



**CARDIOME PHARMA CORP.**

**ANNUAL INFORMATION FORM**

**FOR THE YEAR ENDED DECEMBER 31, 2016**

**MARCH 28, 2017**

## TABLE OF CONTENTS

	<u>Page</u>
REFERENCE INFORMATION	2
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	2
CORPORATE STRUCTURE	6
GENERAL DEVELOPMENT OF THE BUSINESS	6
Three Year History	7
NARRATIVE DESCRIPTION OF THE BUSINESS	10
General	10
Summary of Our Products and Product Candidates	11
Our Strategy	11
Our Products and Product Candidates	12
Production Methods and Components	18
Specialized Skill and Knowledge	18
Foreign Operations	18
U.S. Export Controls and Economic Sanctions	18
Competition	18
Patents and Proprietary Protection	19
Regulatory Environment	19
Employees	23
RISK FACTORS	23
DIVIDENDS AND DISTRIBUTIONS	39
CAPITAL STRUCTURE	39
MARKET FOR SECURITIES	40
PRIOR SALES	40
DIRECTOR AND EXECUTIVE OFFICERS	41
CEASE TRADE ORDERS, BANKRUPTCIES, PENALTIES OR SANCTIONS	45
CONFLICTS OF INTEREST	46
AUDIT COMMITTEE INFORMATION	46
LEGAL PROCEEDINGS AND REGULATORY ACTIONS	47
INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS	47
TRANSFER AGENT AND REGISTRARS	47
MATERIAL CONTRACTS	47
INTERESTS OF EXPERTS	48
ADDITIONAL INFORMATION	48
SCHEDULE “A” AUDIT COMMITTEE MANDATE	49

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### **REFERENCE INFORMATION**

In this annual information form, a reference to the “Corporation”, “Company”, “Cardiome”, “we”, “us”, “our” and similar words refer to Cardiome Pharma Corp. and its subsidiaries, or any one of them, as the context requires.

All references herein to “dollars” and “\$” are to U.S. dollars, unless otherwise indicated. All references to “Cdn.\$” are to Canadian dollars. On March 27, 2017, the exchange rate for conversion of U.S. dollars into Canadian dollars was \$1.00 = Cdn.\$1.3368 based upon the Bank of Canada noon rate.

Unless otherwise stated, the information set forth in this annual information form is as of December 31, 2016.

### **CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

Certain statements and information in this annual information form are not based on historical facts and constitute forward-looking statements or forward-looking information within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and applicable Canadian securities legislation (“forward-looking statements”), including, without limitation, statements containing the words “believe”, “may”, “plan”, “will”, “estimate”, “continue”, “anticipate”, “intend”, “expect” and similar expressions.

Forward-looking statements are necessarily based on estimates and assumptions made by us in light of our experience and perception of historical trends, current conditions and expected future developments, as well as other factors we believe are appropriate. Forward-looking statements in this annual information form include but are not limited to statements relating to:

- our intention to expand the indications for which we may market AGGRASTAT<sup>®</sup>;
- our expected commercialization of XYDALBA<sup>™</sup> in Belgium, Nordic nations, Canada, certain other European countries and select countries in the Middle East;
- our plans to develop and commercialize product candidates and the timing of these development programs;
- the expected commercialization of BRINAVESS<sup>™</sup> in Canada;
- whether we will receive, and the timing and costs of obtaining, regulatory approvals in the United States, Canada, Europe and other countries;
- our intended use of proceeds raised from equity and debt financings;
- the cost of post-market regulation if we receive necessary regulatory approvals;
- our ability to meet certain revenue milestones under the Term Loan Agreement with CRG (as defined below);
- clinical development of our product candidates, including the results of current and future clinical trials;
- our ability to enroll patients in our clinical trials;

- the benefits and risks of our product candidates as compared to others;
- our maintenance and establishment of intellectual property rights in our product candidates;
- our need for additional financing and our estimates regarding our capital requirements and future revenues and profitability;
- our estimates of the size of the potential markets for our product candidates;
- our selection and licensing of product candidates;
- our potential relationships with distributors and collaborators with acceptable development, regulatory and commercialization expertise and the benefits to be derived from such collaborative efforts;
- our distributors' and licensees' compliance with the terms of their agreements and with relevant regulations and licenses;
- sources of revenues and anticipated revenues, including contributions from distributors and collaborators, product sales, license agreements and other collaborative efforts for the development and commercialization of product candidates;
- our creation and maintenance of an effective direct sales and marketing infrastructure for approved products we elect to market and sell directly;
- our creation and maintenance of an effective logistics infrastructure for supply and delivery of our approved products;
- the rate and degree of market acceptance of our products;
- the pricing of our products;
- whether we will receive and the timing and amount of reimbursement for our products;
- the success and pricing of other competing therapies that may become available;
- our retention and hiring of qualified employees in the future;
- the manufacturing capacity of third-party manufacturers for our product candidates;
- our ability to negotiate and maintain third-party manufacturing and supply contracts and the party's performance under contract;
- our ability to maintain or reduce third-party manufacturing costs;
- the competition we face from other companies, research organizations, academic institutions and government agencies, and the risks such competition pose to our products;
- the confidential information we possess about patients, customers and core business functions, and the information technologies we use to protect it;
- our intention to continue directing a significant portion of our resources into international sales expansion;
- our ability to get our products approved for use in hospitals; and
- government legislation in all countries in which we already, or hope to, sell our products, and its effect on our ability to set prices, enforce patents and obtain product approvals or reimbursements.

Such forward-looking statements reflect our current views with respect to future events and are subject to risks and uncertainties and are necessarily based upon a number of estimates and assumptions that, while considered reasonable by us, are inherently subject to significant business, economic, competitive, political and social uncertainties and contingencies, many of which, with respect to future events, are subject to change. The factors and assumptions used by us to develop such forward-looking statements include, but are not limited to, the assumption that we will be able to reach agreements with regulatory agencies on executable development programs, the assumption that recruitment to clinical trials will continue at rates similar to our completed trials, the assumption

that the regulatory requirements, including patient exposure, for approval of marketing authorization applications/new drug approvals will be maintained, the assumption that genericisation of markets for AGGRASTAT® will proceed according to estimates, the assumption that the time required to analyze and report the results of our clinical studies will be consistent with past timing, the assumption that market data and reports reviewed by us are accurate, the assumption that our current good relationships with our suppliers and service providers will be maintained, the assumptions relating to the availability of capital on terms that are favourable to us and the assumptions relating to the feasibility of future clinical trials.

