. These agreements may not provide adequate protection for our trade secrets, know-how, or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. If any of our trade secrets, know-how, or other proprietary information is disclosed, the value of our trade secrets, know-how, and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

Owning a patent does not per se prevent competition. To stop third-party infringement, a patent owner and/or licensee must take steps to enforce the patent through court proceedings. This can be a very lengthy and costly process and the outcome may be uncertain.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The Canadian Intellectual Property Office (“CIPO”) and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Periodic maintenance fees on any issued patent are due to be paid to CIPO and various foreign national or international patent agencies in several stages over the lifetime of the patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents.

If we fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

While a patent may be granted by a national patent office, there is no guarantee that the granted patent is valid. Options exist to challenge the validity of the patent which, depending upon the jurisdiction, may include re-examination, opposition proceedings before the patent office, and/or invalidation proceedings before the relevant court. Patent validity may also be the subject of a counterclaim to an allegation of patent infringement.

Pending patent applications may be challenged by third parties in protest or similar proceedings. Third parties can typically submit prior art material to patentability for review by the patent examiner. Regarding Patent Cooperation Treaty applications, a positive opinion regarding patentability issued by the International Searching Authority does not guarantee allowance of a national application derived from the Patent Cooperation Treaty application. The coverage claimed in a patent application can be significantly reduced before the patent is issued, and the patent's scope can be modified after issuance. It is also possible that the scope of claims granted may vary from jurisdiction to jurisdiction.

The grant of a patent does not have any bearing on whether the invention described in the patent application would infringe the rights of earlier filed patents. It is possible to both obtain patent protection for an invention and yet still infringe the rights of an earlier granted patent.

We may become subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Our commercial success depends upon our ability to develop, manufacture, market, and sell our product candidates, and to use our related proprietary technologies without violating the intellectual property rights of others. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates, including interference or derivation proceedings before CIPO, United States Patent and Trademark Office, and other applicable patents offices in foreign jurisdictions. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Under certain circumstances, we could be forced, including by court order, to cease commercializing the applicable product candidate. In addition, in any such proceeding or litigation, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Therefore, we have filed applications and/or obtained patents only in key markets, such as the United States, Canada, and certain countries internationally. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and their products may compete with ours.

We rely and will continue to rely on third parties to conduct and monitor many of our pre-clinical studies and our clinical trials, and their failure to perform as required could cause substantial harm to our business.

We rely and will continue to rely on third parties to conduct a significant portion of our pre-clinical and clinical development activities. Pre-clinical activities include in vivo studies providing access to specific disease models, pharmacology and toxicology studies, and assay development. Clinical development activities include trial design, regulatory submissions, clinical patient recruitment, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management, contract manufacturing, and quality assurance. If there is any dispute or disruption in our relationship with third parties, or if they are unable to provide quality services in a timely manner and at a feasible cost, our active development programs will face delays. Further, if any of these third parties fails

to perform as we expect or if their work fails to meet regulatory requirements, our testing could be delayed, cancelled, or rendered ineffective.

Failure to comply with cannabis laws in Canada and controlled substances laws elsewhere may adversely affect the results of our business operations.

Our ability to successfully produce our product candidates is dependent on extensive ongoing regulatory compliance and reporting requirements by the DEA, the FDA, Health Canada and other foreign regulatory authorities. Failure to comply with such requirements could have a material adverse impact on our business, financial condition and operating results. There is no assurance that regulatory approval will be granted or continued for our product candidates. Should regulatory approval not be granted or continued, our business, financial condition and operating results would be materially adversely affected. Even if we receive regulatory approval for our product candidates, this approval may carry conditions that limit the market for the products or put the products at a competitive disadvantage relative to alternative therapies. For instance, regulatory approval may limit the indicated uses for which we can market a product (if approved) or the patient population that may utilize the product or may be required to carry a warning on its packaging. Once a product candidate is approved, we remain subject to continuing regulatory obligations, such as safety reporting requirements and additional post-marketing obligations, including regulatory oversight of promotion and marketing.

If our operations are found to be in violation of any of the federal and state laws or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private “qui tam” actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into supply contracts, including government contracts, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates (if approved) are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

In both domestic and foreign markets, the development, formulation, manufacturing, packaging, labelling, handling, distribution, import, export, licensing, sale, and storage of pharmaceuticals are affected by a body of laws, governmental regulations, administrative determinations, including those by the Canadian Food Inspection Agency and the FDA, court decisions, and similar constraints. Such laws, regulations and other constraints can exist at the federal, provincial or local levels in Canada and at all levels of government in foreign jurisdictions. We and our partners may be required to incur significant costs to comply with such laws and regulations in the future, and such laws and regulations may have an adverse effect on the business. The failure of us or our partners to comply with current or future regulatory requirements could lead to the imposition of significant penalties or claims and may have a material adverse effect on our business. In addition, the adoption of new laws, regulations or other constraints or changes in the interpretations of such requirements might result in significant compliance costs or lead us and our partners to discontinue product development and could have an adverse effect on our business.

Our ability to research, develop, and commercialize product candidates, if approved, is dependent on our ability to obtain and maintain licenses relating to possession and supply of controlled substances

Our research and manufacturing facilities are located in Canada. In Canada, various licenses are required to produce pharmaceutical cannabinoids. Our continued ability to research, develop, and commercialize our product candidates is dependent on our ability to obtain, and subsequently maintain, licenses relating to possession and supply of controlled substances. Loss of such licenses or inability to obtain such licenses could have an adverse effect on our business.

Controlled substance legislation differs between countries and legislation in certain countries may restrict or limit ability to sell products

Most countries are parties to the Single Convention on Narcotic Drugs 1961, which governs international trade and domestic control of narcotic substances, including cannabis. Countries may interpret/implement their treaty obligations in a way that creates a legal obstacle to our obtaining marketing approval for our product candidates in those countries. These countries may not be willing or able to amend or otherwise modify their laws and regulations to permit our product candidates to be marketed, if approved, or achieving such amendments to the laws and regulations may take a prolonged period of time.

Changes in laws and regulations may make compliance challenging, costly and time consuming for us.

Our operations are subject to a variety of laws, regulations and guidelines relating to pharmacology, cannabinoids, and drug delivery, as well as laws and regulations relating to health and safety, the conduct of operations, and the protection of the environment. While, to our knowledge, we are currently in material compliance with all such laws, changes to such laws, regulations and guidelines due to matters beyond our control may cause adverse effects to our operations and financial condition. These changes may require us to incur substantial costs associated with legal and compliance fees and ultimately require us to alter our business plan.

In addition, if the governments of Canada or the U.S. were to enact or amend laws relating to our industry, it may decrease the size of, or eliminate entirely, the market for our product candidates, if approved, may introduce significant new competition into the market and may otherwise potentially materially and adversely affect our business, results of operations, and financial condition.

Tax and accounting requirements may change in ways that are unforeseen to the Corporation and the Corporation may face difficulty or be unable to implement and/or comply with any such changes.

The Corporation is subject to numerous tax and accounting requirements, and changes in existing accounting or taxation rules or practices, or varying interpretations of current rules or practices, could have a significant adverse effect on the Corporation's financial results, the manner in which it conducts its business, or the marketability of any of its products. In the future, the geographic scope of the Corporation's business may expand, and such expansion will require the Corporation to comply with the tax laws and regulations of multiple jurisdictions. Requirements as to taxation vary substantially among jurisdictions. Complying with the tax laws of these jurisdictions can be time consuming and expensive and could potentially subject the Corporation to penalties and fees in the future if the Corporation were to inadvertently fail to comply. In the event the Corporation was to inadvertently fail to comply with applicable tax laws, this could have a material adverse effect on the business, results of operations, and financial condition of the Corporation.

Management may not be able to successfully implement adequate internal controls over financial reporting ("ICFR").

Proper systems of internal controls over financial accounting and disclosure are critical to the operation of a public company. However, the Corporation does not expect that its Disclosure, Controls, and Procedures or ICFR will prevent all error and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. Due to the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and may not be detected in a timely manner or at all. If the Corporation cannot provide reliable financial reports or prevent fraud, its reputation and operating results could be materially adversely affected, which could cause investors to lose confidence in the Corporation's reported financial information, which in turn could result in a reduction in the value of the common shares.

Medical research of cannabinoids remains limited.

Research in Canada, the United States, and internationally regarding the medical benefits, viability, safety, efficacy, and dosing of cannabinoids remains limited. There have been relatively few clinical trials conducted on the benefits of cannabinoids. The statements made in this MD&A concerning the potential medical benefits of cannabinoids are based on published articles and reports with details of research studies and clinical trials. As a result, the statements made in this MD&A are subject to the experimental parameters, qualifications, and limitations in the studies that have been completed.

Although the Corporation believes that the articles and reports with details of research studies and clinical trials referenced in this MD&A reasonably support its beliefs regarding the medical benefits, viability, safety, efficacy, and dosing of cannabinoids as set out in this MD&A, future research and clinical trials in pursuit of our development efforts may prove such statements to be incorrect, or could raise concerns regarding and perceptions relating to, cannabinoids. Given these risks, uncertainties and assumptions, undue reliance should not be placed on such articles and reports. Future research studies and clinical trials may draw opposing conclusions to those stated in this MD&A or reach negative conclusions regarding the viability, safety, efficacy, dosing, social acceptance or other facts and perceptions related to cannabinoids, which could have a material adverse effect on the demand for the Corporation's product candidates, if approved, and therefore materially impact the business, financial condition, and operating results of the Corporation.

Pharmaceutical cannabinoid and other product candidates, if approved, may be unable to achieve the expected market acceptance and, consequently, limit our ability to generate revenue from new products.

Even if product development is successful and regulatory approval is obtained, our ability to generate significant revenue depends on the acceptance of our products by physicians and patients. We cannot assure you that our pharmaceutical cannabinoid product candidates will achieve the expected market acceptance and revenue if and when they obtain the requisite regulatory approvals. The market acceptance of any product depends on a number of factors, including the indication statement and warnings approved by regulatory authorities on the product label, continued demonstration of efficacy and safety in commercial use, physicians' willingness to prescribe the product, reimbursement from third-party payers such as government health care systems and insurance companies, the price of the product, the nature of any post-approval risk management plans mandated by regulatory authorities, competition, and marketing and distribution support. Any factors preventing or limiting the market acceptance of our products could have a material adverse effect on our business, results of operations, and financial condition.

We currently have no commercialized products.

Even if we obtain regulatory approval for a product candidate, our future success will still depend on our ability to successfully commercialize our products, which depends on a number of factors beyond our control, including the willingness of physicians to prescribe our products to patients, payers' willingness and ability to pay for the product, the level of pricing achieved, patients' response to our products, the ability of our marketing partners to generate sales, and our ability to manufacture products on a cost-effective and efficient basis. If we are not successful in the commercialization of our products, our business, results of operations, and financial condition may be harmed.

We rely on contract manufacturers over whom we have limited control. If we are subject to quality, cost, or delivery issues with the pre-clinical and clinical grade materials supplied by contract manufacturers, our business operations could suffer significant harm.

We currently have no manufacturing experience and rely on Dalton and other contract manufacturing organizations ("CMOs") to manufacture our product candidates for pre-clinical studies and clinical trials. We rely on CMOs for manufacturing, filling, packaging, storing, and shipping of product candidates in compliance with current good manufacturing practice, or cGMP, regulations applicable to our product candidates. The FDA ensures the quality of drug products by carefully monitoring drug manufacturers' compliance with cGMP regulations. The cGMP regulations for drugs contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packaging of a drug product. If our CMOs increase their prices or fail to meet our quality standards, or those of regulatory agencies such as the FDA, and cannot be replaced by other acceptable CMOs, our ability to obtain regulatory approval for andcommercialize our product candidates may be materially adversely affected.

Business disruptions affecting our third-party suppliers, manufacturers, and CROs could harm our future revenues and financial condition and increase our costs and expenses.

We rely on third parties to supply the materials for and manufacture our APIs for our pre-clinical and clinical trials. There are only a limited number of suppliers and manufacturers of our APIs and our ability to obtain these materials could be disrupted if the operations of these manufacturers are affected by earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, including the ongoing COVID-19 pandemic, and other natural or man-made disasters or business interruptions. We also rely on CROs, clinical data management organizations, and consultants to design, conduct, supervise, and monitor pre-clinical studies of our product candidates and will do the same for our planned clinical trials. If their facilities are unable to operate because of an accident or incident, even for a short period of time, some or all of our research and development programs may be harmed or delayed, and our operations and financial condition could suffer.

Our existing collaboration agreements and any such agreement entered into in the future may not be successful, which would have adverse consequences.

We are a party to, and may seek additional, collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our current and potential product candidates. We may enter into new arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for each product candidate, both in Canada and internationally. To the extent that we decide to enter into collaboration agreements, we will face significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document, and implement. We may not be successful in our efforts to establish, implement, and maintain collaborations or other alternative arrangements if we choose to enter into such arrangements. In addition, the terms of any collaboration or other arrangements that we may establish may not be favorable to us.

Any existing or future collaboration that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations.

Disagreements between parties to a collaboration arrangement regarding development, intellectual property, regulatory or commercialization matters, can lead to delays in the development process or commercialization of the applicable product candidate, if approved, and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority.

Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Product candidate shipment delays would have an adverse effect on the business.

The shipment, import, and export of our product candidates may require import and export licenses. In the United States, the FDA, United States Customs and Border Protection, and in other countries, similar regulatory authorities, regulate the import and export of pharmaceutical products that contain controlled substances. Specifically, the import and export process requires the issuance of import and export licenses by the relevant controlled substance authority in both the importing and exporting country. Once we are in the production phase, we may not be granted, or if granted, maintain, such licenses from the authorities in certain countries. Even if we obtain the relevant licenses, shipments of our product candidates may be held up in transit, which could cause significant delays and may lead to product batches being stored outside required temperature ranges. Inappropriate storage may damage the product shipment resulting in a partial or total loss of revenue from one or more shipment of our other product candidates. A partial or total loss of revenue from one or more shipment of our product candidates could have a material adverse effect on our business, results of operations and financial condition.

Our ability to generate product revenues will be diminished if our pharmaceutical cannabinoid products (if approved) sell for inadequate prices or patients are unable to obtain adequate levels of reimbursement

Our ability to commercialize our pharmaceutical cannabinoid products, if approved, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from:

- government and health administration authorities;
- private health maintenance organizations and health insurers; and
- other healthcare payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers are challenging the prices charged for medical products and services. Government and other healthcare payers increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs. Even if our product candidates are approved by the FDA or Health Canada, insurance coverage may not be available, and reimbursement levels may be inadequate, to cover our pharmaceutical cannabinoid (if approved). If government and other healthcare payers do not provide adequate coverage and reimbursement levels for our pharmaceutical cannabinoid, once approved, market acceptance of such pharmaceutical cannabinoid could be reduced.

We do not have a history of selling, marketing, or distributing products.

We may not be able to market, sell, and distribute our product candidates, if approved, successfully. Our future success may depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the product candidates under development, and such collaborator's ability to successfully market and sell any such product candidates, if approved. Although we intend to pursue collaborative arrangements regarding the sale and marketing of our product candidates, if approved, there can be no assurance that we will be able to establish or maintain our own sales operations or effect collaborative arrangements, or that if we are able to do so, our collaborators will have effective sales forces. There can also be no assurance that we will be able to establish or maintain effective relationships with third party collaborators or develop in-house sales and distribution capabilities. To the extent that we will in the future depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful. In addition, there can also be no assurance that we will be able to market and sell our product candidates, if approved, internationally.

We may face intense competition from other companies which may be larger and better financed.

Competition from pharmaceutical companies, biotechnology companies and universities is intense and is expected to increase. Increased competition by larger and better financed competitors could materially and adversely affect the business, financial condition, and results of operations of the Corporation. The Corporation's future success depends in part on its ability to maintain a competitive position, including the ability to further progress its portfolio candidates through the necessary pre-clinical and clinical trials towards regulatory approval for sale and commercialization. Other companies may succeed in commercializing products earlier than the Corporation is able to commercialize its product candidates, if approved, or they may succeed in developing products that are more effective. While the Corporation will seek to expand its capabilities in order to remain competitive, there can be no assurance that developments by others will not render its product candidates, if approved, non-competitive or that the Corporation or its licensors will be able to keep pace with technological developments. Competitors have developed or could develop technologies that could be the basis for competitive products. Some of those products may have an entirely different approach or means of accomplishing the desired therapeutic effect than the Corporation's product candidates and may be more effective or less costly than the Corporation's product candidates, if approved. In addition, other forms of medical treatment may offer competition to the Corporation's product candidates, if approved. The success of the Corporation's competitors and their products relative to the Corporation's capabilities and competitiveness could have a material adverse effect on the future of pre-clinical and clinical trials of the Corporation's product candidates, including its ability to obtain the necessary regulatory approvals for the conduct of such trials.