By their very nature, forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, events or developments, or industry results, to be materially different from any future results, events or developments expressed or implied by such forward-looking statements or information. In evaluating these forward-looking statements, prospective purchasers should specifically consider various factors, including the risks outlined under the heading “Risk Factors” in the annual information form. Specifically, certain risks and uncertainties that could cause such actual events or results expressed or implied by such forward-looking statements and information to differ materially from any future events or results expressed or implied by such statements and information include, but are not limited to, the risks and uncertainties related to the fact that:

- we will have significant additional future capital needs and there are uncertainties as to our ability to raise additional funding;
- we have a history of significant losses and a significant accumulated deficit;
- we have a history of negative operating cash flow and may continue to experience negative operating cash flow;
- we may not realize the anticipated benefits of past or future acquisitions or product licenses and integration of these acquisitions and any products acquired or licensed may disrupt our business and management;
- if we are unable to make our regularly scheduled payments under our term loan, we could have a covenant violation;
- we are subject to certain restrictive covenants;
- we are dependent on two products for substantially all of our current revenues;
- we are exposed to generic product risk which may result in a decline in sales of AGGRASTAT®;
- we have substantial competition in the life sciences industry and with respect to our products;
- we are subject to the risks associated with product liability claims, insurance and recalls;
- we rely on third parties for the supply and manufacture of our products, which can be unpredictable in terms of quality, cost and availability;
- we rely on our supply chain and the supply chain of third parties to provide our products, and supply chains may fail due to inadequacies in their systems and processes, in execution and for unforeseen reasons;
- we rely on third parties for the execution of a significant portion of our regulatory, pharmacovigilance, medical information and logistical responsibilities and such third parties may fail to meet their obligations as a result of inadequacies in their systems and processes or execution failure;
- we rely on third party distributors in many markets to sell our products and such third parties may fail to meet their obligations;
- government legislation could adversely impact our ability to obtain product reimbursement and economically price our products and may be difficult to interpret or comply with, resulting in additional costs to conduct our business in certain countries;
- compulsory licensing and/or generic competition may affect our business in certain countries;

- if we are not able to convince public payors and hospitals to include our products on their approved formulary lists, our revenues may not meet expectations and our business, results of operations and financial condition may be adversely affected;
- our hospital customers may be late in their payments and in some cases may not pay monies owed;
- our business may be materially adversely affected by new legislation, new regulatory requirements, and the continuing efforts of governmental and third party payors to contain or reduce the costs of healthcare through various means;
- we rely on proprietary technology, the protection of which can be unpredictable and costly;
- there may be an unauthorized disclosure of a significant amount of confidential information under our control;
- clinical trials for our product candidates are expensive and time-consuming, and their outcome is uncertain;
- the results of pre-clinical studies and initial clinical trials are not necessarily predictive of future results, and our current product candidates may not have favourable results in later trials or in the commercial setting;
- our industry is subject to health and safety risks;
- our approved products may not achieve or maintain expected levels of market acceptance;
- we are dependent upon our key personnel to achieve our business objectives;
- we are exposed to concentration of credit risk relating to major distribution relationships and customers in certain geographic regions;
- our policies and estimates regarding returns, allowances and chargebacks may reduce revenue in future periods;
- our inventory has a limited shelf life and may require write-downs;
- we are exposed to risks relating to the write-down of intangible assets, which comprises a significant portion of our total assets;
- we may face exposure to adverse movements in foreign currency exchange rates;
- if we were to lose our foreign private issuer status under United States federal securities laws, we would likely incur additional expenses associated with compliance with the United States securities laws applicable to United States domestic issuers;
- we are subject to risks inherent in foreign operations;
- there are uncertainties with respect to data protection laws in Europe;
- failure to comply with the United States *Foreign Corrupt Practices Act* (the “FCPA”), as well as the anti-bribery laws of the nations in which we conduct business (such as the United Kingdom’s *Bribery Act* or the *Corruption of Foreign Public Officials Act of Canada*) (the “CFPOA”) could subject us to penalties and other adverse consequences;
- legislative actions, potential new accounting pronouncements, and higher insurance costs are likely to impact our future financial position or results of operations;
- our product candidates are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays, or prevent the receipt of the required approvals to commercialize products;
- any of our product candidates that receive regulatory approval could be subject to extensive post-market obligations that can affect sales, marketing and profitability;
- obtaining regulatory approval in the European Union does not ensure we will obtain regulatory approval in other countries; and

- our business depends heavily on the use of information technologies.

Other factors are described in detail in this annual information form and our filings with the United States Securities and Exchange Commission (the “SEC”) (available through the SEC’s Electronic Document Gathering and Retrieval System (“EDGAR”) at <http://www.sec.gov>) and the Canadian securities regulatory authorities (available on the Canadian Securities Administrators System for Electronic Document Analysis and Retrieval (“SEDAR”) at <http://www.sedar.com>).

Should one or more of these risks or uncertainties or a risk that is not currently known to us materialize, or should assumptions underlying those forward-looking statements prove incorrect, actual results may vary materially from those described herein. These forward-looking statements are made as of the date of this annual information form and we do not intend, and do not assume any obligation, to update these forward-looking statements, except as required by law. Investors are cautioned that forward-looking statements are not guarantees of future performance and accordingly investors are cautioned not to put undue reliance on forward-looking statements due to their inherent uncertainty.

In addition to the disclosure contained in this annual information form, readers are encouraged to review our Management’s Discussion and Analysis of Financial Condition and Results of Operations for the year ended December 31, 2016, for an additional discussion of factors that could affect our future performance.

## **CORPORATE STRUCTURE**

We were incorporated under the Company Act (British Columbia) on December 12, 1986 under the name Nortran Resources Ltd. In June 1992, we changed our name to Nortran Pharmaceuticals Inc. In June 2001, we changed our name to Cardiome Pharma Corp. On March 8, 2002, we continued under the Canada Business Corporations Act (the “CBCA”) and effected a four-to-one share consolidation. On March 1, 2009, we amalgamated with Cardiome Research and Development (Barbados), Inc. (previously our wholly-owned subsidiary). On March 20, 2009, we registered under the Business Corporations Act (British Columbia) as an extra-provincial company. On April 9, 2013, we effected a five-to-one share consolidation of our common shares and began trading on a post-consolidation basis on April 12, 2013. Our common shares trade on the Toronto Stock Exchange (the “TSX”) under the symbol “COM” and on the NASDAQ Stock Market (the “NASDAQ”) under the symbol “CRME”.

The following table lists the principal subsidiaries of Cardiome and their jurisdictions of incorporation or organization. All such entities are 100% owned, directly or indirectly, by Cardiome:

<b>Subsidiary Name</b>	<b>Jurisdiction of Incorporation or Organization</b>
Cardiome International SA	Switzerland
Cardiome UK Limited	United Kingdom
Correvio LLC	Delaware, U.S.A.
Correvio International S.a.r.l.	Switzerland
Correvio (UK) Ltd.	United Kingdom

Our registered office is located at Suite 2600, 595 Burrard Street, Three Bentall Centre, Vancouver, British Columbia, Canada, V7X 1L3 and our head office and principal place of business are located at 1441 Creekside Drive, 6<sup>th</sup> Floor, Vancouver, British Columbia, Canada, V6J 4S7.

## **GENERAL DEVELOPMENT OF THE BUSINESS**

We are a specialty pharmaceutical company dedicated to offering patients and healthcare providers innovative therapeutic options that effectively, safely, and conveniently manage acute medical conditions to improve health and quality of life. We strive to find innovative, differentiated medicines that provide therapeutic and

economic value to patients, physicians and healthcare systems. We currently have two marketed, in-hospital cardiology products, BRINAVESS™ and AGGRASTAT®, which are commercially available in markets outside of the United States. We have licensed an approved antibiotic, XYDALBA™ (dalbavancin) that we launched in Germany and the United Kingdom in the fourth quarter of 2016 and in France in the first quarter of 2017. We expect to commercialize in Belgium, Nordic nations, Canada, certain other European countries and select countries in the Middle East over time. In addition, we have also licensed commercialization rights to a pre-registration drug/device combination product, TREVYENT®, for the treatment of pulmonary arterial hypertension (“PAH”) in certain regions outside the United States and commercialization rights to cardiology products ESMOCARD® and ESMOCARD LYO® (esmolol hydrochloride) in certain European countries.

### **Three Year History**

#### *Acquisition of Correvio*

On November 18, 2013, we completed the acquisition of Correvio LLC (“Correvio”), a privately held pharmaceutical company headquartered in Geneva, Switzerland, focused on the worldwide marketing, excluding the United States, of AGGRASTAT®, a branded prescription pharmaceutical. We acquired 100% of Correvio in exchange for 19.9% of our outstanding common shares (pro forma ownership of approximately 16.6%) and a deferred cash consideration of \$12.0 million. The deferred cash consideration is being repaid monthly at an amount equal to 10% of cash receipts from product sales and any applicable interest accrued at 10% compounded annually. The deferred cash consideration must be repaid in full by December 1, 2019. The Company filed a business acquisition report on Form 51-102F4 dated January 29, 2014 in respect of the acquisition of Correvio.

#### *Prospectus Offerings*

On February 18, 2014, we filed a prospectus supplement in each of the provinces of Canada, other than Québec, and the United States to qualify and register the distribution of common shares for aggregate gross proceeds of up to \$8.9 million in “at the market” distributions effected from time to time pursuant to an At Market Issuance Sales Agreement (the “Sales Agreement”) that we entered into on the same day with MLV & Co. LLC (“MLV”) as agent. We did not issue any common shares under the Sales Agreement for the year ended December 31, 2016. During the year ended December 31, 2015, we issued 554,247 of our common shares under the Sales Agreement for gross proceeds of \$5.3 million.

On March 11, 2014, we completed a prospectus offering of 1,500,000 common shares from treasury at Cdn.\$10.00 per common share for net proceeds of Cdn.\$12.4 million. Additionally, 1,500,000 common shares were sold in a secondary offering from CarCor Investment Holdings LLC (“CarCor”), the shareholder from which we purchased Correvio, at Cdn.\$10.00 per common share. We did not receive any of the proceeds of the sale of common shares by CarCor. This short form prospectus offering was made on a bought deal basis pursuant to an underwriting agreement with Canaccord Genuity Corp., acting as sole bookrunner and co-lead underwriter, and Cormark Securities Inc., acting as co-lead underwriter.

#### *Senior Secured Term Loan Facility*

On July 18, 2014, we announced the closing of the term loan facility with MidCap Financial, LLC (“Midcap”) for up to \$22.0 million in two tranches bearing interest at a rate of LIBOR plus 8%. The first tranche of \$12.0 million was drawn and was used for working capital and general corporate purposes. The second tranche of up to \$10.0 million was available to support a product or company acquisition. The second tranche was never drawn. The Term Loan Facility carried a term of 48 months and was secured by substantially all of our assets. We extinguished this term loan facility with Midcap on June 13, 2016.

#### *Board and Management*

On February 16, 2015, we announced the resignation of Karim Lalji as Chief Commercial Officer. On June 1, 2015, we announced the appointment of David Dean as Vice President, Investor Relations and Business Development. On June 22, 2015, we announced the resignation of Robert W. Rieder and Peter W. Roberts from the

board of directors and announced the appointment of Arthur H. Willms and Mark H. Corrigan to the board of directors. On September 8, 2015, we announced the addition of Robert James Meyer to our board of directors.

*Commercialization Agreement for ESMOCARD<sup>®</sup> and ESMOCARD LYO<sup>®</sup>*

On May 12, 2015, we entered into a Commercialization Agreement with AOP Orphan Pharmaceuticals AG (“AOP”) to sell AOP’s cardiovascular products, ESMOCARD<sup>®</sup> and ESMOCARD LYO<sup>®</sup> (esmolol hydrochloride) in Italy, France and Belgium. The addition of the ESMOCARD<sup>®</sup> franchise increases our offering of cardiovascular products in these countries.

*Exclusive License and Supply Agreement with SteadyMed Ltd. for TREVYENT<sup>®</sup>*

On June 28, 2015, we entered into an Exclusive License and Supply Agreement with SteadyMed Ltd. (“SteadyMed”) to commercialize TREVYENT<sup>®</sup> in Europe, Canada and the Middle East. We made an upfront payment of \$3.0 million upon execution of the agreement.

*United Kingdom BRINAVESS<sup>™</sup> Pricing Approval*

On August 10, 2015, we announced that the Secretary of State for the U.K. Department of Health approved pricing for BRINAVESS<sup>™</sup>. The approved amount represents a maximum price per vial of BRINAVESS<sup>™</sup> in the United Kingdom. It is consistent with pricing in other territories and our economic forecasts. Pricing approval is a step on the path to formulary coverage.

*Prospectus Offering*

On August 13, 2015, we completed an offering of 2,875,000 common shares at \$8.00 per common share for gross proceeds of \$23.0 million. We used the net proceeds for business development and growth opportunities, including potential product licensing opportunities, the advancement of our business objectives, and working capital and general corporate purposes. The majority of proceeds were put toward selling, general and administration (“SG&A”) expenses.

*Co-Promotion Agreement with Mitsubishi Tanabe Pharma Europe*

On September 30, 2015, we entered into a Co-Promotion Agreement with Mitsubishi Tanabe Pharma Europe Ltd. (“MTPE”), a subsidiary of Mitsubishi Tanabe Pharma Corporation headquartered in Japan, to co-promote Cardiome’s AGGRASTAT<sup>®</sup> and MTPE’s EXEMBOL<sup>®</sup> (argatroban monohydrate) in the United Kingdom. Cardiome and MTPE will co-promote the two products, thereby leveraging the existing sales force and investments in this market for an initial term of three years.

*New Drug Submission for Intravenous Vernakalant with Health Canada*

On December 22, 2015, we announced the filing of a New Drug Submission (“NDS”) with Health Canada’s Therapeutic Products Directorate (the “TPD”) seeking Canadian approval of vernakalant (IV) for the rapid conversion of recent onset atrial fibrillation (“AF”) to sinus rhythm in adults with AF for up to seven days. Following completion of screening in May 2016, the TPD initiated a detailed review of the NDS. On March 14, 2017, we announced that BRINAVESS<sup>™</sup> received a Notice of Compliance from Health Canada which enables us to begin commercializing BRINAVESS<sup>™</sup> in Canada.

*Centralized Review of TREVYENT<sup>®</sup> by the European Medicines Agency*

On January 6, 2016, we announced that the European Medicines Agency (the “EMA”) has approved our request to review TREVYENT<sup>®</sup> under the Centralised Authorisation Procedure drug review process. This procedure results in a single marketing authorization that is valid in all 28 European Union countries as well as three European Economic Area countries.

### *Base Shelf Prospectus Filings*

On March 1, 2016, we filed a short form base shelf prospectus with the securities regulatory authorities in Canada, other than Quebec, and the SEC in the United States under a registration statement on Form F-10 (together, the “Base Shelf Prospectuses”). The Base Shelf Prospectuses provide for the potential offering in Canada and the United States of up to an aggregate of \$250.0 million of our common shares, preferred shares, debt securities, warrants, subscription receipts and units from time to time over a 25-month period.

### *Purchase Agreement*

We filed a prospectus supplement on January 12, 2016 pertaining to sales under a Purchase Agreement dated January 12, 2016 (the “Purchase Agreement”) with Lincoln Park Capital Fund, LLC (“LPC”). We may terminate the Purchase Agreement at any time, at our sole discretion, without any monetary cost or penalty to us upon one business day’s written notice to LPC. Under the terms of the agreement, LPC will not cause or engage, in any manner whatsoever, any direct or indirect short selling or hedging of our common shares and is obligated to purchase our common shares at such times and in such amounts as determined by us in accordance with the terms and conditions of the Purchase Agreement. In consideration for entering into the agreement, we issued 48,856 common shares to LPC as a commitment fee. We plan to use the net proceeds, if any, for general corporate purposes. In connection with the filing of the Base Shelf Prospectuses, we filed a new prospectus supplement pertaining to the Purchase Agreement on March 7, 2016.