The Corporation expects to face intense competition from other companies in the sale of cannabidiol, some of which can be expected to have more financial resources and manufacturing and marketing experience than the Corporation. Increased competition by larger and better financed competitors could materially and adversely affect the business, financial condition, and results of operations of the Corporation.

The sale of cannabinoid products is regulated under the Cannabis Act and various provincial regimes in Canada. With the opening of the cannabinoids market under the Cannabis Act, the Corporation expects to face additional competition from new entrants. If the number of users of medical cannabis in Canada increases, the demand for products will increase and the Corporation expects that competition will become more intense, as current and future competitors begin to offer an increasing number of diversified products. To remain competitive, the Corporation will require a continued high level of investment in research and development, marketing, sales, and client support. The Corporation may not have sufficient resources to maintain research and development, marketing, sales, and client support efforts on a competitive basis which could materially and adversely affect the business, financial condition, and operating results of the Corporation.

Research and development, and evolving technology and products, may render our product candidates (if approved) obsolete, if we are unable to continue to improve our product offerings in the future.

Rapidly changing markets, technology, emerging industry standards and frequent introduction of new products characterize the Corporation's business. The introduction of new products embodying new technologies, including new manufacturing processes, and the emergence of new industry standards may render the Corporation's product candidates, if approved, obsolete, less competitive, or less marketable. The process of developing the Corporation's product candidates is complex and requires significant continuing costs, development efforts, and third-party commitments. The Corporation's failure to develop new technologies and product candidates and the obsolescence of existing technologies could adversely affect the business, financial condition, and operating results of the Corporation. The Corporation may be unable to anticipate changes in its potential customer requirements that could make the Corporation's existing technology obsolete. The Corporation's success will depend, in part, on its ability to continue to enhance its existing technologies, develop new technology that addresses the increasing sophistication and varied needs of the market, and respond to technological advances and emerging industry standards and practices on a timely and cost-effective basis. The development of the Corporation's proprietary technology entails significant technical and business risks. The Corporation may not be successful in using its new technologies or exploiting its niche markets effectively or adapting its businesses to evolving customer or medical requirements or preferences or emerging industry standards.

Negative public or consumer perception around cannabinoid may negatively affect he development and commercialization of our product candidates.

The Corporation believes the cannabinoid industry is highly dependent upon consumer perception regarding the safety, efficacy, and quality of the cannabinoid produced. Consumer perception of the Corporation's pharmaceutical cannabinoid product candidates can be significantly influenced by scientific research or findings, regulatory investigations, litigation, media attention, and other publicity regarding the consumption of cannabinoids. There can be no assurance that future scientific research, findings, regulatory proceedings, litigation, media attention, or other research findings or publicity will be favourable to the cannabinoid market or any particular product, or consistent with earlier publicity. Future research reports, findings, regulatory proceedings, litigation, media attention, or other publicity that are perceived as less favourable than, or that question, earlier research reports, findings, or publicity could have a material adverse effect on the demand for the Corporation's pharmaceutical cannabinoids, if approved, and the business, results of operations, financial condition, and cash flows of the Corporation. The Corporation's dependence upon consumer perceptions means that adverse scientific research reports, findings, regulatory proceedings, litigation, media attention, or other publicity, whether or not accurate or with merit, could have a material adverse effect on the Corporation, the demand for the Corporation's pharmaceutical cannabinoids, if approved, and the business, results of operations, financial condition, and cash flows of the Corporation. Further, adverse publicity reports or other media attention regarding the safety, efficacy, and quality of cannabinoid in general, or the Corporation's pharmaceutical cannabinoids, if approved, specifically, or associating the consumption of cannabinoid with illness or other negative effects or events, could have such a material adverse effect. Such adverse publicity reports or other media attention could arise even if the adverse

effects associated with such products resulted from consumers' failure to consume such products legally, appropriately, or as directed.

We may face risks from product liability claims, if our product candidates are approved.

If we become a manufacturer and distributor of products designed to be ingested by humans, the Corporation faces an inherent risk of exposure to product liability claims, regulatory action, and litigation if its product candidates (once approved) are alleged to have caused significant loss or injury. In addition, the manufacture and sale of cannabis products involve the risk of injury to consumers due to tampering by unauthorized third parties or product contamination. Previously unknown adverse reactions resulting from human consumption of cannabis products alone or in combination with other medications or substances could occur. The Corporation may be subject to various product liability claims, including, among others, that the products produced by the Corporation caused injury or illness, include inadequate instructions for use or include inadequate warnings concerning possible side effects or interactions with other substances. A product liability claim or regulatory action against the Corporation could result in increased costs, could adversely affect the Corporation's reputation with its clients and consumers generally, and could have a material adverse effect on the business, financial condition, and operating results of the Corporation. There can be no assurances that the Corporation will be able to obtain or maintain product liability insurance on acceptable terms or with adequate coverage against potential liabilities. Such insurance is expensive and may not be available in the future on acceptable terms, or at all. The inability to obtain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims could prevent or inhibit the commercialization of product candidates (if approved).

The Corporation's product candidates, if approved, may be subject to product recalls.

Manufacturers and distributors of products are sometimes subject to the recall or return of their products for a variety of reasons, including product defects, such as contamination, unintended harmful side effects or interactions with other substances, packaging safety and inadequate or inaccurate labeling disclosure. If any of the product candidates (if approved) that the Corporation produces or intends to produce are recalled due to an alleged product defect or for any other reason, the Corporation could be required to incur the unexpected expense of the recall and any legal proceedings that might arise in connection with the recall. The Corporation may lose a significant amount of sales and may not be able to replace those sales at an acceptable margin or at all. In addition, a product recall may require significant Management attention. Although the Corporation has detailed procedures in place for testing finished products (if our product candidates are approved), there can be no assurance that any quality, potency, or contamination problems will be detected in time to avoid unforeseen product recalls, regulatory action, or lawsuits. Additionally, if one of Corporation's product candidates, if approved, were subject to recall, the image of that product and the Corporation could be harmed. A recall for any of the foregoing reasons could lead to decreased demand for products produced by the Corporation and could have a material adverse effect on the results of operations and financial condition of the Corporation. Additionally, product recalls may lead to increased scrutiny of the operations of the Corporation by Health Canada or other regulatory agencies, requiring further Management attention and potential legal fees and other expenses.

The Corporation may seek to expand its business and operations into jurisdictions outside of Canada, and there are risks associated with doing so.

The Corporation may in the future expand its operations and business into jurisdictions outside of Canada. There can be no assurance that any market for the Corporation's product candidates (if approved) will develop in any such foreign jurisdiction. The Corporation may face new or unexpected risks or significantly increase its exposure to one or more existing risk factors, including economic instability, changes in laws and regulations, and the effects of competition. These factors may limit the Corporation's capability to successfully expand its operations and may have a material adverse effect on the Corporation's business, financial condition, and results of operations.

The Corporation may become subject to liability arising from any fraudulent or illegal activity by its employees, contractors, and consultants.

The Corporation is exposed to the risk that its employees, independent contractors, and consultants may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to the Corporation that violates: (i) government regulations; (ii) manufacturing standards; (iii) federal and provincial healthcare fraud and abuse laws and regulations; or (iv) laws that require the true, complete, and accurate reporting of financial information or data. It is not always possible for the Corporation to identify and deter misconduct by its employees and other third parties, and the precautions taken by the Corporation to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting the Corporation from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against the Corporation, and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of the Corporation's operations, any of which could have a material adverse effect on the Corporation's business, financial condition and results of operations.

Corporation's business is dependent on key inputs, and the inability to secure such inputs may negatively affect our business.

The Corporation's business is dependent on a number of key inputs and their related costs including raw materials and supplies related to its growing operations, as well as electricity, water, and other local utilities. Any significant interruption or negative change in the availability or economics of the supply chain, including as a result of the ongoing COVID-19 pandemic, for key inputs could materially impact the business, financial condition, and operating results of the Corporation. Any inability to secure required supplies and services or to do so on appropriate terms could have a materially adverse impact on the business, financial condition, and operating results of the Corporation.

Our insurance coverage may be insufficient to protect us from our operating risk.

The Corporation has insurance to protect its assets, operations, and employees. While the Corporation believes its insurance coverage addresses all material risks to which it is exposed and is adequate and customary in its current state of operations, such insurance is subject to coverage limits and exclusions and may not be available for all risks and hazards to which the Corporation is exposed. In addition, no assurance can be given that such insurance will be adequate to cover the Corporation's liabilities or will be generally available in the future or, if available, that premiums will be commercially justifiable. If the Corporation were to incur substantial liability and such damages were not covered by insurance or were in excess of policy limits, or if the Corporation were to incur such liability at a time when it is not able to obtain liability insurance, its business, results of operations, and financial condition could be materially adversely affected.

We may be unable to manage our growth effectively.

The Corporation may be subject to growth-related risks, including capacity constraints and pressure on its internal systems and controls. The ability of the Corporation to manage growth effectively will require it to continue to implement and improve its operational and financial systems and to expand, train, and manage its employee base. The inability of the Corporation to deal with this growth may have a material adverse effect on the Corporation's business, financial condition, results of operations, and prospects.

Some of our directors and/or officers may have conflicts of interest from other business activities.

The Corporation may be subject to various potential conflicts of interest because of the fact that some of its officers and directors may be engaged in a range of business activities. In addition, the Corporation's executive officers and Directors may devote time to their outside business interests, so long as such activities do not materially or adversely interfere with their duties to the Corporation. In some cases, the Corporation's executive officers and Directors may have fiduciary obligations associated with these business interests that interfere with their ability to

devote time to the Corporation's business and affairs and that could adversely affect the Corporation's operations. These business interests could require significant time and attention of the Corporation's executive officers and Directors. In addition, the Corporation's executive officers and Directors control a large percentage of common shares and may have ability to control matters affecting the Corporation.

The Corporation may also become involved in other transactions which conflict with the interests of its Directors and the officers who may from time-to-time deal with persons, firms, institutions, or Companies with which the Corporation may be dealing, or which may be seeking investments similar to those desired by it. The interests of these persons could conflict with those of the Corporation. In addition, from time to time, these persons may be competing with the Corporation for available investment opportunities. Conflicts of interest, if any, will be subject to the procedures and remedies provided under applicable laws. In particular, in the event that such a conflict of interest arises at a meeting of the Corporation's Directors, a director who has such a conflict will abstain from voting for or against the approval of such participation or such terms. In accordance with applicable laws, the Directors of the Corporation are required to act honestly, in good faith, and in the best interests of the Corporation.

Certain publicity may cause damage to our reputation.

Damage to the Corporation's reputation could be the result of the actual or perceived occurrence of any number of events, and could include any negative publicity, whether true or not. The increased usage of social media and other web-based tools used to generate, publish, and discuss user generated content and to connect with other users has made it increasingly easier for individuals and groups to communicate and share opinions and views in respect to the Corporation and its activities, whether true or not. Although the Corporation believes that it operates in a manner that is respectful to all stakeholders and that it takes care in protecting its image and reputation, the Corporation does not ultimately have direct control over how it is perceived by others. Reputation loss may result in decreased investor confidence, increased challenges in developing and maintaining community relations, and an impediment to the Corporation's overall ability to advance its product candidates, thereby having a material adverse impact on financial performance, financial condition, cash flows, and growth prospects.

Third parties may perceive reputational risk for doing business with us as a company involved in the medical cannabis business.

The parties with which the Corporation does business may perceive that they are exposed to reputational risk as a result of the Corporation's medical cannabis business activities. This may impact the Corporation's ability to retain current partners, such as its banking relationship, or source future partners as required for growth or future expansion in Canada or internationally. Failure to establish or maintain business relationships could have a material adverse effect on the Corporation.

Our relationships with healthcare providers, patients and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings

Healthcare providers, customers, and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our products for which we obtain marketing approval. As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid, or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and

administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs.

We and our third-party providers may face security threats to information systems.

The Corporation has entered into agreements with third parties for hardware, software, telecommunications, and other information technology ("IT") services in connection with its operations. The Corporation's operations depend, in part, on how well it and its suppliers protect networks, equipment, IT systems, and software against damage from a number of threats, including, but not limited to, cable cuts, damage to physical plants, natural disasters, terrorism, fire, power loss, hacking, computer viruses, vandalism, and theft. The Corporation's operations also depend on the timely maintenance, upgrade, and replacement of networks, equipment, IT systems and software, as well as pre-emptive expenses to mitigate the risks of failures. Any of these and other events could result in information system failures, delays and/or increase in capital expenses. The failure of information systems or a component of information systems could, depending on the nature of any such failure, adversely impact the Corporation's reputation and results of operations.

The Corporation has not experienced any material losses to date relating to cyber-attacks or other information security breaches, but there can be no assurance that the Corporation will not incur such losses in the future. The Corporation's risk and exposure to these matters cannot be fully mitigated because of, among other things, the evolving nature of these threats. As a result, cybersecurity and the continued development and enhancement of controls, processes, and practices designed to protect systems, computers, software, data, and networks from attack, damage, or unauthorized access is a priority. As cyber threats continue to evolve, the Corporation may be required to expend additional resources to continue to modify or enhance protective measures or to investigate and remediate any security vulnerabilities.

We do not currently, and have no plans to, pay dividends on our common shares.

Our current policy is to retain earnings to finance the development and enhancement of our product candidates and to otherwise reinvest in the Corporation. Therefore, we do not anticipate paying cash dividends on the common shares in the foreseeable future. Our dividend policy will be reviewed from time to time by our board of directors in the context of our earnings, financial condition, and other relevant factors. Until the time that we do determine to pay dividends, which we might never do, our shareholders will not be able to receive a return on their common shares unless they sell them.

Future sales of common shares by existing shareholders.

Holders of options to purchase common shares will have an immediate income inclusion for tax purposes when they exercise their options (that is, tax is not deferred until they sell the underlying common shares). As a result, these holders may need to sell common shares purchased on the exercise of options in the same year that they exercise their options. This might result in a greater number of common shares being sold in the public market, and fewer long- term holds of common shares by Management and our employees.

Cardiol may be subject to securities litigation which is expensive and could divert Management's attention.

The market price of the common shares may be volatile, and in the past companies that have experienced volatility in the market price of their shares have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our Management's attention from other business concerns, which could seriously harm our business.

Our common shares are subject to market price volatility

The market price of common shares may be adversely affected by a variety of factors relating to the Corporation's business, including fluctuations in the Corporation's operating and financial results, the results of any public announcements made by the Corporation and its failure to meet analysts' expectations. In addition, from time to

time, the stock market experiences significant price and volume volatility that may affect the market price of common shares for reasons unrelated to the Corporation's performance. Additionally, the value of common shares is subject to market value fluctuations based upon factors that influence the Corporation's operations, such as legislative or regulatory developments, competition, technological change, global capital market activity and changes in interest and currency rates. There can be no assurance that the market price of common shares will not experience significant fluctuations in the future, including fluctuations that are unrelated to the Corporation's performance.

The market value of common shares may also be affected by the Corporation's financial results and political, economic, financial, and other factors that can affect the capital markets generally, the stock exchanges on which common shares are traded and the market segments in which the Corporation is a part.

Issuances of our equity securities in the future may result in dilution to current shareholders.

Our articles of incorporation and by-laws allow it to issue an unlimited number of common shares for such consideration and on such terms and conditions as established by the Corporation's board of directors, in many cases, without shareholder approval. The Corporation may issue additional common shares in future offerings (including through the sale of securities convertible into or exchangeable for common shares) and on the exercise of stock options or other securities exercisable for common shares. The Corporation cannot predict the size of future issuances of common shares or the effect that future issuances and sales of common shares will have on the market price of common shares. Issuances of a substantial number of additional common shares, or the perception that such issuances could occur, may adversely affect prevailing market prices for common shares. With any additional issuance of common shares, investors will suffer dilution to their voting power and may experience dilution in its earnings per share.

Failure to comply with the U.S. Foreign Corrupt Practices Act ("FCPA"), the Canadian Corruption of Foreign Public Officials Act ("CFPOA"), and other global anti-corruption and anti-bribery laws could subject the Corporation to penalties and other adverse consequences.