### *Amendment to the Purchase Agreement*

On December 22, 2016, we filed an amendment to our prospectus supplement dated March 7, 2016 to the Base Shelf Prospectuses in connection with an amendment to the Purchase Agreement with LPC.

Under the terms of the amended Purchase Agreement, we may sell to LPC, at our sole discretion from time to time, up to 4,027,453 common shares for an aggregate offering amount of up to \$20.0 million until December 31, 2018, subject to the conditions and limitations set forth in the Purchase Agreement. The purchase price of any common shares sold to LPC will be based on the then prevailing market prices of the common shares. We may terminate the Purchase Agreement at any time, at our sole discretion, without any monetary cost or penalty to us upon one business day’s written notice to LPC. Our closing share price must be equal to or greater than \$1.00 in order for a purchase to be effected. We plan to use the net proceeds, if any, for general corporate purposes. As of the date of this annual information form, we have sold 160,000 common shares to LPC for gross proceeds of \$0.8 million.

### *Amended and Restated Sales Agreement*

We also filed a new prospectus supplement dated March 7, 2016 pertaining to sales under an amended and restated Sales Agreement dated March 7, 2016 with FBR Capital Markets & Co. (“FBR”) and MLV. Under the terms of the amended and restated Sales Agreement, we may sell, from time to time, through “at-the-market” offerings with FBR and MLV as agents, such common shares as would have an aggregate offer price of up to \$30.0 million. FBR and MLV, at our discretion and instruction, will use their commercially reasonable efforts to sell the common shares at market prices from time to time. The amended and restated Sales Agreement amends and restates the Sales Agreement. We entered into the amended and restated Sales Agreement only as a result of the acquisition by FBR of MLV. We did not issue any common shares under the amended and restated Sales Agreement for the year ended December 31, 2016.

### *License Agreement*

On May 5, 2016, we announced the execution of a license agreement with Allergan plc (“Allergan”), for the rights to commercialize dalbavancin (branded DALVANCE<sup>®</sup> in the United States and XYDALBA<sup>™</sup> in the rest of the world) in the United Kingdom, Germany, France, Denmark, Iceland, Finland, Malta, Norway, Sweden, Belgium, the Netherlands, Luxemburg, Ireland, Switzerland, Canada and certain countries in the Middle East. As consideration for the rights and licenses granted, we made non-refundable payments to Allergan of \$13.0 million.

Additional non-refundable milestone payments will be due to Allergan upon our achievement of various milestones. Royalty payments may also be due to Allergan based on achievement of pre-determined levels of annual net sales. We began our commercial launch of XYDALBA™ in the United Kingdom and Germany in the fourth quarter of 2016 and in France in the first quarter of 2017.

#### *Term Loan Agreement with CRG Servicing LLC*

On June 13, 2016, we entered into a term loan agreement (the “Term Loan Agreement”) with CRG Servicing LLC as administrative and collateral agents (“CRG”) among other lenders as parties thereto, for up to \$30 million consisting of three tranches bearing interest at 14% per annum (the “CRG Term Loan”). The first tranche of \$20 million has been drawn and was used to extinguish existing long-term debt from Midcap and for general corporate purposes. The second and third tranches of \$5 million each are available to us if we reach certain revenue milestones, as at December 2016 and June 2017, respectively. We reached the revenue milestone at December 31, 2016 and the second tranche of \$5 million is available to us. The loan matures on March 31, 2021. Under the terms of the agreement, an interest-only period is provided such that principal repayment begins in June 2019; interest is payable on a quarterly basis through the full term of the loan. If we meet certain revenue milestones, the interest-only period may be extended such that principal repayment begins in June 2020. We expect to begin principal repayment in June 2019.

We are required to meet certain annual revenue covenants, starting for the year ending December 31, 2016. If the revenue covenants are not met, we may exercise a cure right by issuing additional common shares in exchange for cash or by borrowing subordinated debt in an amount equal to two times the difference between the minimum required revenue and our revenue. The cash received from the cure right would be considered repayment of principal. We were in compliance with this revenue covenant for the year ended December 31, 2016.

#### *Common Share Offering*

On July 29, 2016, we closed an underwritten public offering (the “Offering”) of 11,500,000 common shares from treasury, including the underwriters' full exercise of their option to purchase 1,500,000 common shares, at a price to the public of \$3.00 per common share, for aggregate gross proceeds of \$34.5 million before deducting the underwriting commission and estimated Offering expenses payable by us.

We used some of the net proceeds from the Offering for the payment of the upfront licensing fee pursuant to the exclusive license agreement with Allergan, for the in-licensing of dalbavancin, and for general corporate purposes. Any remaining net proceeds from the Offering will be used for milestone payments related to pricing reimbursements and launches of dalbavancin and for general corporate purposes.

## **NARRATIVE DESCRIPTION OF THE BUSINESS**

### **General**

We are a specialty pharmaceutical company dedicated to offering patients and healthcare providers innovative therapeutic options that effectively, safely, and conveniently manage acute medical conditions to improve health and quality of life. We strive to find innovative, differentiated medicines that provide therapeutic and economic value to patients, physicians and healthcare systems. We currently have two marketed, in-hospital cardiology products, BRINAVESS™ and AGGRASTAT®, which are commercially available in markets outside of the United States. We have licensed an approved antibiotic, XYDALBA™ (dalbavancin) that we launched in Germany and the United Kingdom in the fourth quarter of 2016 and in France in the first quarter of 2017. We expect to commercialize in Belgium, Nordic nations, Canada, certain other European countries and select countries in the Middle East over time. In addition, we have also licensed commercialization rights to a pre-registration drug/device combination product, TREVYENT®, for the treatment of PAH in certain regions outside the United States and commercialization rights to cardiology products ESMOCARD® and ESMOCARD LYO® (esmolol hydrochloride) in certain European countries.

## Summary of Our Products and Product Candidates

BRINAVESS™ (vernakalant (IV)) was approved in the European Union in September 2010 and is currently registered and approved in approximately 50 countries for the rapid conversion of recent onset AF to sinus rhythm in adults (for non-surgery patients with AF of seven days or less) and for use in post-cardiac surgery patients with AF of three days or less. BRINAVESS™ is mentioned as a first-line therapy in the European Society of Cardiology AF guidelines for the cardioversion of recent onset AF in patients with no, or minimal/moderate, structural heart disease.

AGGRASTAT® (tirofiban hydrochloride) is a reversible GP IIb/IIIa inhibitor (an intravenous anti-platelet drug) for use in patients with Acute Coronary Syndrome (“ACS”). AGGRASTAT® is currently registered and approved in more than 60 countries worldwide. We acquired the marketing rights outside of the United States to AGGRASTAT® as part of the transaction in which we also acquired Correvio in November 2013.

Both BRINAVESS™ and AGGRASTAT® are available commercially outside of the United States either directly through our own sales force in Europe or via our global distributor and partner network. We have a comprehensive global distributor and partner network that allows our products to be commercialized in many countries worldwide.

XYDALBA™ (dalbavancin) was centrally approved by the EMA in February 2015 as a treatment for Acute Bacterial Skin and Skin Structure Infections in adults. Dalbavancin is commercialized under the trade name XYDALBA™ in certain countries outside the United States and DALVANCE® in the United States. Cardiome launched XYDALBA™ in Germany and the United Kingdom in December 2016 and in France in February 2017.

TREVVYENT® (treprostinil sodium) is a development stage drug product that combines SteadyMed’s PatchPump technology, a drug delivery device, with treprostinil, a vasodilatory prostacyclin analogue to treat PAH. PatchPump is a proprietary, disposable, parenteral drug administration platform that is prefilled and preprogrammed at the site of manufacture.

ESMOCARD® is indicated for the treatment of supraventricular tachycardia (except for pre-excitation syndromes) and for the rapid control of the ventricular rate in patients with AF or atrial flutter in perioperative, postoperative, or other circumstances where short-term control of the ventricular rate with a short-acting agent is desirable. ESMOCARD® is also indicated for tachycardia and hypertension occurring in the perioperative phase and non-compensatory sinus tachycardia where, in the physician’s judgement, the rapid heart rate requires specific intervention. ESMOCARD® is not intended for use in chronic settings.

## Our Strategy

Our core strategy is to offer patients and healthcare providers innovative therapeutic options that effectively, safely, and conveniently manage acute medical conditions to improve health and quality of life. We strive to find innovative, differentiated medicines that provide therapeutic and economic value to patients, physicians and healthcare systems. Key elements of our strategy include:

- *Successfully commercializing XYDALBA™ in currently approved countries and seeking approvals in additional countries.* We intend to launch XYDALBA™ in countries where we have received approval to sell. Initially, we intend to focus our sales efforts on launching XYDALBA™ in the United Kingdom, Germany and France through our direct sales force. We also intend to commercialize XYDALBA™ in countries where the product has not yet launched, including the Nordic nations, Belgium, Ireland, and certain European countries, and to pursue approvals and subsequently launch XYDALBA™ in Canada and select countries in the Middle East.
- *Continuing to support the worldwide marketing of AGGRASTAT®.* We intend to continue to sell AGGRASTAT® in countries where it is presently approved, marketed and reimbursed for as long as these markets are economically viable. Further, we are seeking to expand the indications for which we may market AGGRASTAT® through extension of the indication statement for AGGRASTAT® to include “the reduction of major cardiovascular events in patients with acute myocardial infarction (ST-elevated myocardial infarction) intended for primary percutaneous coronary intervention.” AGGRASTAT® has already been granted this expanded label in some countries.

- *Attaining Approval to Commercialize TREVYENT® in Europe, Canada and the Middle East.* We licensed TREVYENT® from SteadyMed and anticipate preparing the marketing authorization application dossiers in Europe, Canada and the Middle East in 2017. Cardiome anticipates filing a marketing authorization application in 2017.
- *Successfully commercializing BRINAVESS™ in currently approved countries.* We intend to continue to sell BRINAVESS™ in countries where it is presently approved, marketed and reimbursed. We intend to focus our sales efforts on promoting BRINAVESS™ product sales in Europe via a fully dedicated direct sales force in Europe. We also intend to seek reimbursement in countries where the product has regulatory approval but has not launched in order to broaden the commercial opportunities for BRINAVESS™.
- *Successfully obtaining approval for vernakalant worldwide.* We intend to seek the approval of the U.S. Food and Drug Administration (the “FDA”) to restart the development program for vernakalant (IV) in the United States (which is currently on clinical hold) and to continue to advance the approval and development of vernakalant (IV) elsewhere. We intend to pursue a regulatory strategy to further develop intravenous vernakalant in order to achieve its maximum potential in the treatment of acute forms of atrial fibrillation.
- *Launching ESMOCARD® in Italy, France and Belgium.* We have licensed commercial rights for Italy, France and Belgium from AOP. We anticipate commercializing ESMOCARD® using our existing infrastructure.
- *Expanding our product offering and product pipeline through in-licensing and/or acquisitions.* We continuously evaluate in-licensing and acquisition opportunities that complement our product and operational capabilities. At any given time, we may have entered into confidentiality agreements, non-binding letters of intent or may be in the process of conducting due diligence with respect to potential opportunities. Priority will be given to later-stage or approved product opportunities that could be sold through our existing European in-hospital acute care sales force.
- *Building Product Offerings in Canada.* We intend to continue to sell AGGRASTAT® in Canada and to extend the indication to better align AGGRASTAT®’s Canadian label with its label in Europe, and to more accurately reflect the most recent evidence and actual clinical use, while making the drug more competitive. Further, we intend to build on our Canadian presence through advancing NDS for XYDALBA™ and TREVYENT® in Canada. On March 14, 2017, we announced that BRINAVESS™ received a Notice of Compliance from Health Canada which enables us to begin commercializing BRINAVESS™ in Canada. We hope to add additional products to our Canadian commercial effort through business development activities.
- *Leveraging external resources.* We focus our internal resources on those activities that we believe add or create the most value. We maintain a core team of professionals, consultants and staff with the necessary skill base for our operations, and contract out the specialized work required, such as pharmacovigilance, regulatory, medical information systems, commercial manufacturing and distribution to external organizations.

## **Our Products and Product Candidates**

We currently have two marketed, in-hospital cardiology products, BRINAVESS™ and AGGRASTAT®, which are commercially available in markets outside of the United States. We have licensed a European-approved antibiotic, XYDALBA™ (dalbavancin) that we have launched commercially in Germany and the United Kingdom in the fourth quarter of 2016 and in France in the first quarter of 2017. We expect to commercialize in Belgium, Nordic nations, Canada, certain other European countries and select countries in the Middle East over time. In addition, we have also licensed commercialization rights to a pre-registration drug/device combination product, TREVYENT®, for the treatment of PAH in certain regions outside the United States and commercialization rights to cardiology products ESMOCARD® and ESMOCARD LYO® (esmolol hydrochloride) in certain European countries.

### ***Vernakalant for Atrial Fibrillation***

AF is the most common cardiac arrhythmia (abnormal heart rhythm). It is characterized by an erratic and often rapid heart rate where the electrical activity of the heart's two small upper chambers (the atria) are not coordinated, resulting in inefficient pumping of blood and an increased risk of developing a blood clot in the heart, which could lead to embolic stroke. If a blood clot in the atria leaves the heart, enters the circulation, and becomes lodged in an artery in the brain, a stroke may result. Approximately 15% of all strokes occur in people with AF.

The risk of developing AF increases with age. The lifetime risk of developing AF at age 55 has been estimated at 24% in men and 22% in women. In addition, during the past 20 years, there has been a 60% increase in hospital admissions for atrial fibrillation independent of changes in known risk factors. Third party research estimates that 5.5 million patients are treated for atrial fibrillation in the seven leading industrialized nations each year.

Vernakalant is a chemical entity designed by Cardiome's scientists to treat AF by converting the heart back into normal rhythm and possesses the potential to overcome several limitations of current drugs and devices which are currently utilized to treat AF. Its mechanism of action involves the selective blockade of multiple ion channels in the heart that are known to be active during episodes of AF. The drug is being developed for two potential applications: (a) vernakalant (IV) was developed as an intravenous pharmacological converting agent designed to terminate an atrial fibrillation episode and return the heart to normal rhythm; and (b) vernakalant (oral) is being evaluated as an oral maintenance therapy for the long-term prevention of AF recurrence in patients who have had one or more previous episodes of AF.

### ***BRINAVESS™ (Vernakalant (IV))***

We have exclusive, global development and marketing rights to BRINAVESS™, the intravenous formulation of vernakalant, and are responsible for all and future development and commercialization of the product, subject to ongoing transfer of certain rights from Merck, Sharpe & Dohme ("Merck") and its affiliates. Transfers have been delayed in certain jurisdictions due to routine regulatory requirements.