The FCPA and the CFPOA, as well as any other applicable domestic or foreign anti-corruption or anti-bribery laws to which the Corporation is or may become subject generally prohibit corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity and requires companies to maintain accurate books and records and internal controls, including at foreign-controlled subsidiaries.

Compliance with these anti-corruption laws and anti-bribery laws may be expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, these laws present particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and physicians and other hospital employees are considered to be foreign officials. Certain payments by other companies to hospitals in connection with clinical trials and other work have been deemed to be improper payments to governmental officials and have led to FCPA enforcement actions.

The Corporation's internal control policies and procedures may not protect it from reckless or negligent acts committed by the Corporation's employees, distributors, licensees, or agents. The Corporation can make no assurance that they will not engage in prohibited conduct, and the Corporation may be held liable for their acts under applicable anti- corruption and anti-bribery laws. Noncompliance with these laws could subject the Corporation to investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension or debarment from contracting with certain persons, the loss of export privileges, whistleblower complaints, reputational harm, adverse media coverage, and other collateral consequences. Any investigations, actions or sanctions or other previously mentioned harm could have a material adverse effect on the Corporation's business, operating results, and financial condition.

The Corporation may be classified as a "passive foreign investment company" for U.S. federal income tax purposes, which would subject U.S. investors that hold the Corporation's Common Shares to potentially significant adverse U.S. federal income tax consequences.

If the Corporation is classified as a passive foreign investment company ("PFIC") for U.S. federal income tax purposes in any taxable year, U.S. investors holding the Corporation's Common Shares generally will be subject, in that taxable year and all subsequent taxable years (whether or not the Corporation continued to be a PFIC), to certain adverse

U.S. federal income tax consequences. The Corporation will be classified as a PFIC in respect of any taxable year in which, after taking into account its income and gross assets (including the income and assets of 25% or more owned subsidiaries), either (i) 75% or more of its gross income consists of certain types of "passive income" or (ii) 50% or more of the average quarterly value of its assets is attributable to "passive assets" (assets that produce or are held for the production of passive income). Based upon the current and expected composition of the Corporation's income and assets, the Corporation believes that it was a PFIC for the taxable year ended December 31, 2020 and expects that it may be a PFIC for the current taxable year. Because the Corporation's PFIC status must be determined annually with respect to each taxable year and will depend on the composition and character of the Corporation's assets and income, including the Corporation's use of proceeds from offerings, and the value of the Corporation's assets (which may be determined, in part, by reference to the market value of Common Shares, which may be volatile) over the course of such taxable year, the Corporation may be a PFIC in any taxable year. Because there are uncertainties in the application of the relevant rules and PFIC status is a factual determination made annually after the close of each taxable year, there can be no assurance that the Corporation will not be a PFIC for any future taxable year. In addition, it is possible that the U.S. Internal Revenue Service may challenge the Corporation's classification of certain income and assets as non-passive, which may result in the Corporation being or becoming a PFIC in the current or subsequent years.

If the Corporation is a PFIC for any year during a U.S. Holder's (as defined below) holding period, then such U.S. Holder generally will be required to treat any gain realized upon a disposition of Common Shares, or any "excess distribution" received on its Common Shares, as ordinary income, and to pay an interest charge on a portion of such gain or distribution, unless the U.S. Holder makes a timely and effective "qualified electing fund" election ("QEF Election") or a "mark-to-market" election with respect to its Common Shares. A U.S. Holder who makes a QEF Election generally must report on a current basis its share of the Corporation's net capital gain and ordinary earnings for any year in which the Corporation is a PFIC, whether or not the Corporation distributes any amounts to its shareholders. However, U.S. Holders should be aware that there can be no assurance that the Corporation will satisfy the record keeping requirements that apply to a QEF, or that the Corporation will supply U.S. Holders with information that such U.S. Holders require to report under the QEF Election rules, in the event that the Corporation is a PFIC and a U.S. Holder wishes to make a QEF Election. Thus, U.S. Holders may not be able to make a QEF Election with respect to their Common Shares. A U.S. Holder who makes a mark-to-market election generally must include as ordinary income each year the excess of the fair market value of the Common Shares over the taxpayer's basis therein. Each U.S. Holder should consult its own tax advisors regarding the PFIC rules and the U.S. federal income tax consequences of the acquisition, ownership, and disposition of Common Shares.

As used in this discussion, the term "U.S. Holder" means a beneficial owner of Common Shares that is, for U.S. federal income tax purposes, (1) an individual who is a citizen or resident of the United States, (2) a corporation (or entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia, (3) an estate the income of which is subject to U.S. federal income tax regardless of its source or (4) a trust (x) with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of its substantial decisions or (y) that has elected under applicable U.S. Treasury regulations to be treated as a domestic trust for U.S. federal income tax purposes.

It may be difficult for United States investors to obtain and enforce judgments against the Corporation because of the Corporation's Canadian incorporation and presence.

The Corporation is a corporation existing under the laws of Ontario, Canada. Most of the Corporation's directors and officers are residents of Canada, and all or a substantial portion of their assets, and a substantial portion of

the Corporation's assets, are located outside the United States. Consequently, it may be difficult for holders of the Corporation's securities who reside in the United States to effect service of process within the United States upon those directors, officers, and experts who are not residents of the United States. It may also be difficult for holders of the Corporation's securities who reside in the United States to realize in the United States upon judgments of courts of the United States predicated upon the Corporation's civil liability and the civil liability of the Corporation's directors, officers and experts under United States federal securities laws. Investors should not assume that Canadian courts would (i) enforce judgments of United States courts obtained in actions against the Corporation or such directors or officers predicated upon the civil liability provisions of the United States federal securities laws or the securities or "blue sky" laws of any state or jurisdiction of the United States or (ii) would enforce, in original actions, liabilities against the Corporation or such directors, officers or experts predicated upon the United States federal securities laws or any securities or "blue sky" laws of any state or jurisdiction of the United States. In addition, the protections afforded by Canadian securities laws may not be available to investors in the United States.

As a foreign private issuer, the Corporation is subject to different U.S. securities laws and rules than a U.S. domestic issuer, which may limit the information publicly available to U.S. investors.

The Corporation is a "foreign private issuer", under applicable U.S. federal securities laws, and is, therefore, not subject to the same requirements that are imposed upon U.S. domestic issuers by the Securities and Exchange Commission ("SEC"). Under the U.S. Securities Exchange Act of 1934, as amended (the "US Exchange Act"), the Corporation is subject to reporting obligations that, in certain respects, are less detailed and less frequent than those of U.S. domestic reporting companies. As a result, the Corporation does not file the same reports that a U.S. domestic issuer would file with the SEC, although the Corporation is required to file with or furnish to the SEC the continuous disclosure documents that it is required to file in Canada under Canadian securities laws. In addition, the Corporation's officers, directors, and principal shareholders are exempt from the reporting and short-swing profit recovery provisions of Section 16 of the U.S. Exchange Act. Therefore, the Corporation's shareholders may not know on as timely a basis as with U.S. domestic issuers when the Corporation's officers, directors and principal shareholders purchase or sell Common Shares, as the reporting periods under the corresponding Canadian insider reporting requirements are longer. As a foreign private issuer, the Corporation is exempt from the rules and regulations under the U.S. Exchange Act related to the furnishing and content of proxy statements. The Corporation is also exempt from Regulation FD, which prohibits issuers from making selective disclosures of material non-public information. While the Corporation complies with the corresponding requirements relating to proxy statements and disclosure of material non-public information under Canadian securities laws, these requirements differ from those under the U.S. Exchange Act and Regulation FD and shareholders should not expect to receive the same information at the same time as such information is provided by U.S. domestic companies. In addition, the Corporation may not be required under the U.S. Exchange Act to file annual and quarterly reports with the SEC as promptly as U.S. domestic companies whose securities are registered under the U.S. Exchange Act. In addition, as a foreign private issuer, the Corporation has the option to follow certain Canadian corporate governance practices, except to the extent that such laws would be contrary to U.S. securities laws, and provided that the Corporation disclose the requirements it is not following and describe the Canadian practices it follows instead. The Corporation has elected to follow home country practices in Canada with regard to certain corporate governance matters. As a result, the Corporation's shareholders may not have the same protections afforded to shareholders of U.S. domestic companies that are subject to all corporate governance requirements.

The Corporation may lose its foreign private issuer status in the future, which could result in significant additional costs and expenses to the Corporation.

In order to maintain its status as a foreign private issuer, a majority of the Corporation's Common Shares must be either directly or indirectly owned by non-residents of the U.S. unless the Corporation also satisfies one of the additional requirements necessary to preserve this status. The Corporation may in the future lose its foreign private issuer status if a majority of its Common Shares are held in the U.S. and if the Corporation fails to meet the additional requirements necessary to avoid loss of its foreign private issuer status. The regulatory and compliance costs under

U.S. federal securities laws as a U.S. domestic issuer may be significantly more than the costs incurred as a Canadian foreign private issuer eligible to use the multi-jurisdictional disclosure system adopted by the securities regulatory authorities in Canada and the United States (the "MJDS"). If the Corporation is not a foreign private issuer, it would not be eligible to use the MJDS or other foreign issuer forms and would be required to file periodic and current reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive than the forms available to a foreign private issuer, and would be required to file financial statements prepared in accordance with United States generally accepted accounting principles. In addition, the Corporation may lose the ability to rely upon exemptions from Nasdaq corporate governance requirements that are available to foreign private issuers.

The Corporation relies upon certain accommodations available to it as an "emerging growth company."

The Corporation is an "emerging growth company" as defined in section 3(a) of the U.S. Exchange Act (as amended by the JOBS Act, enacted on April 5, 2012), and the Corporation will continue to qualify as an emerging growth company until the earliest to occur of: (a) the last day of the fiscal year during which the Corporation has total annual gross revenues of US$1,070,000,000 (as such amount is indexed for inflation every five years by the SEC) or more; (b) the last day of the fiscal year of the Corporation following the fifth anniversary of the date of the first sale of common equity securities of the Corporation pursuant to an effective registration statement under the U.S. Securities Act; (c) the date on which the Corporation has, during the previous three year period, issued more than US$1,000,000,000 in non-convertible debt; and (d) the date on which the Corporation is deemed to be a "large accelerated filer", as defined in Rule 12b-2 under the U.S. Exchange Act. The Corporation will qualify as a large accelerated filer (and would cease to be an emerging growth company) at such time when on the last business day of its second fiscal quarter of such year the aggregate worldwide market value of its common equity held by non-affiliates will be US$700,000,000 or more. For so long as the Corporation remains an emerging growth company, it is permitted to and intends to rely upon exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. The Corporation cannot predict whether investors will find the Common Shares less attractive because the Corporation relies upon certain of these exemptions. If some investors find the Common Shares less attractive as a result, there may be a less active trading market for the Common Shares and the Common Share price may be more volatile. On the other hand, if the Corporation no longer qualifies as an emerging growth company, the Corporation would be required to divert additional management time and attention from the Corporation's development and other business activities and incur increased legal and financial costs to comply with the additional associated reporting requirements, which could negatively impact the Corporation's business, financial condition, and results of operations.

The impacts of the ongoing COVID-19 pandemic on the Corporation's business are uncertain.

On March 11, 2020, the World Health Organization declared the outbreak of COVID-19 a global pandemic. In response to the outbreak, governmental authorities in Canada and internationally have introduced various recommendations and measures to try to limit the pandemic, including travel restrictions, border closures, non-essential business closures, quarantines, self-isolations, shelters-in-place, and social distancing. The COVID-19 outbreak and the response of governmental authorities to try to limit it are having a significant impact on the private sector and individuals, including unprecedented business, employment, and economic disruptions.

Although the Corporation has taken steps to mitigate the impact of COVID-19, the continued presence and spread of COVID-19 nationally and globally could have a material adverse impact on the Corporation's business, operations, financial results and position and prospects, including through employee attrition, disruptions to the Corporation's activities, as well as a deterioration of general economic conditions including a possible national or global recession. Due to the speed with which the COVID-19 situation is developing and the uncertainty of its magnitude, outcome, and duration, it is not possible to estimate its impact on the Corporation's business, operations, financial results and position or prospects at this time.

The Corporation continues to monitor the situation and work with its stakeholders (including customers, employees, and suppliers) in order to assess further possible implications to its business, supply chain and customers, and,

where practicable, mitigate adverse consequences and responsibly address this global pandemic.

DIVIDENDS

We have not declared dividends on our Common Shares in the past. We currently intend to reinvest all future earnings in order to finance the development and growth of our business. As a result, we do not intend to pay dividends on our Common Shares in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors and will depend on the financial condition, business environment, operating results, capital requirements, any contractual restrictions on the payment of dividends, and any other factors that the Board of Directors deems relevant.

CAPITAL STRUCTURE

Common Shares

As of the date hereof, 61,925,499 Common Shares are issued and outstanding. Each Common Share entitles the holder to receive notice of and attend all meetings of the Shareholders. Each Common Share carries the right to one vote. The holders of Common Shares are entitled to receive any dividends declared by the Corporation in respect of the Common Shares at such time and in such amount as may be determined by the Board, in its discretion. In the event of the liquidation, dissolution, or winding-up of the Corporation, whether voluntary or involuntary, holders of Common Shares are also entitled to participate, rateably, in the distribution of the assets of the Corporation, subject to the rights of the holders of any other class of shares ranking in priority to the Common Shares.

Share Purchase Warrants

The following table reflects the share purchase warrants of the Corporation issued and outstanding, excluding 1,020,000 Meros Special Warrants convertible automatically into Common Shares for no additional consideration in accordance with the original escrow release terms as described in the Meros License Agreement:

Expiry date	Exercise price ($)	Warrants outstanding	
August 31, 2022	4.00	824,000	CARO Compensation Warrants
May 12, 2024	4.60	3,453,178	May 2021 Warrants
November 5, 2024	3.75[1]	8,175,000	November 2021 Warrants
Total		**12,452,178**	

[1]Exercise price denoted in USD.

May 2021 Warrants

Each May 2021 Warrant entitles the holder to acquire, subject to adjustment in certain circumstances, one Common Share at an exercise price of $4.60 until 4:00 p.m. (Eastern time) on May 12, 2024 in accordance with the terms of a warrant indenture entered into between the Corporation and Computershare Trust dated May 12, 2021 (the “May 2021 Warrant Indenture”), after which time the May 2021 Warrants will be void and of no value.

The subscription rights in effect under the May 2021 Warrant Indenture shall be subject to adjustment from time to time upon the occurrence of certain events, including:

i. the subdivision, redivision or change of the Common Shares into a greater number of shares;

ii. the reduction, combination, or consolidation of the Common Shares into a lesser number of shares;

iii. the issuance of Common Shares or securities exchangeable for or convertible into Common Shares to all or substantially all of the holders of the Common Shares as a stock dividend or other distribution (other than a distribution of Common Shares upon the exercise of May 2021 Warrants or any outstanding options);

iv. the issuance to all or substantially all of the holders of the Common Shares of rights, options or warrants under which such holders are entitled, during a period expiring not more than 45 days after the record date for such issuance, to subscribe for or purchase Common Shares, or securities exchangeable for or convertible into Common Shares, at a price per share to the holder (or at an exchange or conversion price per share) of less than 95% of the "current market price", as defined in the May 2021 Warrant Indenture, for the Common Shares on such record date; and

v. the issuance or distribution to all or substantially all the holders of Common Shares of (i) securities of any class of the Corporation (other than Common Shares), (ii) rights, options or warrants to subscribe for or purchase Common Shares (or other securities convertible into or exchangeable for Common Shares), other than pursuant to a rights offering; (iii) evidences of its indebtedness; or (iv) any property or other assets.

The May 2021 Warrant Indenture also provides for adjustments in the class and/or number of securities issuable upon exercise of the May 2021 Warrants and/or exercise price per security in the event of the following additional events: (a) reclassification of the Common Shares or a capital reorganization of the Corporation (other than as described in clauses i or ii above), (b) consolidations, amalgamations, arrangements or merger of the Corporation with or into another entity, or (c) any sale or conveyance of the property and assets as an entirety or substantially as an entirety to another entity, in which case each holder of a May 2021 Warrant which is thereafter exercised will receive, in lieu of Common Shares, the kind and number or amount of other securities or property which such holder would have been entitled to receive as a result of such event if such holder had exercised the May 2021 Warrants prior to the event.

The Corporation also covenants in the May 2021 Warrant Indenture that, during the period in which the May 2021 Warrants are exercisable, it will give notice to holders of May 2021 Warrants of certain stated events, including events that would result in an adjustment to the exercise price for the May 2021 Warrants or the number of Common Shares issuable upon exercise of the May 2021 Warrants, at least 14 days prior to the record date or effective date, as the case may be, of such events.