### ***North America***

In December 2006, our former partner, Astellas Pharma US, Inc. ("Astellas"), filed a New Drug Application ("NDA") for vernakalant with the FDA. In August 2008, Astellas received an action letter from the FDA, informing Astellas that the FDA had completed its review of the NDA for vernakalant (IV) and that the application was approvable. The letter requested additional information associated with the risk of previously identified events experienced by a subset of patients during the clinical trials as well as a safety update from ongoing or completed studies of vernakalant (IV), regardless of indication, dosage form or dose level. The action letter further indicated that if the response to their requests was not satisfactory, additional clinical studies may be required.

In August 2009, we, together with our former partner Astellas, announced that Astellas would undertake a single confirmatory additional Phase 3 clinical trial ("ACT 5") under a Special Protocol Assessment. The decision to conduct another trial was reached following extended discussions between Astellas and the FDA to define the best regulatory path forward for vernakalant (IV). ACT 5 began enrolment of recent onset AF patients without a history of heart failure in October 2009.

In October 2010, a clinical hold was placed on the ACT 5 study by the FDA following a single unexpected serious adverse event of cardiogenic shock experienced by a patient with AF who received vernakalant (IV). The ACT 5 study was terminated. The FDA-mandated clinical hold on the vernakalant (IV) program remains in effect in the United States.

In 2013, when sponsorship of the U.S. Investigational New Drugs ("INDs") for vernakalant (IV) and vernakalant (oral) and the NDA for vernakalant (IV) were transferred to us from Merck, we initiated discussions with the FDA to determine the next steps for the development of vernakalant (IV) in the United States. The program

remains on clinical hold pending agreement of a suitable development path. In pursuit of alternative development scenarios, and after dialogue with the FDA, Cardiome has initiated additional nonclinical studies. Upon completion of these studies, it is Cardiome's intention to re-engage with the Cardiorenal Division to discuss paths forward.

In December 2015, we announced the filing of a NDS with Health Canada's Therapeutic Products Directorate (the "TPD") seeking Canadian approval of vernakalant (IV) for the rapid conversion of recent onset AF to sinus rhythm in adults with AF for up to seven days. Following completion of screening in May 2016, the TPD initiated a detailed review of the NDS. On March 14, 2017, we announced that BRINAVESS™ received a Notice of Compliance from Health Canada which enables us to begin commercializing BRINAVESS™ in Canada.

#### *Rest of World (Outside North America)*

In April 2009, we entered into two collaboration and license agreements (the "Collaboration Agreements") with Merck for the development and commercialization of vernakalant. The Collaboration Agreements provided an affiliate of Merck with exclusive rights outside of North America to vernakalant (IV).

Under the terms of the Collaboration Agreements, Merck paid us an initial fee of \$60 million. In addition, we were eligible to receive up to an additional \$200 million in payments, of which we received \$45 million. In July 2009, Merck submitted a Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA") seeking marketing approval for vernakalant (IV) in the European Union. In September 2010, vernakalant (IV) received marketing approval under the trade name BRINAVESS™ in the European Union, Iceland and Norway. After receipt of marketing approval, Merck began its commercial launch of BRINAVESS™ in a number of European countries.

In September 2012, Merck gave notice to us of its termination of the Collaboration Agreements. In April 2013 we took responsibility for worldwide sales, marketing, and promotion of vernakalant (IV) and in September 2013 we completed the transfer of commercialization responsibility for BRINAVESS™ in the European Union and of the responsibility to complete the post-marketing study for BRINAVESS™. Since this date, we have been supplying BRINAVESS™ under our own trade dress.

In September 2013, we entered into an agreement with Merck for the continued transfer of marketing authorizations. On a per country basis, regulatory and commercialization responsibilities have been transferred to us upon agencies' approvals of marketing authorization transfers. As a result of routine regulatory requirements, the transfers have been delayed in certain jurisdictions.

In December 2014, Eddingpharm (Asia) Macao Commercial Offshore Limited ("Eddingpharm") acquired rights to develop and commercialize BRINAVESS™ in China, Taiwan, and Macau and to re-launch BRINAVESS™ in Hong Kong. Eddingpharm will be responsible for any clinical trials and regulatory approvals required to commercialize BRINAVESS™ in the countries covered by the agreement. Under the terms of the agreement, Eddingpharm agreed to an upfront payment of \$1 million and specific annual commercial goals for BRINAVESS™. We are also eligible to receive regulatory milestone payments of up to \$3 million.

In August 2015, we announced that the Secretary of State for the U.K. Department of Health approved pricing for BRINAVESS™. The approved amount represents a maximum price per vial of BRINAVESS™ in the United Kingdom. It is consistent with pricing in other territories and our economic forecasts. Pricing approval is a step on the path to formulary coverage.

In January and March 2016, we filed MAAs with the Kingdom of Saudi Arabia's Saudi Food and Drug Authority and the United Arab Emirates' Ministry of Health, respectively, seeking approval of BRINAVESS™.

#### *Clinical Trials*

The clinical effect of BRINAVESS™ in the treatment of patients with atrial fibrillation has been evaluated in three, randomised, double-blind, placebo-controlled Phase 3 studies (ACT I, ACT II and ACT III) and in an active comparator trial versus intravenous amiodarone. Based on data from 1,203 patients in nine Phase 2 and Phase

3 trials, BRINAVESS™ has been approved in the European Union, Canada and countries in Central America, South America, Asia and the Middle East for the rapid conversion of recent onset atrial fibrillation to sinus rhythm in adults who have experienced atrial fibrillation for the following periods:

- For non-surgery patients: ≤ 7 days duration
- For post-cardiac surgery patients: ≤ 3 days duration.

In August 2010, Merck initiated a 615 patient Phase 3 Asia Pacific vernakalant (IV) study that was expected to support regulatory applications in additional territories for which marketing approval has not yet been obtained. In 2013, the study was terminated as part of the transfer of rights and responsibilities under the collaboration and license agreements from Merck to us. In November 2014, we announced results from this clinical trial. The study was originally planned to recruit 615 patients, however the study was completed after randomising 123 patients. The study remained sufficiently powered and showed that of the 111 treated patients with recent onset AF lasting three hours to seven days, 53% of those receiving an intravenous dose of BRINAVESS™ converted to normal heart rhythm within 90 minutes, compared to 12% of placebo patients.

Since transfer of rights for BRINAVESS™ from Merck to Cardiome, in China, our partner Eddingpharm has completed a Phase 1 study and planning is underway for a Phase 3 clinical trial.

In 2011, Merck initiated a 2,000 patient post-approval study for vernakalant (IV). This non-interventional prospective study is a post-authorization safety study of vernakalant (IV) conducted to collect information about normal conditions of use and appropriate dosing, and to quantify possible medically significant risks associated with the use of vernakalant in real-world clinical practice. In 2013, the transfer of this post-approval safety study (“PASS”) from Merck to us was completed. After the transfer, we recognized that the study had enrolled less quickly than initially anticipated and we filed an application to reduce the number of patients required for this study to 1,300. Our application to the EMA was unsuccessful and we are exploring methods to accelerate recruitment of the full complement of patients.

### ***Vernakalant (oral)***

Vernakalant (oral) is being developed as an oral maintenance therapy for the long-term prevention of AF recurrence. Two Phase 2 clinical trials have been completed. As part of the Collaboration Agreements, Merck acquired exclusive rights for the development and commercialization of vernakalant (oral). In March 2012, Merck informed us of its decision to discontinue further development and in September 2012, Merck returned global marketing and development rights to us. The IND was transferred to us in 2013. In January 2016, we submitted an application for orphan drug designation for vernakalant (oral) for the prevention of post-operative AF in patients undergoing coronary artery bypass graft surgery to the FDA’s Office of Orphan Products Development (the “OOPD”). In June 2016, we received notification from the OOPD that we were unsuccessful with our application.

### ***AGGRASTAT® for Acute Coronary Syndrome***

AGGRASTAT® contains tirofiban hydrochloride, which is a reversible GP IIb/IIIa inhibitor for use in indicated ACS patients. AGGRASTAT® is used to help assist the blood flow to the heart and to prevent chest pain and/or heart attacks (both STEMI – ST-elevation myocardial infarction, and NSTEMI-ACS – non-ST-elevation acute myocardial infarction). It works by preventing platelets, cells found in the blood, from forming into blood clots within the coronary arteries and obstructing blood flow to the heart muscle which can result in a heart attack. The medicine may also be used in patients whose heart vessels are dilated with a balloon (percutaneous coronary intervention), a procedure used to open up blocked or obstructed arteries in the heart in order to improve the blood flow to the heart muscle (myocardium) with or without the placement of a coronary stent. AGGRASTAT® is administered intravenously, and has been on the market for many years.

AGGRASTAT® contains tirofiban hydrochloride, which is a reversible GP IIb/IIIa inhibitor for use in indicated Acute Coronary Syndrome patients. AGGRASTAT® is used to help assist the blood flow to the heart and to prevent chest pain and/or heart attacks (both STEMI – ST-elevation myocardial infarction, and NONSTEMI – non-ST-elevation myocardial infarction). It works by preventing platelets, cells found in the blood, from forming

into blood clots within the coronary arteries and obstructing blood flow to the heart muscle which can result in a heart attack. The medicine may also be used in patients whose heart vessels are dilated with a balloon (percutaneous coronary intervention (“PCI”)), a procedure used to open up blocked or obstructed arteries in the heart in order to improve the blood flow to the heart muscle (myocardium) with or without the placement of a coronary stent. AGGRASTAT<sup>®</sup> is administered intravenously, and has been on the market for many years with an excellent safety and efficacy profile.

Cardiome has exclusive global marketing rights to AGGRASTAT<sup>®</sup> outside of the United States. Tirofiban hydrochloride was first approved in the United States in 1998, and to date is authorised in more than 70 countries worldwide, including almost all European Union and European Economic Area (“EEA”) member states.

The original indication approved for AGGRASTAT<sup>®</sup> was for the management of patients with unstable angina or non-Q-wave myocardial infarction, including patients who may subsequently undergo percutaneous transluminal coronary angioplasty, to decrease the rate of refractory ischemic conditions, new myocardial infarction and death.

### *Extension of Indication*

Since the original approvals of tirofiban hydrochloride, evidence emerged as result of a number of independent studies indicating that a higher degree of platelet inhibition was beneficial for patients in need of an urgent PCI and thus at a high risk for ischaemic events. When PCI is performed urgently, as in high risk non-ST elevation acute coronary syndrome (“NSTE-ACS”) or STEMI patients, platelet inhibition must be achieved rapidly and to a high degree. Consequently, a number of investigator-initiated studies demonstrated the clinical benefit of tirofiban hydrochloride using a high dose bolus (“HDB”) regimen employing a bolus of 25 mcg/kg administered over three minutes followed by a maintenance infusion of 0.15 mcg/kg/min in patients with ACS who undergo PCI early.

The original indication terminology was no longer in common use and described a population of ACS patients including those with unstable angina and NONSTEMI, but not STEMI. Therefore, in the interest of aligning the current label for tirofiban hydrochloride with the most recent evidence and actual clinical use, Corveio extended the therapeutic indication to include treatment of patients with STEMI intended for primary PCI and to add HDB as the appropriate dosing regimen.

In the European Union, a variation for the introduction of the HDB tirofiban hydrochloride regimen and concomitant use of oral antiplatelet drugs was approved in September 2010. The data for the approval of the HDB regimen was derived from independent investigator-initiated studies including patients with UA/NONSTEMI and STEMI. The European Union approval of the indication for patients suffering from STEMI with the intention to undergo primary PCI was granted in October 2013. In Switzerland, a combined variation extending the indication to STEMI patients and recommending the HDB regimen for NSTE-ACS patients undergoing PCI within four hours and STEMI primary PCI patients, was approved by Swiss regulatory authorities in December 2014.

In October 2013, the United States AGGRASTAT<sup>®</sup> label was updated to include the HDB posology. At the same time, the indication statement was refined to “AGGRASTAT is indicated to reduce the rate of thrombotic cardiovascular events (combined endpoint of death, myocardial infarction, or refractory ischemia/repeat cardiac procedure) in patients with NSTE-ACS.

Applications for the extension of the indication statement for AGGRASTAT<sup>®</sup> are continuing worldwide, most recently with the submission of a supplemental NDS in Canada in July 2015. In September 2015, we entered into an agreement with Mitsubishi Tanabe Pharma Europe Ltd. (“MTPE”), a subsidiary of Mitsubishi Tanabe Pharma Corporation headquartered in Japan, to co-promote AGGRASTAT<sup>®</sup> and MTPE’s EXEMBOL<sup>®</sup> (argatroban monohydrate) in the United Kingdom. EXEMBOL<sup>®</sup> is indicated for anticoagulation in adult patients with heparin-induced thrombocytopenia type II who require parenteral antithrombotic therapy. The co-promotion agreement is for an initial term of three years.

***XYDALBA<sup>TM</sup>***

In May 2016, we announced the execution of an exclusive license agreement with Allergan plc (“Allergan”), for the rights to commercialize dalbavancin (branded DALVANCE<sup>®</sup> in the United States, where it is marketed by Allergan, and XYDALBA<sup>™</sup> in the rest of the world) in the United Kingdom, Germany, France, Denmark, Iceland, Finland, Malta, Norway, Sweden, Belgium, the Netherlands, Luxemburg, Ireland, Switzerland, Canada and certain countries in the Middle East. XYDALBA<sup>™</sup> fits Cardiome’s commercial footprint as a differentiated specialty pharmaceutical company focused on commercializing proprietary growth pharmaceuticals in Europe and Canada. In December 2016, we initiated the launch of XYDALBA<sup>™</sup> in the United Kingdom and Germany and expect to continue to commercialize in other countries over time.

XYDALBA<sup>™</sup> is a second generation, semi-synthetic lipoglycopeptide. XYDALBA<sup>™</sup> is the first and only IV antibiotic approved in Europe for the treatment of ABSSSI with a single dose regimen of 1500 mg administered over 30 minutes or a two-dose regimen of 1000 mg followed one week later by 500 mg, each administered over 30 minutes. This dosing regimen makes it possible to treat patients with ABSSSI in an outpatient setting, avoiding hospitalization or potentially allowing earlier discharge, without compromising efficacy. XYDALBA<sup>™</sup> demonstrates bactericidal activity in vitro against a range of Gram-positive bacteria, such as Staphylococcus aureus (including methicillin-resistant, also known as MRSA, strains) and Streptococcus pyogenes, as well as certain other streptococcal species.

### **TREVVYENT<sup>®</sup>**

In June 2015, we entered into an exclusive license and supply agreement (the “License Agreement”) with SteadyMed to commercialize the development-stage product TREVVYENT<sup>®</sup> (treprostinil) in Europe, Canada and the Middle East.