No fractional Common Shares will be issuable to any holder of May 2021 Warrants upon the exercise thereof, and no cash or other consideration will be paid in lieu of fractional shares. The holding of May 2021 Warrants will not make the holder thereof a shareholder of the Corporation or entitle such holder to any right or interest in respect of the May 2021 Warrants except as expressly provided in the May 2021 Warrant Indenture. Holders of May 2021 Warrants will not have any voting or pre-emptive rights or any other rights of a holder of Common Shares.

The May 2021 Warrant Indenture provides that, from time to time, Computershare Trust and the Corporation, without the consent of the holders of May 2021 Warrants, may be able to amend or supplement the May 2021 Warrant Indenture for certain purposes, including, among other things, rectifying any ambiguities, defective or inconsistent provisions, errors, mistakes or omissions contained in the May 2021 Warrant Indenture or in any deed or indenture supplemental or ancillary to the May 2021 Warrant Indenture, provided that, in the opinion of Computershare Trust, relying on counsel, the rights of Computershare Trust and of the holders of May 2021 Warrants are in no way prejudiced.

Holders of May 2021 Warrants may also agree to amend or supplement the May 2021 Warrant Indenture if an Extraordinary Resolution (as defined below) is passed at a meeting of holders of May 2021 Warrants. An "Extraordinary Resolution" is defined in the May 2021 Warrant Indenture as a resolution either: (i) passed at a meeting of the holders of May 2021 Warrants at which there are holders of May 2021 Warrants present in person or represented by proxy representing at least 50% of the aggregate number of the then outstanding May 2021 Warrants and passed by the affirmative vote of holders of May 2021 Warrants representing not less than 66⅔%

of the aggregate number of all the then outstanding May 2021 Warrants represented at the meeting and voted on the poll upon such resolution.

November 2021 Warrants

Each November 2021 Warrant entitles the holder to acquire, subject to adjustment in certain circumstances, one Common Share at an exercise price of USD$3.75 until 5:00 p.m. (Eastern time) on November 5, 2024 in accordance with the terms of a warrant indenture entered into between the Corporation and Computershare Trust dated November 5, 2021 (the "November 2021 Warrant Indenture"), after which time the November 2021 Warrants will be void and of no value. In accordance with a covenant in the November 2021 Warrant Indenture, the Corporation must use commercially reasonable best effort to maintain an effective registration statement in respect of the warrant shares. The Corporation filed a prospectus supplement dated February 9, 2022 to register the warrant shares.

The subscription rights in effect under the November 2021 Warrant Indenture shall be subject to adjustment from time to time upon the occurrence of certain events, including:

i. the issuance of Common Shares or securities exchangeable for or convertible into Common Shares to all or substantially all of the holders of the Common Shares as a stock dividend or other distribution (other than a distribution of Common Shares upon the exercise of November 2021 Warrants or pursuant to the exercise, conversion or exchange of securities of the Corporation outstanding as of the date hereof);

ii. the subdivision, redivision or change of the Common Shares into a greater number of shares;

iii. the reduction, combination, or consolidation of the Common Shares into a lesser number of shares;

iv. the distribution to all or substantially all of the holders of the Common Shares of rights, options or warrants under which such holders are entitled, during a period expiring not more than 45 days after the record date for such issuance, to subscribe for or purchase Common Shares, or securities exchangeable for or convertible into Common Shares, at a price per share to the holder (or at an exchange or conversion price per share) of less than 95% of the "current market price", as defined in the November 2021 Warrant Indenture, for the Common Shares on such record date; and

v. the issuance or distribution to all or substantially all the holders of Common Shares of (i) shares of any class of the Corporation (other than Common Shares), (ii) rights, options or warrants to acquire Common Shares (or other securities convertible into or exchangeable for Common Shares); (iii) evidences of indebtedness; or (iv) cash, securities or any property or other assets.

The November 2021 Warrant Indenture also provides for adjustments in the class and/or number of securities issuable upon exercise of the November 2021 Warrants and/or exercise price per security in the event of the following additional events: (i) the Corporation effects any merger or consolidation of the Corporation with or into another person, in which the Corporation is not the surviving entity or the shareholders of the Corporation immediately prior to such merger or consolidation do not own, directly or indirectly, at least 50% of the voting power of the surviving entity immediately after such merger or consolidation, (ii) the Corporation effects any sale to another person of all or substantially all of its assets in one or a series of related transactions, (iii) pursuant to any tender offer or exchange offer (whether by the Corporation or another person), shareholders who tender shares representing more than 50% of the voting power of the Common Shares and the Corporation or such other person, as applicable, accepts such tender for payment, (iv) the Corporation consummates a share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off, merger or plan of arrangement) with another person whereby such other person acquires more than the 50% of the voting power of the Common Shares or (v) the Corporation effects any reclassification of the Common Shares or any compulsory share exchange pursuant to which the Common Shares are effectively converted into or exchanged for other securities, cash or property (other than as a result of a subdivision or combination of Common Share covered above) (in any such case, a "Fundamental Transaction")

The Corporation also covenants in the November 2021 Warrant Indenture that, during the period in which the Warrants are exercisable, it will give notice to holders of November 2021 Warrants of certain stated events, including events that would result in an adjustment to the exercise price for the November 2021 Warrants or the number of Common Shares issuable upon exercise of the November 2021 Warrants, at least 14 days prior to the record date or effective date, as the case may be, of such events.

No fractional Common Shares will be issuable to any holder of November 2021 Warrants upon the exercise thereof, and no cash or other consideration will be paid in lieu of fractional shares. The holding of November 2021 Warrants will not make the holder thereof a shareholder of the Corporation or entitle such holder to any right or interest in respect of the November 2021 Warrants except as expressly provided in the November 2021 Warrant Indenture. Holders of November 2021 Warrants will not have any voting or pre-emptive rights or any other rights of a holder of Common Shares.

The November 2021 Warrant Indenture provides that, from time to time, Computershare Trust and the Corporation, without the consent of the holders of November 2021 Warrants, may be able to amend or supplement the November 2021 Warrant Indenture for certain purposes, including, among other things, rectifying any ambiguities, defective or inconsistent provisions, errors, mistakes or clerical omissions contained in the November 2021 Warrant Indenture or in any deed or indenture supplemental or ancillary to the November 2021 Warrant Indenture, provided that, in the opinion of Computershare Trust, relying on counsel, the rights of Computershare Trust and of the holders of November 2021 Warrants are in no way prejudiced.

Holders of November 2021 Warrants may also agree to amend or supplement the November 2021 Warrant Indenture if an Extraordinary Resolution (as defined below) is passed at a meeting of holders of November 2021 Warrants. An “Extraordinary Resolution” is defined in the November 2021 Warrant Indenture as a resolution either: (i) passed at a meeting of the holders of November 2021 Warrants at which there are holders of November 2021 Warrants present in person or represented by proxy representing at least 20% of the aggregate number of the then outstanding November 2021 Warrants and passed by the affirmative vote of holders of November 2021 Warrants representing not less than 66⅔% of the aggregate number of all the then outstanding November 2021 Warrants represented at the meeting and voted on the poll upon such resolution.

CARO Compensation Warrants

See “Business of Cardiol - Commercialization Relationships - TecSalud (CARO Development Agreement)”.

Meros Special Warrants

See “Business of Cardiol - Commercialization Relationships - Meros”.

Stock Options and other Share-Based Awards

The Board of Directors has adopted a Legacy Equity Compensation Plan, and subsequently an Omnibus Equity Incentive Plan under which options to purchase Common Shares and other Share-Based Awards (as defined below) may be granted to the Corporation’s Directors, officers, employees, and consultants. See below “Summary of Legacy Equity Compensation Plan” and “Summary of Omnibus Equity Incentive Plan”. The following table sets out the current number of options outstanding and details, the expiry date, the grant date, the exercise price, and options exercisable:

Expiry date	Grant Date	Exercise price ($)	Options outstanding	Options exercisable
June 22, 2022	June 23, 2020	2.58	83,334	83,334
February 8, 2023	February 9, 2021	4.56	416,666	416,666
February 18, 2023	February 19, 2021	4.80	560,000	560,000
February 22, 2023	February 23, 2021	4.46	130,000	130,000
October 15, 2024	October 16, 2019	3.23	60,000	40,000
December 2, 2024	December 3, 2019	4.08	60,000	40,000
December 5, 2024	December 6, 2019	3.69	60,000	60,000
February 23,2025	February 24, 2020	3.54	81,800	81,800
August 16, 2025	August 16, 2018	5.00	200,000	200,000
August 19, 2025	August 20, 2020	2.12	100,000	33,333
August 30, 2025	September 5, 2018	5.00	480,000	480,000
October 7, 2025	October 8, 2020	2.90	35,000	11,667
December 2, 2025	December 3, 2020	2.59	130,000	43,333
January 2, 2026	January 3, 2019	4.30	150,000	150,000
January 24, 2026	January 24, 2019	5.34	60,000	60,000
March 29, 2026	March 30, 2021	4.51	400,000	-
April 1, 2026	April 2, 2019	5.77	140,000	93,333
April 4, 2026	April 5, 2019	5.42	60,000	40,000
May 12, 2026	May 13, 2021	3.00	75,000	50,000
June 5, 2026	June 6, 2021	3.26	60,000	-
August 16, 2026	August 17, 2021	3.26	60,000	-
August 24, 2026	August 25, 2021	3.81	140,000	25,000
September 13, 2026	September 14, 2021	4.88	55,000	-
December 8, 2026	December 9, 2021	2.65	380,000	-
December 8, 2026	December 9, 2021	3.59	325,000	-
January 11, 2027	January 12, 2022	2.18	220,000	-
March 14, 2027	March 15, 2022	2.07	60,000	-
Total			**4,581,800**	**2,598,466**

In addition to the options noted above, the following Share-Based Awards were granted in 2021: 12,054 on January 11, 2021 at a price of $2.80, 2,500 on January 27, 2021 at a price of $3.19, and 106,618 on March 18, 2021 at a price of $4.14, 37,000 on March 19, 2021 at a price of $4.50, 2,478 on March 31, 2021 at a price of $4.54, 153,500 on April 12, 2021 at a price of $4.28, 30,500 on May 19, 2021 at a price of $2.93, 159,606 on August 25, 2021 at a price of $3.22, 175,000 on September 17, 2021 at a price of $3.22, 4,336 on September 30, 2021 at a price of $5.70, 175,000 on October 17, 2021 at a price of $3.22, 175,000 on November 17, 2021 at a price of $3.22, 18,500 on December 1, 2021 at a price of $2.76, and 175,000 on December 17, 2021 at a price of $3.22. Of the previously listed grants, 75,000 common shares are subject to vesting of 1/3 on each of March 29, 2022, September 29, 2022, and March 29, 2023, and 50,000 common shares are subject to vesting of 1/2 on each of May 17, 2022, and August 17, 2022.

During 2021, 700,000 Performance Share Units were exercised for one Common Shares. 100,000 of these were valued at a price of $4.60 and the remaining 600,000 were valued at a price of $4.77. The Corporation currently has 1,200,000 PSUs outstanding that are due to expire on June 30, 2022 and were valued at $2.67 per share.

EQUITY PLANS

Summary of the Legacy Equity Compensation Plans

The Legacy Equity Compensation Plan was designed to give individuals an interest in preserving and maximizing shareholder value in the longer term, to enable the Corporation to attract and retain individuals with experience and ability and to reward individuals for current performance and expected future performance. The Legacy Equity Compensation Plan amended and restated the Corporation's stock option plan was effective April 22, 2020, and was approved by the Corporation's shareholders on June 1, 2020. As of May 21, 2021, the Legacy Equity Compensation Plan was replaced (see "Summary of Omnibus Equity Incentive Plan" below) and no additional awards will be granted under it. Previously granted awards under the Legacy Equity Compensation Plan will continue to be governed by it.

A description of the Legacy Equity Compensation Plan is set out below.

Eligible Participants: Directors, Employees and Service Providers (as those terms are defined in the Legacy Equity Compensation Plan, and referred to as "Participants") are eligible to be granted Awards under the Legacy Equity Compensation Plan and are Participants. "Award" is defined to mean, individually or collectively, a grant under the Legacy Equity Compensation Plan of Options or a grant or issue under the Legacy Equity Compensation Plan of Share-Based Awards. "Option" is defined to mean a stock option granted to a Director, Employee or Service Provider to purchase a Common Share. A Share-Based Award is defined to mean a Common Share award granted or issued to a Non-Executive Employee, an Independent Director, or a Service Provider (as those terms are defined in the Legacy Equity Compensation Plan).

Number of Shares Reserved: The number of Common Shares which may be issued pursuant to the Legacy Equity Compensation Plan may not exceed 13% of the issued Common Shares from time to time. The number of Common Shares which may be issuable pursuant to exercise of Options shall not exceed 10% of issued Common Shares from time to time. The maximum number of Share-Based Awards granted or issued in any fiscal year shall not exceed 3% of the issued Common Shares, on the first day of such fiscal year. Common Shares covered by an option that have been exercised, terminated, or expired shall again be available for an option grant. As of the date hereof, the total number of Common Shares issuable upon exercise of options granted under the Option Plan is 3,281,800 Common Shares (representing approximately 5.3% of the Common Shares issued and outstanding). Upon adoption of the Omnibus Equity Incentive Plan during fiscal 2021, no further Options or Common Shares grants are permitted under the Legacy Equity Compensation Plan

Limitations on Grants: The aggregate number of Common Shares issuable to insiders of the Corporation within any one-year period under the Legacy Equity Compensation Plan, or when combined with all of the Corporation's other security-based compensation arrangements, shall not exceed 10% of the Corporation's total issued and outstanding Common Shares. The aggregate number of Common Shares reserved for issuance to insiders of the Corporation at any time under the Legacy Equity Compensation Plan, or when combined with all of the Corporation's other security-based compensation arrangements, shall not exceed 10% of the Corporation's total issued and outstanding Common Shares. Share-Based Awards cannot be granted to employees who are insiders of the Corporation.

Exercise Price: The exercise price of the Common Shares covered by each Option is determined by the Board. While the Common Shares are listed on the TSX, the exercise price shall not be less than the "Market Price" of the Common Shares at the time the option is granted. "Market Price" is defined in the Legacy Equity Compensation Plan as the closing price of the Common Shares on the TSX, or another stock exchange where the majority of the trading volume and value of the Common Shares occurs, on the day immediately preceding the relevant date. If the Common Shares are listed on an exchange other than the TSX, the exercise price will be determined in accordance with the policies of such other exchange, or in the absence thereof, will be determined as the closing

sales price of such Shares as quoted on such exchange for the market trading date immediately prior to the time of determination less any discount permitted by such exchange.

Vesting: The Legacy Equity Compensation Plan provides that an option may be exercised (in each case to the nearest full share) during the term of the Option as follows unless determined otherwise by the Board by resolution: (a) one-third on the first anniversary of the date of the Option certificate relating to the options; (b) one-third on the second anniversary of the date of the Option certificate; and (c) the remaining one-third shall vest on the third anniversary of the date of the Option certificate.

Term of Options: Subject to the termination and change of control provisions noted below, the term of any option granted under the Legacy Equity Compensation Plan is determined by the Board and may not exceed ten years from the date of grant. Should the expiry date for an option fall within a blackout period or within nine business days following the expiration of a blackout period, such expiry date shall be automatically extended without any further act or formality to that date which is the tenth business day after the end of the blackout period, such tenth business day to be considered the expiry date for such option for all purposes under the Legacy Equity Compensation Plan. A “blackout period” is a period during which designated persons cannot trade Common Shares of the Corporation pursuant to any policy of the Corporation respecting restrictions on trading.

Termination: If the Participant is a director, Employee, or Service Provider of the Corporation and ceases to be such, other than by reason of death, then the expiry date of the Option is 90 days following the termination date, provided that, the Board has the discretion to waive the 90-day termination requirement, to permit the Participant to exercise any options for the full term of the Options, unless the Participant is terminated as a result of certain specified circumstances (including termination for cause for Employees and Service Providers) in which case the expiry date will be the date the Participant is terminated. The date that the Participant ceases to be an Employee or Service Provider of the Corporation for the purposes of the Legacy Equity Compensation Plan means the date designated by the Corporation as the effective date on which the Participant ceases, for any reason whatsoever, to perform services for or to be employed by the Corporation, as determined in the sole discretion of the Corporation.

In the event of the death of a Participant, the Participant’s Option may be exercised only within one year next succeeding such death and then only (i) by the person or persons to whom the Participant’s rights under the Option shall pass by the Participant’s will or the laws of descent and distribution, and (ii) to the extent that the Participant was entitled to exercise the Option at the date of death. Each Share-Based Award agreement shall set forth the extent to which the Participant shall have the right to receive Share-Based Awards following termination of the Participant’s employment or other relationship wit the Corporation. Such provisions shall be determined at the sole discretion of the Administrator. The Administrator is any director or employee of the Corporation that has been delegated by the Board to administer the Legacy Equity Compensation Plan.

Change of Control: In the event of an actual or potential change of control, the Board has the right to deal with any Awards in the manner it deems equitable and appropriate in the circumstances, including the right to: (i) determine that any Awards will remain in full force and effect in accordance with their terms after the change of control; (ii) cause any Awards to be converted or exchanged for options to acquire shares of another entity involved in the change of control, having the same value and terms and conditions as the Awards; (iii) accelerate the vesting of any unvested Awards; (iv) provide Participants with the right to surrender any Awards for an amount per underlying Common Share equal to the positive difference, if any, between the fair market value of the Common Share on the date of surrender and the Option exercise price of such Awards; and (v) accelerate the date by which any Awards must be exercised.

Assignability: The benefits, rights, and Awards accruing to any Participant in accordance with the terms and conditions of the Legacy Equity Compensation Plan are not transferable or assignable. During the lifetime of a Participant any benefits, rights and Awards may only be exercised by the Participant.

Amendment Provisions: The Legacy Equity Compensation Plan provides that the Board may from time to time amend the Legacy Equity Compensation Plan and the terms and conditions of any Award granted thereunder, provided that any such amendment, modification, or change to the provisions of the Legacy Equity Compensation Plan shall: (a) not adversely alter or impair any Award previously granted except as permitted by the adjustment

provisions in the Legacy Equity Compensation Plan; (b) be subject to any regulatory approvals, where required, including the approval of the TSX, where necessary; (c) be subject to Shareholder approval in accordance with the rules of the TSX in circumstances where the amendment, modification or change to the Legacy Equity Compensation Plan would (i) reduce the exercise price of an option held by an insider of the Corporation; (ii) extend the term of an Option held by an insider of the Corporation beyond the original term of the Option (other than pursuant to the blackout period provisions); (iii) amend to remove or to exceed the insider participation limits in the Legacy Equity Compensation Plan; (iv) increase the fixed maximum percentage of issued and outstanding Common Shares which may be issued pursuant to the Legacy Equity Compensation Plan or change from a fixed maximum percentage of issued and outstanding Common Shares to a fixed maximum number of Common Shares; or (v) amend the amendment provisions and (d) not be subject to Shareholder approval in circumstances where the amendment, modification or change to the Legacy Equity Compensation Plan or Award would (i) be of a "housekeeping nature"; (ii) be necessary for Awards to qualify for favourable treatment under applicable tax laws; (iii) alter, extend or accelerate any vesting terms or condition in the Legacy Equity Compensation Plan or any option; (iv) introduce, amend or modify any mechanics for exercising any Option (including relating to a cashless exercise feature or an automatic exercise feature); (v) change the term of an Option or change any termination provision in the Equity Compensation or any Award (for example, relating to termination of employment, resignation, retirement or death), provided that such change does not entail an extension beyond the original term of such Award (other than such period being extended by virtue of the blackout provisions); (vi) introduce a share appreciation right feature payable in cash or Common Shares, provided that such feature provides for a full deduction of the number of underlying Common Shares from the Legacy Equity Compensation Plan maximum as applicable; (vii) change the application of the adjustment or change of control provisions; (viii) add a form of financial assistance or amend a financial assistance provision which is adopted; or (ix) change the eligible participants under the Legacy Equity Compensation Plan.

Financial Assistance: The Legacy Equity Compensation Plan does not provide for the Corporation to give financial assistance to facilitate the purchase of Common Shares under the Legacy Equity Compensation Plan.

Taxes and Source Deductions: The Legacy Equity Compensation Plan provides that the Corporation or any subsidiary may take such reasonable steps for the deduction and withholding of any taxes and other required source deductions that the Corporation or the subsidiary, as the case may be, is required by any law or regulation of any governmental authority whatsoever to withhold, deduct or remit in connection with the Legacy Equity Compensation Plan, any exercise or surrender of any option, or a portion thereof, by an Participant or any issuance of Common Shares to an Participant.

In addition, the delivery of any Common Shares to be issued to a Participant on the exercise or termination of options by the Participant, may be made conditional upon the Participant (or other person) reimbursing or compensating the Corporation or making arrangements satisfactory to the Corporation for the payment to it in a timely manner of all taxes required to be remitted for the account of the Participant.

Summary of the Omnibus Equity Incentive Plan

The purpose of the Omnibus Equity Incentive Plan is to provide the Corporation with a share–related mechanism to attract, retain and motivate qualified Omnibus Participants (as defined below) and to reward such Omnibus Participants as may be granted Omnibus Awards (as defined below) by the Board from time to time for their contributions toward the long–term goals and success of the Corporation and to enable and encourage such Omnibus Participants to acquire Common Shares as long–term investments and proprietary interests in the Corporation.

A description of the Omnibus Equity Incentive Plan is set out below.

Common Shares Subject to the Omnibus Equity Incentive Plan: The Omnibus Equity Incentive Plan is a rolling plan which, subject to the adjustment provisions provided for therein, provides that the aggregate maximum number of Common Shares that may be issued upon the exercise or settlement of awards granted under the Omnibus Equity Incentive Plan shall not exceed 15% of the Corporation's issued and outstanding Common Shares from time to time (including Common Shares reserved for issuance in respect of 3,281,800 stock options outstanding under the Legacy Equity Compensation Plan and in respect of any other security based compensation

arrangement), such number being 9,288,824 as at the date hereof. The Omnibus Equity Incentive Plan is considered an "evergreen" plan, since the Common Shares covered by awards which have been exercised, settled, or terminated shall be available for subsequent grants under the Omnibus Equity Incentive Plan and the number of awards available to grant increases as the number of issued and outstanding Common Shares increases.

Insider Participation Limit: The Omnibus Equity Incentive Plan provides that the aggregate number of Common Shares (a) issuable to insiders at any time (under all of the Corporation's security-based compensation arrangements) cannot exceed 10% of the Corporation's issued and outstanding Common Shares and (b) issued to insiders within any one year period (under all of the Corporation's security-based compensation arrangements) cannot exceed 10% of the Corporation's issued and outstanding Common Shares.

Administration: The Plan Administrator (as defined in the Omnibus Equity Incentive Plan) is determined by the Board, and is initially the Board. The Omnibus Equity Incentive Plan may in the future be administered by a committee of the Board. That committee may in turn sub delegate certain functions to an officer or director. The Plan Administrator determines which directors, officers, consultants, and employees are eligible to receive awards under the Omnibus Equity Incentive Plan, the time or times at which awards may be granted, the conditions under which awards may be granted or forfeited to the Corporation, the number of Common Shares to be covered by any award, the exercise price of any award, whether restrictions or limitations are to be imposed on the Common Shares issuable pursuant to grants of any award, and the nature of any such restrictions or limitations, any acceleration of exercisability or vesting, or waiver of termination regarding any award, based on such factors as the Plan Administrator may determine.

Eligibility: All directors, employees, and consultants of the Corporation and future subsidiaries, if any, are eligible to participate in the Omnibus Equity Incentive Plan (referred to as "Omnibus Participants"). The extent to which any such individual is entitled to receive a grant of an award pursuant to the Omnibus Equity Incentive Plan will be determined in the sole and absolute discretion of the Plan Administrator.

Types of Awards: Awards of Options, Restricted Share Units, Performance Share Units, Deferred Share Units and other share-based awards may be made under the Omnibus Equity Incentive Plan. All of the awards described below are subject to the conditions, limitations, restrictions, exercise price, vesting, settlement, and forfeiture provisions determined by the Plan Administrator, in its sole discretion, subject to such limitations provided in the Omnibus Equity Incentive Plan and will generally be evidenced by an award agreement. In addition, subject to the limitations provided in the Omnibus Equity Incentive Plan and in accordance with applicable law, the Plan Administrator may accelerate or defer the vesting or payment of awards, cancel, or modify outstanding awards, and waive any condition imposed with respect to awards or Common Shares issued pursuant to awards.

Options: An Option entitles a holder thereof to purchase a prescribed number of treasury Common Shares at an exercise price set at the time of the grant. The Plan Administrator will establish the exercise price at the time each Option is granted, which exercise price must in all cases be not less than the five-day volume weighted average closing price (the "5-day VWAP") of the Common Shares on the TSX for the five trading days immediately preceding the date of grant (for the purposes of this section, the "Market Price"). Subject to any accelerated termination as set forth in the Omnibus Equity Incentive Plan, each Option expires on its respective expiry date. The Plan Administrator will have the authority to determine the vesting terms applicable to grants of Options. Once an Option becomes vested, it shall remain vested and shall be exercisable until expiration or termination of the Option, unless otherwise specified by the Plan Administrator, or as otherwise set forth in any written employment agreement, award agreement or other written agreement between the Corporation and the Omnibus Participant. The Plan Administrator has the right to accelerate the date upon which any Option becomes exercisable. The Plan Administrator may provide at the time of granting an Option that the exercise of that Option is subject to restrictions, in addition to those specified in the Omnibus Equity Incentive Plan, such as vesting conditions relating to the attainment of specified performance goals.

Unless otherwise specified by the Plan Administrator at the time of granting an Option and set forth in the particular award agreement, an exercise notice must be accompanied by payment of the exercise price. A Omnibus Participant may, with the consent of the Corporation, in lieu of exercising an Option pursuant to an exercise notice, elect to surrender such Option to the Corporation (a "Cashless Exercise") in consideration for an amount from the

Corporation equal to (i) the Market Price of the Common Shares issuable on the exercise of such Option (or portion thereof) as of the date such Option (or portion thereof) is exercised, less (ii) the aggregate exercise price of the Option (or portion thereof) surrendered relating to such Common Shares (the "In-the-Money Amount") by written notice to the Corporation indicating the number of Options such participant wishes to exercise using the Cashless Exercise, and such other information that the Corporation may require. Subject to the provisions of the Omnibus Equity Incentive Plan, the Corporation will satisfy payment of the In-the-Money Amount by delivering to the participant such number of Common Shares having a fair market value equal to the In-the-Money Amount.

Restricted Share Units: A Restricted Share Unit (“RSU”) is a unit equivalent in value to a Common Share credited by means of a bookkeeping entry in the books of the Corporation which entitles the holder to receive one Common Share (or the value thereof) for each RSU after a specified vesting period. The Plan Administrator may, from time to time, subject to the provisions of the Omnibus Equity Incentive Plan and such other terms and conditions as the Plan Administrator may prescribe, grant RSUs to any Omnibus Participant in respect of a payment for services rendered by the applicable participant in a taxation year.

The number of RSUs (including fractional RSUs) granted at any particular time under the Omnibus Equity Incentive Plan will be calculated by dividing (a) the amount of the payment that is to be paid in RSUs, as determined by the Plan Administrator, by (b) the greater of (i) the Market Price of a Common Share on the date of grant and (ii) such amount as determined by the Plan Administrator in its sole discretion. The Plan Administrator shall have the authority to determine any vesting terms applicable to the grant of RSUs.

Upon settlement, holders will redeem each vested RSU for one Common Share in respect of each vested RSU (or, at the election of the holder and subject to the approval of the Plan Administrator, a cash payment or a combination of Common Shares and cash). Any such cash payments made by the Corporation shall be calculated by multiplying the number of RSUs to be redeemed for cash by the Market Price per Common Share as at the settlement date.

Performance Share Unit: A Performance Share Unit (“PSU”) is a unit equivalent in value to a Common Share credited by means of a bookkeeping entry in the books of the Corporation which entitles the holder to receive one Common Share (or the value thereof) for each PSU after specific performance-based vesting criteria determined by the Plan Administrator, in its sole discretion, have been satisfied. The performance goals to be achieved during any performance period, the length of any performance period, the amount of any PSUs granted, the effect of termination of a participant's service and the amount of any payment or transfer to be made pursuant to any PSU will be determined by the Plan Administrator and by the other terms and conditions of any PSU, all as set forth in the applicable award agreement. The Plan Administrator may, from time to time, subject to the provisions of the Omnibus Equity Incentive Plan and such other terms and conditions as the Plan Administrator may prescribe, grant PSUs to any participant in respect of a bonus or similar payment in respect of services rendered by the applicable participant in a taxation year (the "PSU Service Year").

The Plan Administrator shall have the authority to determine any vesting terms applicable to the grant of PSUs. Upon settlement, holders will redeem each vested PSU for the following at the election of such holder but subject to the approval of the Plan Administrator: (a) one Common Share in respect of each vested PSU, (b) a cash payment, or (c) a combination of Common Shares and cash. Any such cash payments made by the Corporation to a participant shall be calculated by multiplying the number of PSUs to be redeemed for cash by the Market Price per Common Share as at the settlement date. Subject to the provisions of the Omnibus Equity Incentive Plan and except as otherwise provided in an award agreement, no settlement date for any PSU shall occur, and no Common Share shall be issued or cash payment shall be made in respect of any PSU any later than the final business day of the third calendar year following the applicable PSU Service Year.

Deferred Share Units: A Deferred Share Unit (“DSU”) is a unit equivalent in value to a Common Share credited by means of a bookkeeping entry in the books of the Corporation which entitles the holder to receive one Common Share (or, at the election of the holder and subject to the approval of the Plan Administrator, the cash value thereof) for each DSU on a future date. The Board may fix from time to time a portion of the total compensation (including annual retainer) paid by the Corporation to a director in a calendar year for service on the Board that are to be payable in the form of DSUs. In addition, an Omnibus Participant may, with the Corporation's consent, be given,

subject to the provisions of the Omnibus Equity Incentive Plan, the right to elect to receive a portion of the compensation owing to them in the form of DSUs.

Share-Based Awards: The Plan Administrator may grant other types of equity-based or equity-related awards (including the grant or offer for sale of unrestricted Common Shares) in such amounts and subject to such terms and conditions, including, but not limited to, being subject to performance criteria, or in satisfaction of such obligations, as the Plan Administrator shall determine. Such awards may involve the issuance of actual Common Shares to Omnibus Participants, or payment in cash or otherwise of amounts based on the value of Common Shares.

Dividend Equivalents: Except as otherwise determined by the Plan Administrator or as set forth in the particular award agreement, RSUs, PSUs, and DSUs shall be credited, in accordance with the terms of the Omnibus Equity Incentive Plan, with dividend equivalents in the form of additional RSUs, PSUs, and DSUs, as applicable, as of each dividend payment date in respect of which normal cash dividends are paid on Common Shares.

Black-out Periods: In the event an award expires, at a time when a scheduled blackout is in place or an undisclosed material change or material fact in the affairs of the Corporation exists, the expiry of such award will be the date that is ten business days after which such scheduled blackout terminates or there is no longer such undisclosed material change or material fact.

Term: While the Omnibus Equity Incentive Plan does not stipulate a specific term for awards granted thereunder, as discussed below, awards may not expire beyond ten years from its date of grant, except where Shareholder approval is received or where an expiry date would have fallen within a blackout period of the Corporation. All awards must vest and settle in accordance with the provisions of the Omnibus Equity Incentive Plan and any applicable award agreement, which award agreement may include an expiry date for a specific award.

Termination of Employment or Services: The following describes the impact of certain events upon the Omnibus Participants under the Omnibus Equity Plan Incentive Plan, including termination for cause, resignation, termination without cause, disability, death or retirement, subject, in each case, to the terms of an Omnibus Participant's applicable employment agreement, award agreement or other written agreement:

- Termination for Cause / Resignation; Any Option or other award held by the Omnibus Participant that has not been exercised, surrendered, or settled as of the Termination Date (as defined in the Omnibus Equity Incentive Plan) shall be immediately forfeited and cancelled as of the Termination Date.

- Termination without Cause: Any unvested Option or other award which would otherwise vest or become exercisable in accordance with its terms based solely on the Omnibus Participant remaining in the service of the Corporation on or prior to the date that is 90 days after the Termination Date shall immediately vest. Any vested Options may be exercised by the Omnibus Participant within the time period contemplated by the Omnibus Equity Incentive Plan.

- Death or Disability: Any award that is held by the Omnibus Participant that has not vested as of the date of the death or disability (as defined under the Omnibus Equity Incentive Plan) of such Omnibus Participant shall vest on such date. Any vested Options may be exercised by the Omnibus Participant, or Omnibus Participant's beneficiary or legal representative (as applicable), within the time period contemplated by the Omnibus Equity Incentive Plan.

- Retirement: Any (i) outstanding award that vests or becomes exercisable based solely on the Omnibus Participant remaining in the service of the Corporation or its subsidiary will become 100% vested, and (ii) outstanding award that vests based on the achievement of Performance Goals (as defined in the Omnibus Equity Incentive Plan) that has not previously become vested shall continue to be eligible to vest based upon the actual achievement of such Performance Goals. Any vested Options may be exercised by the Omnibus Participant within the time period contemplated by the Omnibus Equity Incentive Plan.

Change in Control: Under the Omnibus Equity Incentive Plan, except as may be set forth in an employment agreement, award agreement or other written agreement between the Corporation or a subsidiary of the Corporation and a participant:

- If within 12 months following the completion of a transaction resulting in a Change in Control (as defined in the Omnibus Equity Inventive Plan), an Omnibus Participant's employment, consultancy or directorship is terminated by the Corporation or a subsidiary of the Corporation without Cause (as defined in the Omnibus Equity Incentive Plan), without any action by the Plan Administrator:
    - any unvested awards held by the participant at the Termination Date shall immediately vest; and
    - any vested awards may be exercised, surrendered to the Corporation, or settled by the participant at any time during the period that terminates on the earlier of: (A) the expiry date of such award; and (B) the date that is 90 days after the Termination Date. Any award that has not been exercised, surrendered, or settled at the end of such period being immediately forfeited and cancelled.
- Unless otherwise determined by the Plan Administrator, if, as a result of a Change in Control, the Common Shares will cease trading on the TSX, the Corporation may terminate all of the awards, other than an Option held by an Omnibus Participant that is a resident of Canada for the purposes of the *Income Tax Act* (Canada), granted under the Omnibus Equity Incentive Plan at the time of and subject to the completion of the Change in Control transaction by paying to each holder at or within a reasonable period of time following completion of such Change in Control transaction an amount for each Award equal to the fair market value of the award held by such participant as determined by the Plan Administrator, acting reasonably.

Non-Transferability of Awards: Except as permitted by the Plan Administrator and to the extent that certain rights may pass to a beneficiary or legal representative upon death of a participant, by will or as required by law, no assignment or transfer of awards, whether voluntary, involuntary, by operation of law or otherwise, vests any interest or right in such awards whatsoever in any assignee or transferee and immediately upon any assignment or transfer, or any attempt to make the same, such awards will terminate and be of no further force or effect. To the extent that certain rights to exercise any portion of an outstanding award pass to a beneficiary or legal representative upon the death of a participant, the period in which such award can be exercised by such beneficiary or legal representative shall not exceed one year from the Omnibus Participant's death.

Amendments to the Omnibus Equity Incentive Plan: The Plan Administrator may also from time to time, without notice and without approval of the holders of voting Common Shares, amend, modify, change, suspend or terminate the Omnibus Equity Incentive Plan or any awards granted pursuant thereto as it, in its discretion, determines appropriate, provided that (a) no such amendment, modification, change, suspension or termination of the Omnibus Equity Incentive Plan or any award granted pursuant thereto may materially impair any rights of a participant or materially increase any obligations of a participant under the Omnibus Equity Incentive Plan without the consent of such participant, unless the Plan Administrator determines such adjustment is required or desirable in order to comply with any applicable securities laws or stock exchange requirements, and (b) any amendment that would cause an award held by a U.S. taxpayer to be subject to the income inclusion under Section 409A of the United States Internal Revenue Code of 1986, as amended, shall be null and void *ab initio*.

Notwithstanding the above, and subject to the rules of the TSX, the approval of Shareholders will be required to effect any of the following amendments to the Omnibus Equity Incentive Plan:

- increasing the number of Common Shares reserved for issuance under the Omnibus Equity Incentive Plan, except pursuant to the provisions in the Omnibus Equity Incentive Plan which permit the Plan Administrator to make equitable adjustments in the event of transactions affecting the Corporation or its capital;
- increasing or removing the 10% limits on Common Shares issuable or issued to insiders;

- reducing the exercise price of an option award (for this purpose, a cancellation or termination of an award of a participant prior to its expiry date for the purpose of reissuing an option award to the same participant with a lower exercise price shall be treated as an amendment to reduce the exercise price of an option award) except pursuant to the provisions in the Omnibus Equity Incentive Plan which permit the Plan Administrator to make equitable adjustments in the event of transactions affecting the Corporation or its capital;

- extending the term of an Option award beyond the original expiry date (except where an expiry date would have fallen within a blackout period applicable to the participant or within ten business days following the expiry of such a blackout period);

- permitting an Option award to be exercisable beyond ten years from its date of grant (except where an expiry date would have fallen within a blackout period);

- permitting awards to be transferred to a person;

- changing the eligible Omnibus Participants; and

- deleting or otherwise limiting the amendments which require approval of the Shareholders.

Except for the items listed above, amendments to the Omnibus Equity Incentive Plan will not require Shareholder approval. Such amendments include (but are not limited to): (a) amending the general vesting provisions of an award, (b) amending the provisions for early termination of awards in connection with a termination of employment or service, (c) adding covenants of the Corporation for the protection of the Omnibus Participants, (d) amendments that are desirable as a result of changes in law in any jurisdiction where an Omnibus Participant resides, and (e) curing or correcting any ambiguity or defect or inconsistent provision or clerical omission or mistake or manifest error.

MARKET FOR SECURITIES

Common Shares

The Common Shares currently trade under the symbol “CRDL” on the TSX and the Nasdaq. The Common Shares commenced trading on the TSX on December 20, 2018 and commenced trading on the Nasdaq on August 10, 2021. The following table sets out the price range and trading volume of the Common Shares, as reported by the TSX, for each month traded in Cardiol’s financial year ended December 31, 2021, and the current fiscal year to date:

Common Shares

Month	Price Range		Total Volume
	High ($)	Low ($)	
January 2021	3.66	2.61	3,321,624
February 2021	5.32	3.05	6,092,761
March 2021	5.06	3.45	5,124,200
April 2021	4.49	3.68	2,456,879
May 2021	4.42	2.72	6,372,940
June 2021	3.35	2.87	2,679,984
July 2021	3.20	2.56	2,126,230
August 2021	4.95	2.63	5,763,058
September 2021	6.19	4.35	8,637,945
October 2021	6.11	4.01	6,164,662
November 2021	4.65	2.48	8,230,143

December 2021	2.85	2.25	5,760,699
January 2022	2.95	1.97	5,855,925
February 2022	2.49	1.73	3,900,132
March 1-22, 2022	2.29	1.58	3,001,709

ESCROWED SECURITIES AND SECURITIES SUBJECT TO CONTRACTUAL RESTRICTIONS ON TRANSFER

As at December 31, 2021, no outstanding Common Shares or other securities of Cardiol were held in escrow or subject to contractual restrictions on transfer, other than as described under “Capital Structure – Stock Options and other Share-Based Awards.

May 2021 Warrants

The May 2021 Warrants currently trade under the symbol “CRDL.WT.A” on the TSX. The May 2021 Warrants commenced trading on the TSX on May 12, 2021. The following table sets out the price range and trading volume of the May 2021 Warrants, as reported by the TSX, for each month traded in Cardiol’s financial year ended December 31, 2021, and the current fiscal year to date:

	May 2021 Warrants		
	Price Range		
Month	High ($)	Low ($)	Total Volume
May 12-31, 2021	1.10	0.48	432,024
June 2021	1.15	0.85	168,300
July 2021	1.00	0.81	156,201
August 2021	2.10	0.75	209,458
September 2021	2.78	1.50	322,625
October 2021	2.65	1.29	53,400
November 2021	2.00	1.72	26,484
December 2021	1.80	1.52	1,290
January 2022	1.46	0.90	2,700
February 2022	0.90	0.70	2,500
March 1-22, 2022	0.76	0.29	133,000

DIRECTORS AND MANAGEMENT

The following table sets out, for each of our directors and executive officers, the person’s name, province or state, and country of residence, position with us, principal occupation and, if a director, the date on which the person became a director. Our directors are expected to hold office until our next annual general meeting of Shareholders. Our directors are elected annually and, unless re-elected, retire from office at the end of the next annual general meeting of Shareholders. As a group, the Directors and executive officers beneficially own, or control or direct, directly or indirectly, a total of 3,251,759 Common Shares, representing 5.25% of the Common Shares outstanding.

Directors and Executive Officers

Name and Province or State and Country of Residence	Position with the Corporation	Since	Principal Occupation
David Elsley Ontario, Canada	Director, President, and Chief Executive Officer	January 19, 2017	President and Chief Executive Officer of Cardiol since January 19, 2017. Self-employed, investigated drug formulations that are the foundation of Cardiol's business (from 2013 to 2017).
Chris Waddick Ontario, Canada	Chief Financial Officer and Corporate Secretary	August 16, 2018	Chief Financial Officer and Corporate Secretary of Cardiol since August 16, 2018. Executive Vice President and CFO of Active Energy Inc., a private energy company, since January 2013 and President of NRJ Consulting Inc., a consulting company, since November 2009.
Bernard Lim Ontario, Canada	Chief Operating Officer	December 3, 2020	Chief Operating Officer of Cardiol since December 3, 2020. Chair of the Board of AndersDx (UK) a technology company since 2009. Chair of the Board for Altus Assessments Inc. a technology company focused on professional screening for academic institutions since 2014. Chair of the Board of Front Line Medical, a vascular trauma medical device company since 2020. Director of Aventamed (Ireland) a medical device company since 2015.
Dr. Andrew Hamer Nelson, New Zealand	Chief Medical Officer (CMO)	March 29, 2021	Chief Medical Officer of Cardiol since March 29, 2021. Served as Executive Director, Global Development-Cardiometabolic at California-based Amgen Inc.
Michael Willner[(1)(3)(5)] Florida, USA	Director	September 7, 2021	Founder of Willner Capital, Inc., an investment company specializing in public and private equities, as well as debt instruments.
Iain Chalmers[(2)(4)(6)] Ontario, Canada	Former Director	August 20, 2018	Professor of Marketing and Alcohol Business Management, Centennial College, Toronto. Previously, Vice-President of Marketing and Innovation for Diageo Canada (from 2000 to 2016).
Peter Pekos[(2)(5)] Ontario, Canada	Director	December 15, 2017	President and Chief Executive Officer of Dalton Pharma Services.
Dr. Guillermo Torre-Amione[(1)(2)(5)] Monterrey, Mexico	Chairman and Director	August 20, 2018	President of TecSalud. Previously, Chief of Heart Failure Division and Medical Director of Cardiac Transplantation, Houston Methodist DeBakey Heart & Vascular Center.

Name and Province or State and Country of Residence	Position with the Corporation	Since	Principal Occupation
Colin Stott[1][5] Southport, United Kingdom	Director	December 3, 2019	Chief Operating Officer of Alterola Biotech Inc. Previously Chief Operating Officer of Alinova Biosciences Ltd. Previously Scientific Affairs Director, International and R&D Operations Director for GW Pharmaceuticals plc.
Jennifer Chao[2][4][5][6] New York, USA	Director	March 15, 2022	Founder of CoreStrategies Management, LLC. Previously Managing Director and Senior Lead Biotechnology Securities Analyst at Deutsche Bank.

Notes:

(1) Member of the Audit Committee
(2) Member of the Corporate Governance and Compensation Committee ("CG&C Committee")
(3) Chair of the Audit Committee
(4) Chair of the CG&C Committee
(5) Independent
(6) As of March 15, 2022, Iain Chalmers resigned from the Board of Directors, and was replaced by the appointment of Jennifer Chao

Biographies of Directors and Executive Officers

The following are brief profiles of our executive officers and directors, including a description of each individual's principal occupation within the past five years.

David Elsley, MBA – President, Chief Executive Officer, and Director

Mr. David Elsley is a business leader with a proven track record of developing, financing, and managing all aspects of corporate development in biotechnology and high-growth organizations. In 1990, Mr. Elsley founded Vasogen Inc., a biotechnology company focused on the research and commercial development of novel therapeutics for the treatment of heart failure and other inflammatory conditions. Mr. Elsley assembled a team of management, directors, and scientific advisors comprising industry professionals and thought leaders from North America and Europe. He managed and directed Vasogen's growth from start-up to an organization employing over 250 people with operations and R&D programs in Canada, the United States, and Europe. Mr. Elsley established the research and development infrastructure, partnerships, manufacturing capability, and corporate quality systems necessary to advance two anti-inflammatory therapies from concept to completion of international multi-center pivotal phase III clinical trials involving 2,500 patients. Vasogen went public on the TSX and the Nasdaq, raising over $200 million to support corporate development and reached a market capitalization of over USD $1 billion. Mr. Elsley holds a Master of Business Administration from the Ivey School of Business, University of Western Ontario.

Andrew Hamer, MB, ChB – Chief Medical Officer

Dr. Andrew Hamer brings 30 years of experience in the global life sciences industry, medical affairs, and cardiology practice to the Corporation. Most recently he served as Executive Director, Global Development-Cardiometabolic at California-based Amgen Inc., where he led the Global Development group for Repatha®, the LDL cholesterol lowering PCSK9 inhibitor evolocumab, which generated revenues of almost USD $900 million in 2020. As development lead, Dr. Hamer headed the Repatha® global evidence generation team collaborating with safety, regulatory, health economics, observational research, scientific communications, publications, medical affairs, and clinical operations teams to design and execute several multi-center clinical trials in support of FDA and international regulatory filings. Prior to his five-year tenure with Amgen, Dr. Hamer served for two years as VP Medical Affairs at Capricor Therapeutics Inc., where he was responsible for the development of novel therapeutics for heart disease and for the supervision of the clinical operations of the company, including clinical trial design and execution.

Prior to joining the life sciences industry, Dr. Hamer practiced cardiology and internal medicine in New Zealand for 19 years. His distinguished career in cardiology culminated as Chief Cardiologist at Nelson Hospital, Nelson Marlborough District Health Board, Nelson, while concurrently leading cardiac services nationally in New Zealand. Dr. Hamer graduated with a medical degree (MB, ChB) from the University of Otago, New Zealand, an internationally recognized medical school which recently ranked among the top twenty universities in the world in several medical subject categories. His clinical research training took place at various centres in New Zealand and London, UK, followed by a cardiology fellowship at Deaconess Hospital, Harvard Medical School, Boston. Dr. Hamer has co-authored many high-quality peer-reviewed scientific publications reflecting his considerable experience as a clinical trialist, having served as a principal or co-investigator for 40 multi-centre clinical trials in therapies for acute coronary syndrome, heart failure, hypertension, cholesterol disorders, atrial fibrillation, and diabetes.

Chris Waddick, MBA, CPA, CA – Chief Financial Officer and Corporate Secretary

Mr. Chris Waddick has 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 in designing, building, and managing financial processes, procedures, and infrastructure. Mr. Waddick most recently served as Executive Vice President and Chief Financial Officer for a private Ontario energy company where he was retained by the shareholders to refinance the company and establish a new strategic direction, as well as the appropriate financial infrastructure. During his tenure, he implemented two corporate restructurings, drove substantial earnings growth, and significantly reduced both cost of capital and debt levels. Mr. Waddick spent more than twelve years at Vasogen Inc., a biotechnology company focused on the research and commercial development of novel therapeutics for the treatment of heart failure and other inflammatory conditions. While serving as Chief Financial Officer and Chief Operating Officer, the company grew from start up to an organization employing over 250 employees that established the necessary systems and infrastructure to advance an anti-inflammatory therapy through to the completion of an international multi-center pivotal trial involving 2,500 patients. Vasogen went public on the TSX and the NASDAQ, raising over $200 million to support corporate development and reached a market capitalization of over US$ 1 billion. Prior to Vasogen, he held progressively senior financial positions at Magna International Inc. and Union Gas Limited. Mr. Waddick is a CPA and earned a business degree from Wilfrid Laurier University and a Master of Business Administration from York University.

Bernard Lim, BSc, PgDip, CEng (UK) – Chief Operating Officer

Mr. Bernard Lim is a senior executive with a proven track record of over thirty years in the life sciences industry spanning biotechnology, diagnostics, medical devices, and high-technology companies in North America and Europe. He was founder and CEO of a highly successful drug delivery company that he led from R&D through to commercialization and its eventual acquisition by Eli Lily. As Chair of the Board of Altus Assessments, he guided the company's spinout from the university and its subsequent rapid growth to become market leader in the US and Canada. As Chair of the Board of AndersDx, a private UK-based technology company, he led its growth to a profitable enterprise. He is currently Chair of the Board of Front Line Medical Technologies, a vascular trauma company and board director of Aventamed (Ireland). Previously, Bernard was Senior Vice President, Operations for Vasogen, as well as head of UK operations for a technology multinational where he scaled its operations exponentially and delivered multifold improvements in quality and financial performance. He was also CEO of a glaucoma, Alzheimer's and an *in-vitro* diagnostics company and prior to that was head of R&D for a leading neonatology and paediatrics company.

Guillermo Torre-Amione, MD, PhD – Chairman and Director

Board certified in Cardiovascular Disease and Advanced Heart Failure/Transplant Cardiology, Dr. Guillermo Torre-Amione is former chief of the Heart Failure Division and former medical director of Cardiac Transplantation at the Houston Methodist DeBakey Heart & Vascular Center. He is a senior member at The Methodist Hospital Research Institute, full professor of medicine at the Weill Cornell Medical College of Cornell University, New York, and, more recently, became President of TecSalud, an academic medical center and medical school of the Instituto Tecnológico y de Estudios Superiores de Monterrey (ITESM) in Mexico. Dr. Torre-Amione spearheads the Gene and Judy Campbell Laboratory for Cardiac Transplant Research, where his primary areas of research include heart

failure, cardiac transplantation, and the role of the immune response in modulating the progression of heart failure. He initiated a series of clinical studies that led to an FDA-approved phase II clinical trial of neurostimulation in heart failure, a novel approach to the treatment of patients with advanced heart failure. Dr. Torre-Amione received his medical degree from the ITESM and a doctorate degree in immunology from the University of Chicago. He has published more than 170 manuscripts in peer-reviewed journals. He currently divides his time between his clinical and academic activities at The Methodist Hospital and ITESM. Prior to being appointed to Cardiol's Board of Directors, Dr. Torre-Amione was a member of the Corporation's Scientific Advisory Board.

Iain Chalmers, MBA, BA, Bed, CAAP – Former Director

Mr. Iain Chalmers is currently a professor of Marketing and Alcohol Business Management at Centennial College in Toronto, Ontario as well as part owner of Niagara Falls Craft Distillery. He recently transitioned to teaching after spending nearly thirty years in the Consumer Packaged Goods business, where for over eight years, he was the Vice President of Marketing & Innovation for Diageo Canada, the world's largest alcohol spirits company. Prior to this, he spent eleven years at Gillette/Procter & Gamble in various senior positions, including General Sales and Marketing Director for the Gillette Grooming Division. Iain is a seasoned marketer and brand builder with experience in Canada and the U.S. He led the Business Development and Sales Planning function for Braun USA and worked in marketing and sales positions at Unilever and Wrigley Canada. While at Diageo Canada, he was recognized by Marketing Magazine as one of the top four Marketers in Canada, based on the strong creative output of his team and consistent business performance for global brands, including Guinness, Smirnoff, Crown Royal, and Captain Morgan. Working in the alcohol industry has given Iain extensive experience building brands in a highly government-regulated environment. He is a past member of the Association of Canadian Advertisers, Advertising Standards Canada (ASC) and was a member of the Judicial Committee for ASC. Iain holds a BA in Political Science from University of Western Ontario, a Graduate Certificate in Management from Harvard University, a Bachelor of Education and an MBA from Charles Sturt University, and is a Certified Advertising Agency Practitioner (CAAP) from the Institute of Canadian Advertising. Iain Chalmers resigned from the Board of Directors on March 15, 2022.

Peter Pekos, BSc, MSc – Director

Mr. Peter Pekos, is a veteran of the pharmaceutical services industry. In 1986, he was a founder of Dalton Pharma Services (Dalton). Over a period of 30 years, he directed Dalton's growth based on strong client relationships. Dalton provides pharma and biotech clients with an array of integrated services in a world-class 42,000 square foot facility, with more than 110 employees, in the heart of one of North America's largest biomedical clusters. This includes premium contract chemistry research, a full range of analytical support, medicinal chemistry, formulation, cGMP manufacture of solid dosage forms, and cGMP aseptic fill-in vials and syringes. Mr. Pekos is currently President and CEO of Dalton, guiding the evolution of the company to best serve the changing needs of its clients throughout the major global economies, including the world's largest pharmaceutical companies. In 1983, he obtained a Chemistry/Biochemistry Double Specialist Degree with a Minor in Biology from the University of Toronto. In 1986, he completed a Master's Degree in synthetic chemistry at York University, and with his Professor, Doug Butler, founded Dalton with a very modest amount of capital. The company used incubator facilities at York University, and initially manufactured and sold specialty chemical compounds. Mr. Pekos also founded Ashbury Biologicals. Inc., a phyto-pharmaceutical company, Jupiter Consumer Products, a company that targeted the development of adult-focused confections, and several other technology-based companies focused on advanced materials and pharmaceutical development tools. Mr. Pekos is currently on the board and was founding Chairman of ventureLAB, a Regional Innovation Center located at IBM's York Region campus. VentureLAB guides government program delivery to support the innovation ecosystem for biotechnology and related industries in southern Ontario.

Colin G. Stott, BSc (Hons) - Director

Mr. Colin Stott is a veteran of the pharmaceutical and biotech industries, having almost 30 years' experience in pre-clinical and clinical development, with specific expertise in the development of cannabinoid-based medicines, and 19 years' experience in the field. Currently Chief Operating Officer of Alterola Biotech Inc., Mr. Stott is the former Scientific Affairs Director, International and R&D Operations Director for GW Pharmaceuticals plc ("GW Pharma"), a world leader in the development of cannabinoid therapeutics. As R&D Operations Director at GW

Pharma for over 16 years, he was a key player in the development of their discovery and development pipeline, and was closely involved in the Marketing Authorization Application submission and approval of Sativex® and the New Drug Application submission of Epidiolex®, which was approved by the U.S. Food and Drug Administration as an orphan drug for the treatment of rare forms of paediatric epilepsy in June 2018, and the European Medicines Agency in September 2019 (as Epidyolex®). More recently, as Scientific Affairs Director, International, he was part of the Medical Affairs team responsible for the preparation of the international launch of Epidiolex®. Mr. Stott holds a BSc (Hons) in Medicinal & Pharmaceutical Chemistry and a Diploma in Industrial Studies from Loughborough University of Technology, U.K., as well as a Post Graduate Diploma in Clinical Research from the Welsh School of Pharmacy, Cardiff University, U.K. He has published over 20 research papers and is a named inventor on 17 international patent applications.

Michael J. Willner, Esq. - Director

Mr. Michael J. Willner has practiced as both an Attorney and a Certified Public Accountant. He graduated from Emory University Law School as a member of the Emory Law Review. Subsequently, he practiced real estate and corporate law with New York City-based Milbank, Tweed, Hadley & McCloy, one of the nation's most prominent international law firms. Prior to his legal career, Mr. Willner was employed by the former Arthur Andersen & Company, a national accounting firm, where he practiced in Arthur Andersen's tax department.

Mr. Willner has been a very active and successful opportunistic investor for over forty years and is the founder of Willner Capital, Inc., an investment company specializing in public and private equities, as well as debt instruments. Willner Capital primarily uses fundamental analysis as an evaluation method and event-driven strategies. Over the past ten years, Willner Capital has made significant investments in both the biotechnology and pharmaceutical cannabinoid industries, focusing primarily on clinical-stage companies that seek to address significant unmet medical needs. Mr. Willner has been quoted in the New York Times business section and has served as a moderator and participant on numerous panel discussions and advisory boards regarding his investments in the pharmaceutical side of the cannabinoid industry.

Jennifer Chao - Director

Ms. Chao has over 25 years of experience in the biotech and life sciences industries focused primarily on finance and corporate strategy. She is Managing Partner of CoreStrategies Management, LLC, a company she founded in 2008 to provide transformational corporate and financial strategies to biotech/life science companies for maximizing core valuation. She currently serves on the Board of Directors of Endo Pharmaceuticals and is a member of the Audit Committee and Compliance Committee. Prior to joining Endo, Ms. Chao served as Chairman of the Board of BioSpecifics Technologies Corp. (BioSpecifics) from October 2019 until its acquisition by Endo for approximately US $660 million in December 2020. She also served as Chair of BioSpecifics' Compensation Committee and as a member of the Audit Committee, Strategy Committee, Intellectual Property Committee, and Nominating and Corporate Governance Committee from 2015 to 2020.

Additionally, from 2004 to 2008, Ms. Chao was Managing Director and Senior Lead Biotechnology Securities Analyst at Deutsche Bank, responsible for U.S. large- and small- to mid-cap biotechnology companies with global client coverage; and was known for differentiated fundamentals securities analysis and high visibility coverage of game changing technologies, paradigm shifting treatment algorithms, industry trends and portfolio risk/reward management. Prior to that, Ms. Chao served as Managing Director and Senior Lead Biotechnology Analyst at RBC Capital Markets and VP, Senior Biotechnology Analyst at Leerink Swann & Co. Ms. Chao was a research fellow at Massachusetts General Hospital/Harvard Medical School, as a recipient of the BioMedical Research Career Award, and received her B.A. in Politics and Greek Classics from New York University.

Corporate Cease-Trade Orders

None of our Directors or executive officers has, within the ten years prior to the date of this AIF, been a director, chief executive officer, or chief financial officer of any company (including Cardiol) that, while such person was acting in that capacity (or after such person ceased to act in that capacity but resulting from an event that occurred while that person was acting in such capacity) was the subject of a cease-trade order, an order similar to a cease-

trade order, or an order that denied the company access to any exemption under securities legislation, in each case for a period of more than 30 consecutive days.

Corporate Bankruptcies

None of our Directors or executive officers has, within the ten years prior to the date of this AIF, become bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency or was subject to or instituted any proceedings, arrangement or compromise with creditors or had a receiver, receiver manager, or trustee appointed to hold its assets, been a director or executive officer of any company, that, while that person was acting in that capacity, or within a year of that person ceasing to act in that capacity, became bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency or was subject to or instituted any proceedings, arrangement or compromise with creditors or had a receiver, receiver manager, or trustee appointed to hold its assets.

Penalties or Sanctions

No Director or executive officer of the Corporation or Shareholder holding sufficient securities of the Corporation to affect materially the control of the Corporation has:

- been subject to any penalties or sanctions imposed by a court relating to securities legislation or by a securities regulatory authority or has entered into a settlement agreement with a securities regulatory authority; or
- been subject to any other penalties or sanctions imposed by a court or regulatory body that would likely be considered important to a reasonable investor making an investment decision.

Conflicts of Interest

Other than as described below, to the best of our knowledge, there are no known existing or potential conflicts of interest among us and our Directors, officers, or other members of Management as a result of their outside business interests except that certain of our Directors and officers serve as directors and officers of other companies, and therefore it is possible that a conflict may arise between their duties to us and their duties as a director or officer of such other companies.

Peter Pekos, one of our Directors, founded Dalton in 1986 and continues to serve as its President and CEO. Cardiol and Dalton are parties to the Dalton Services Agreement pursuant to which Cardiol has subcontracted the manufacturing of its drug product candidates to Dalton. See “Commercialization Relationships – Dalton”.

AUDIT COMMITTEE INFORMATION

Charter of the Audit Committee

The full text of the current Terms of Reference for the Audit Committee is attached as Schedule A to this AIF.

Composition of the Audit Committee

The Corporation’s Audit Committee consists of three directors, all of whom are independent. They are also all financially literate in accordance with NI 52-110. The members of the Audit Committee are Michael Willner (Chair), Guillermo Torre-Amione, and Colin Stott.

Relevant Education and Experience

See the respective biographies of each member of the Audit Committee in “Directors and Management - Biographies of Directors and Executive Officers” for a description of the experience that is relevant to the performance of their responsibilities as Audit Committee members.

Reliance on Certain Exemptions

At no time since the commencement of Cardiol's most recently completed financial year has the Corporation relied on any of the exemptions provided in NI 52-110.

Audit Committee Oversight

At no time since the commencement of the Corporation's most recently completed financial year have any recommendations by the Audit Committee respecting the appointment and/or compensation of the Corporation's external auditors not been adopted by the board of directors of Cardiol.

Pre-Approval Policies and Procedures

The policy and procedures relating to the pre-approval of non-audit services provided to the Corporation are described in the Terms of Reference for the Audit Committee attached as Schedule A to this AIF.

External Auditor Service Fees

The aggregate fees billed by Cardiol's external auditors in each of the last two fiscal years for audit fees are as follows:

Fee Category	Year Ended December 31, 2021	Year Ended December 31, 2020
Audit Fees	$105,000	$90,000
Audit-Related Fees	$58,300	$40,000
Tax Fees	$nil	$nil
All Other Fees	$84,800	$20,000
Total	**$248,100**	**$150,000**

"Audit Fees" are the aggregate fees billed by the Corporation's external auditor for services provided for the audit of Cardiol's annual financial statements.

"Audit-Related Fees" are the aggregate fees billed for assurance and related services by the Corporation's external auditor that are reasonably related to the performance of the audit or review of the Corporation's financial statements.

"Tax Fees" are the aggregate fees billed by Cardiol's external auditor for tax compliance, tax advice and tax planning services.

"All Other Fees" are the aggregate fees billed by Cardiol's external auditor for products and services not included in the other categories of fees described above such as work associated with the filing of prospectuses by the Corporation.

PROMOTERS

Mr. David Elsley may be considered to be a promoter of the Corporation within the meaning of applicable securities legislation. As of the date hereof: Mr. Elsley owns 1,754,500 Common Shares, representing 2.83% of the outstanding Common Shares of the Corporation.

Effective as of the closing of the IPO, the Corporation began paying Mr. Elsley an annual salary of $450,000 pursuant to the terms of Mr. Elsley's employment agreement with the Corporation. Effective December 9, 2021, this was increased to $525,000 per year.

LEGAL PROCEEDINGS AND REGULATORY ACTIONS

Cardiol was not involved in any legal proceedings during the year ended December 31, 2021 that had, or could have, a material adverse effect on Cardiol. Moreover, to the knowledge of Cardiol's management, Cardiol is not currently involved in any outstanding, threatened or pending litigation that could have a material adverse effect on Cardiol.

To the knowledge of Cardiol, during the financial year ended December 31, 2021, there were no: (i) penalties or sanctions imposed against Cardiol by a court relating to securities legislation or by a securities regulatory authority; (ii) any other penalties or sanctions imposed by a court or regulatory body against Cardiol that would likely be considered important to a reasonable investor in making an investment decision; or (iii) settlement agreements Cardiol entered into before a court relating to securities legislation or with a securities regulatory authority.

INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS

Except as described elsewhere in this AIF, there have been no related-party transactions in the three most recently completed financial years of Cardiol that required disclosure under any applicable Canadian securities laws other than disclosed in note 17 to Corporation's 2021 audited financial statements, in note 16 to Corporation's 2020 audited financial statements and note 15 to the Corporation's 2019 audited financial statements, copies of which are available on SEDAR at www.sedar.com.

TRANSFER AGENT AND REGISTRAR

The transfer agent and registrar for the Common Shares is Computershare Investor Services Inc. and the register of transfers of the Common Shares is located in Toronto, Ontario. The warrant agent for the warrants is Computershare Trust Company of Canada and the register of transfers of the Warrants is located in Vancouver, British Columbia.

MATERIAL CONTRACTS

The following are material contracts of Cardiol required to be filed on SEDAR pursuant to NI 51-102:

1. the Meros License Agreement (See "Business of Cardiol - Commercialization Relationships – Meros"),
2. the Dalton Services Agreement (See "Business of Cardiol - Commercialization Relationships – Dalton"),
3. the Purisys Exclusive Supply Agreement (See "Business of Cardiol - Commercialization Relationships – Purisys"),
4. the CARO Development Agreement (See "Business of Cardiol - Commercialization Relationships – TecSalud (CARO Development Agreement)")
5. the May 2021 Warrant Indenture (See "Capital Structure – Share Purchase Warrants" for details regarding the Warrant Indenture, and
6. The November 2021 Warrant Indenture (See "Capital Structure – Share Purchase Warrants" for details regarding the Warrant Indenture.

Copies of the material contracts set out above are available under our profile on SEDAR at www.sedar.com.

INTERESTS OF EXPERTS

BDO is independent with respect to the Corporation within the meaning of the Rules of Professional Conduct of the Chartered Professional Accountants of Ontario.

ADDITIONAL INFORMATION

Additional information relating to Cardiol may be found on SEDAR at www.sedar.com. Additional financial information is provided in Cardiol's audited financial statements and management's discussion and analysis for Cardiol's most recently completed financial year, copies of which have been filed on SEDAR and are available at www.sedar.com.

SCHEDULE A

CARDIOL THERAPEUTICS INC.
(THE "CORPORATION")

AUDIT COMMITTEE CHARTER

1. POLICY STATEMENT

It is the policy of the Corporation to establish and maintain an Audit Committee (the "Committee") to assist the directors (individually a "Director" and collectively the "Board") of the Corporation in carrying out the Board's oversight responsibility for the accounting, internal controls, financial reporting, audits of financial statements, and risk management processes of the Corporation.

The Committee shall be provided with resources commensurate with the duties and responsibilities assigned to it by the Board including appropriate administrative support. Without limiting the generality of the foregoing, the Corporation shall provide for appropriate funding, as determined by the Committee in its capacity as a committee of the Board, for payment of: (a) compensation to any registered public accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for the Corporation; (b) compensation to any advisors engaged by the Committee under Section 4(c)(iii) of this charter; and (c) ordinary administrative expenses of the Committee that are necessary or appropriate in carrying out its duties.

If determined appropriate by the Committee, it shall have the discretion to institute investigations of improprieties, or suspected improprieties, within the scope of its responsibilities, including the standing authority to retain special counsel or other experts. The Committee shall have unrestricted access to the Corporation's External Auditors, is authorized to seek any information that it requires from any employee and all employees are directed to co-operate with any request made by the Committee.

2. COMPOSITION OF COMMITTEE

(a) The Committee shall be established by a resolution of the Board. The Committee shall consist of a minimum of three Directors. The Board shall appoint the members of the Committee and may seek the advice and assistance of the Corporate Governance Committee in identifying qualified candidates. The Board shall appoint one member of the Committee to be the chair of the Committee (the "Chair").

(b) All of the members of the Committee shall be Directors who are independent within the meaning of National Instrument 52-110 – Audit Committees ("NI 52-110"), and the rules of any stock exchange or market on which the Corporation's shares are listed or posted for trading (collectively, "Applicable Governance Rules"). In this charter, the term "independent" includes the meanings given to similar terms by Applicable Governance Rules, including the terms "non-executive", "outside" and "unrelated" to the extent such terms are applicable under Applicable Governance Rules. No member of the Committee shall have participated in the preparation of the financial statements of the Corporation or any current subsidiary of the Corporation at any time during the past three years. In addition, in order to be considered to be independent, a member of the Committee may not, other than in his or her capacity as a member of the Committee, the Board or any other Board committee: (i) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the Corporation or any subsidiary thereof, provided that, unless the rules of any stock exchange or market on which the Corporation's shares are listed or posted for trading provide otherwise, compensatory fees do not include the receipt of fixed amounts of compensation under a retirement plan (including deferred compensation) for prior service with the Corporation (provided that such compensation is not contingent in any way on continued service); or (ii) be an affiliated person of the Corporation or any subsidiary thereof.

(c) All members of the Committee must be able to read and understand fundamental financial statements (including a balance sheet, income statement and cash flow statement) and read and understand a set of financial statements that present a breadth and level of complexity of accounting issues that are generally comparable to the breadth and level of complexity of the issues that can reasonably be expected to be raised by the Corporation's financial statements.

(d) The Committee must have at least one member who has past employment in finance or accounting, requisite professional certification in accounting, or any other comparable experience or background which results in that individual's financial sophistication, including being or having been a chief executive officer, chief financial officer or other senior officer with financial oversight responsibilities.

(e) A Director appointed by the Board to the Committee shall be a member of the Committee until replaced by the Board or until his or her resignation.

3. MEETINGS OF THE COMMITTEE

(a) The Committee shall convene a minimum of four times each year at such times and places as may be determined by the Chair of the Committee and whenever a meeting is requested by the Board, a member of the Committee, the auditors or senior management of the Corporation. Scheduled meetings of the Committee shall correspond with the review of the quarterly and year-end financial statements and management discussion and analysis.

(b) Notice of each meeting of the Committee shall be given to each member of the Committee.

(c) Notice of a meeting of the Committee shall:

(i) be in writing, which includes electronic communication facilities;

(ii) state the nature of the business to be transacted at the meeting in reasonable detail;

(iii) to the extent practicable, be accompanied by a copy of any documentation to be considered at the meeting; and

(iv) be given at least two business days prior to the time stipulated for the meeting or such shorter period as the members of the Committee may permit.

(d) A quorum for the transaction of business at a meeting of the Committee shall consist of a majority of the members of the Committee. However, it shall be the practice of the Committee to require review, and, if necessary, approval of important matters by all members of the Committee.

(e) A member or members of the Committee may participate in a meeting of the Committee by means of such telephonic, electronic, or other communication facilities as permits all persons participating in the meeting to communicate with each other. A member participating in such a meeting by any such means is deemed to be present at the meeting.

(f) In the absence of the Chair of the Committee, the members of the Committee shall choose one of the members present to chair the meeting. In addition, the members of the Committee shall choose one of the persons present to be the secretary of the meeting.

(g) The Committee may invite such persons to attend meetings of the Committee as the Committee considers appropriate, except to the extent exclusion of certain persons is required pursuant to this charter or by applicable laws.

(h) The Committee may invite the External Auditors to be present at any meeting of the Committee and to comment on any financial statements, or on any of the financial aspects, of the Corporation.

(i) The Committee (A) shall meet with the External Auditors separately from individuals other than the Committee, and (B) may meet separately with management of the Corporation.

(j) Minutes shall be kept of all meetings of the Committee and shall be signed by the chair and the secretary of the meeting. The Chair of the Committee shall circulate the minutes of the meetings of the Committee to all members of the Board.

4. DUTIES AND RESPONSIBILITIES OF THE COMMITTEE

(a) The Committee, in its capacity as a committee of the Board, is directly responsible for selecting the public accounting firm to be nominated for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for the Corporation (the "External Auditor") as well as the compensation of the External Auditor. The Committee shall also be directly responsible for the oversight of the work of the External Auditor (including resolution of disagreements between management and the auditor regarding financial reporting) and each such External Auditor must report directly to the Committee.

(b) The other primary duties and responsibilities of the Committee are to:

(i) identify and monitor the management of the principal risks that could impact the financial reporting of the Corporation;

(ii) monitor the integrity of the Corporation's financial reporting process and system of internal controls regarding financial reporting and accounting compliance;

(iii) monitor the independence, objectivity, and performance of the External Auditors, including, without limitation: (A) ensuring the Committee's receipt from the External Auditors at least annually of a formal written statement delineating all relationships between the External Auditors and the Corporation; (B) actively engaging in dialogue with the External Auditors with respect to any disclosed relationships or services that may impact the objectivity and independence of the External Auditor; and (C) taking, or recommending that the Board take, appropriate action to oversee the independence of the External Auditors;

(iv) evaluate the performance of the External Auditors at least annually; deal directly with the External Auditors to approve external audit plans, other services (if any), and fees;

(v) directly oversee the external audit process and results (in addition to items described in Section 4(e) below);

(vi) provide an avenue of communication between the External Auditors, management, and the Board;

(vii) review annually with management of the Corporation the anti-fraud, anti-bribery, anti-corruption, and risk assessment programs of the Corporation;

(viii) carry out a review designed to ensure that an effective "whistle blowing" procedure exists to permit stakeholders to express any concerns regarding accounting or financial matters to an appropriately independent individual; and

(c) The Committee shall have the authority to:

(i) inspect any and all of the books and records of the Corporation and its subsidiaries;

(ii) discuss with the management of the Corporation and its subsidiaries, any affected party and the External Auditors, such accounts, records, and other matters as any member of the Committee considers appropriate;

(iii) engage independent counsel and other advisors as it determines necessary to carry out its duties; and

(iv) set and pay the compensation for any advisors engaged by the Committee.

Relationship with the Board

(d) The Committee shall, at the earliest opportunity after each meeting, report to the Board the results of its activities and any reviews undertaken and make recommendations to the Board as considered appropriate.

Relationship with External Auditors

(e) The Committee shall:

(i) review the audit plan with the External Auditors and with management;

(ii) review with the External Auditors the critical accounting policies and practices used by the Corporation, all alternative treatments of financial information within IFRS that the External Auditors have discussed with management, the ramifications of the use of such alternative disclosures and treatments, and the treatment preferred by the External Auditors;

(iii) discuss with management and the External Auditors any proposed changes in major accounting policies or principles, the presentation and impact of material risks and uncertainties and key estimates and judgments of management that may be material to financial reporting;

(iv) review with management and with the External Auditors material financial reporting issues arising during the most recent financial period and the resolution or proposed resolution of such issues;

(v) review any problems experienced or concerns expressed by the External Auditors in performing any audit, including any restrictions imposed by management or any material accounting issues on which there was a disagreement with management;

(vi) review with the External Auditors any accounting adjustments that were noted or proposed by the independent auditor but that were “passed” (as immaterial or otherwise), any communications between the audit team and the External Auditor’s national office respecting auditing or accounting issues presented by the engagement, any “management” or “internal control” letter or schedule of unadjusted differences issued, or proposed to be issued, by the External Auditors to the Corporation, or any other material written communication provided by the External Auditors to the Corporation’s management;

(vii) review with senior management the process of identifying, monitoring, and reporting the principal risks affecting financial reporting;

(viii) review and discuss with management and the External Auditors any off-balance sheet transactions or structures and their effect on the Corporation's financial results and operations, as well as the disclosure regarding such transactions and structures in the Corporation's public filings;

(ix) review the audited annual financial statements (including management discussion and analysis) and related documents in conjunction with the report of the External Auditors and obtain an explanation from management of all material variances between comparative reporting periods;

(x) consider and review with management the internal control memorandum or management letter containing the recommendations of the External Auditors and management's response, if any, including an evaluation of the adequacy and effectiveness of the internal financial controls and procedures for financial reporting of the Corporation and subsequent follow-up to any identified weaknesses;

(xi) review with financial management and the External Auditors the quarterly unaudited financial statements and management discussion and analysis before release to the public;

(xii) periodically meet separately with management and the External Auditors;

(xiii) oversee the financial affairs of the Corporation and its subsidiaries and, if deemed appropriate, make recommendations to the Board, External Auditors, or management;

(xiv) discuss with management and the External Auditors any correspondence with regulatory or governmental agencies that raise material issues regarding the Corporation's financial statements or accounting policies;

(xv) consider the recommendations of management in respect of the appointment and terms of engagement of the External Auditor;

(xvi) pre-approve all audit and non-audit services to be provided to the Corporation or its subsidiaries by its External Auditors, or the External Auditors of subsidiaries of the Corporation, subject to the overriding principle that the External Auditors not be permitted to be retained by the Corporation to perform internal audit outsourcing services or financial information systems services; provided that notwithstanding the above, the foregoing pre-approval of non-audit services may be delegated to a member of the Committee, with any decisions of the member with the delegated authority reporting to the Committee at the next scheduled meeting;

(xvii) approve the engagement letter for non-audit services to be provided by the External Auditors or affiliates of External Auditors, together with estimated fees, and consider the potential impact of such services on the independence of the External Auditors;

(xviii) when there is to be a change of External Auditors, review all issues and provide documentation related to the change, including the information to be included in the notice of change of auditors and documentation required pursuant to the then current legislation, rules, policies and instruments of applicable regulatory authorities and the planned steps for an orderly transition period; and

(xix) review all reportable events, including disagreements, unresolved issues and consultations, as defined by applicable laws, on a routine basis, whether or not there is to be a change of the External Auditors.

(f) In connection with the public disclosure of financial information and other public disclosure, the Committee shall:

(i) review the Corporation's financial statements, management discussion and analysis, and annual and interim profit or loss press releases before the Corporation publicly discloses this information;

(ii) review with management its evaluation of the Corporation's procedures and controls designed to assure that information required to be disclosed in the Corporation's periodic public reports is recorded, processed, summarized, and reported in such reports within the time periods specified by applicable securities laws for the filing of such reports ("Disclosure Controls") and consider whether any changes are appropriate in light of management's evaluation of the effectiveness of such Disclosure Controls;

(iii) establish a policy, which may include delegation to an appropriate member or members of management, for release of earnings press releases, as well as for the release of financial information and earnings guidance provided to analysts and rating agencies;

(iv) satisfy itself that adequate procedures are in place for the review of the Corporation's public information extracted from the Corporation's financial statements, other than the public information reviewed in accordance with Section 4(f)(i), and periodically assess the adequacy of those procedures;

(v) to the extent deemed appropriate, review and supervise the preparation by management of:

(A) the annual information forms, management information circulars, and annual and interim financial statements of the Corporation and any other information of the Corporation filed by the Corporation with applicable securities regulators;

(B) press releases of the Corporation containing financial information, earnings guidance, forward-looking statements, information about operations, or any other material information;

(C) correspondence broadly disseminated to shareholders of the Corporation; and

(D) other relevant written and oral communications or presentations;

(vi) before release, review and if appropriate, recommend for approval by the Board, all public disclosure documents containing audited or unaudited financial information, including any prospectuses, annual reports, annual information forms, management discussion and analysis, and press releases, focusing particularly on:

(A) any changes in accounting policies and practices;

(B) any important areas where judgment must be exercised;

(C) significant adjustments resulting from the audit;

(D) the going concern assumption, if any;

(E) compliance with accounting standards; and

(F) compliance with stock exchange and legal requirements.

(g) The Committee shall enquire into and determine the appropriate resolution of any conflict of interest in respect of audit or financial matters which are directed to the Committee by any member of the Board, a shareholder of the Corporation, the External Auditors, or senior

management.

(h) The Committee shall periodically review with management the need for an internal audit function.

(i) The Committee shall review the accounting and reporting of costs, liabilities, and contingencies of the Corporation.

(j) The Committee shall periodically discuss with management the Corporation's major financial risk exposures and the steps management has taken to monitor and control such exposures.

(k) The Committee shall establish, monitor, and review policies and procedures for internal accounting, financial control, and management information.

(l) The Committee shall periodically discuss with management the Corporation's process for performing its quarterly certifications pursuant to Multilateral Instrument 52-109 – Certification of Disclosure in Issuers' Annual and Interim Filings and the U.S. Sarbanes-Oxley Act.

(m) The Committee shall review with the Chief Executive Officer and Chief Financial Officer of the Corporation any report on significant deficiencies in the design or operation of the internal controls that could adversely affect the Corporation's ability to record, process, summarize, or report financial data, any material weaknesses in internal controls identified to the auditors, and any fraud, whether or not material, that involves management or other employees who have a significant role in the Corporation's internal controls.

(n) The Committee shall establish and maintain procedures for:

(i) the receipt, retention, and treatment of complaints received by the Corporation regarding accounting, internal accounting controls, or auditing matters;

(ii) the confidential, anonymous submission by employees of the Corporation of concerns regarding questionable accounting or auditing matters; and

(iii) reviewing arrangements by which staff of the Corporation may, in confidence, raise concerns about possible improprieties in matters of financial reporting and ensuring that arrangements are in place for proportionate and independent investigation and follow-up action.

(o) At each meeting of the Committee, the Committee shall review any complaints or concerns of employees of the Corporation regarding accounting, internal accounting controls, or auditing matters relating to the Corporation and violations of any applicable law, rule, or regulation and shall follow the procedures established under the Corporation's Whistleblower Policy regarding such concerns and complaints.

(p) The Committee shall review all related-party transactions and discuss the business rationale for these transactions and determine whether appropriate disclosures have been made. For this purpose, the term "related-party transactions" includes any "material transaction" required to be disclosed under Item 13 of Form 51-102F2 under National Instrument 51-102 – Continuous Disclosure Obligations.

(q) The Committee shall review the Corporation's compliance and ethics programs, including consideration of legal and regulatory requirements, and shall review with management its periodic evaluation of the effectiveness of such programs.

(r) The Committee shall review and approve the Corporation's hiring policies regarding partners, employees, and former partners and employees of the present and former External Auditors.

(s) The Committee shall receive any reports from legal counsel of evidence of a material violation of securities laws or breaches of fiduciary duty by the Corporation.

(t) The Committee shall review with the Corporation's legal counsel, on no less than an annual basis, any legal matter that could have a material impact on the Corporation's financial statements and any enquiries received from regulators or government agencies.

(u) The Committee shall assess, on an annual basis, the adequacy of this charter and the performance of the Committee.