Pursuant to the License Agreement, SteadyMed granted us an exclusive royalty-bearing license to commercialize TREVVYENT<sup>®</sup> in Europe, Canada and the Middle East if TREVVYENT<sup>®</sup> is approved for the treatment of pulmonary arterial hypertension (“PAH”) in such regions. Under the License Agreement, SteadyMed will receive up to \$12.3 million in connection with regulatory and sales milestones, including an upfront payment of \$3 million. We have agreed to pay to SteadyMed a transfer price on finished goods and a scaling double-digit royalty on future TREVVYENT<sup>®</sup> sales.

PAH is a type of high blood pressure that occurs in the right side of the heart and in the arteries that supply blood to the lungs. PAH worsens over time and is life-threatening because the pressure in a patient’s pulmonary arteries rises to dangerously high levels, putting a strain on the heart. There is no cure for PAH, but several medications are available to treat symptoms, such as Remodulin<sup>®</sup> (treprostinil sodium), the market-leading prostacyclin PAH therapy produced by United Therapeutics Corporation.

TREVVYENT<sup>®</sup> is a development stage drug product that combines SteadyMed’s PatchPump technology with treprostinil, a vasodilatory prostacyclin analogue to treat PAH. PatchPump is a proprietary, disposable, parenteral drug administration platform that is prefilled and preprogrammed at the site of manufacture.

In January 2016, we announced that the EMA approved our request to review TREVVYENT<sup>®</sup> under the Centralised Authorisation Procedure drug review process. This procedure results in a single marketing authorization that is valid in all 28 European Union countries and three European Economic Area countries.

### **ESMOCARD<sup>®</sup> and ESMOCARD LYO<sup>®</sup>**

In May 2015, we entered a commercialization agreement with AOP Orphan Pharma (“AOP”) to sell AOP’s cardiovascular products, ESMOCARD<sup>®</sup> and ESMOCARD LYO<sup>®</sup> in Italy, France, Spain and Belgium.

Supraventricular tachycardia refers to a rapid heart rhythm of the upper heart chambers (atria). Electrical signals in the atria fire abnormally, which interferes with electrical signals coming from the sinoatrial node - the heart’s natural pacemaker. A series of early beats in the atria speeds up the heart rate. The rapid heartbeat does not allow enough time for the heart to fill before it contracts so blood flow to the rest of the body is compromised.

ESMOCARD<sup>®</sup> is indicated for the treatment of supraventricular tachycardia (except for pre-excitation syndromes) and for the rapid control of the ventricular rate in patients with AF or atrial flutter in perioperative, postoperative, or other circumstances where short-term control of the ventricular rate with a short-acting agent is desirable. ESMOCARD<sup>®</sup> is also indicated for tachycardia and hypertension occurring in the perioperative phase and

non-compensatory sinus tachycardia where, in the physician's judgement the rapid heart rate requires specific intervention. ESMOCARD<sup>®</sup> is not intended for use in chronic settings.

### **Production Methods and Components**

All of our products are manufactured by third parties and require the use of raw materials obtained by third parties. The sources and quantities of such raw materials may be limited. See "Risk Factors – *We rely on third parties for the supply and manufacture of our products, which can be unpredictable in terms of quality, cost and availability.*"

### **Specialized Skill and Knowledge**

We focus our internal resources on those activities that we believe add or create the most value. We maintain a core team of professionals, consultants and staff with the necessary skill base for our operations, and contract out the specialized work required, such as pharmacovigilance, regulatory, medical information services, commercial manufacturing, and distribution to external organizations. In addition, we support our pre-clinical programs by collaborating with external researchers, many of whom have extensive knowledge and understanding of these programs. This collective knowledge, experience and expertise helps ensure that the ideas pursued are of a high caliber and are therefore more likely to result in a drug which impacts a specific disease state. See "Risk Factors – *We are dependent upon our key personnel to achieve our business objectives.*"

### **Foreign Operations**

We have operations in Canada, the United States, as well as various countries in Europe. Our direct sales force responsible for the sale and promotion of all our products are primarily based in Europe. See "Risk Factors – *We are subject to risks inherent in foreign operations.*"

### **U.S. Export Controls and Economic Sanctions**

Cardiome is a global, innovation-driven pharmaceutical business with worldwide operations (directly and through distributors). Prior to the acquisition of Correvio, Cardiome did not have operations in the United States and was not subject to U.S. export controls and economic sanctions regulations, such as those instituted by the U.S. Treasury Department's Office of Foreign Assets Control ("OFAC"). Correvio, however, does have operations in the United States, and in 2012 it voluntarily reported to OFAC that it had made inadvertent sales of AGGRASTAT<sup>®</sup>, which treats chest pain and certain heart conditions, into Iran by a third-party Lebanese distributor, as well as reimbursement costs which were paid to another third-party Iranian distributor. Along with the voluntary report, Correvio applied for a specific license to sell AGGRASTAT<sup>®</sup> through specified intermediaries and distributors into certain hospitals in Iran. Although OFAC has not yet acted on the voluntary report, OFAC did grant Correvio the requested license. Cardiome (or any of our subsidiaries) may generate revenue in the future by way of sales into Iran through a third-party distributor. To the extent required, such sales would be made as permitted by OFAC under either a general or specific license.

### **Competition**

The life sciences industry is characterized by extensive research efforts, rapid technology change and intense competition. Competition in the life sciences industry is based primarily on product performance, including efficacy, safety, ease of use and adaptability to various modes of administration, patient compliance, price, acceptance by physicians, manufacturing, sales, marketing and distribution. Barriers to entry into the market include the availability of patent protection in the United States and other jurisdictions of commercial interest and the ability and time needed and cost required to obtain governmental approval for testing, manufacturing, sales, marketing and distribution.

We are aware of a number of companies engaged in the development of drugs within our areas of focus. Due to the size of the cardiovascular market and the large unmet medical need, a number of the world's largest pharmaceutical companies are developing or could potentially develop products that could compete with our

products. In addition, AGGRASTAT<sup>®</sup> is a mature product which is beginning to face generic competition. See “*Risk Factors – We are exposed to generic product risk which may result in a decline in sales of AGGRASTAT<sup>®</sup>*,” and “*Risk Factors – We have substantial competition in the life sciences industry and with respects to our products.*”

## **Patents and Proprietary Protection**

We consider our patent portfolio to be an important contributor to our business and therefore devote resources to maintaining and augmenting our patent portfolio. Our patent strategy is to pursue the broadest possible patent protection on our proprietary products and technology in selected jurisdictions and to achieve the maximum duration of patent protection available. Accordingly, for novel compounds or therapeutic use claims for the compound, we have made or will make claims related to composition, manufacturing, mechanism of action, dosing, plasma levels, combination with other drugs and therapeutic use. We plan to protect our technology, inventions and improvements to our inventions by filing patent applications in selected key countries according to industry standards in a timely fashion. See “*Risk Factors – We rely on proprietary technology, the protection of which can be unpredictable and costly.*”

In addition to our patents, we also rely upon trade secrets, know-how and continuing technological innovations to develop our competitive position. It is our policy to require our directors, employees, consultants, members of our scientific advisory board and parties to collaborative agreements to execute confidentiality agreements upon the commencement of employment, consulting or collaborative relationships with us. In the case of employees and consultants, the agreements provide that all inventions resulting from work performed for us utilizing our property or relating to our business and conceived of or completed by the individual during employment are our exclusive property.

We currently have no royalty obligations associated with any of the patents and patent applications in our portfolio relating to vernakalant.

## **Regulatory Environment**

The research, development, manufacture, distribution, sale, and marketing of pharmaceutical products are subject to extensive regulation. A comprehensive regulatory scheme requires licensing of manufacturing facilities, carefully controlled research and testing products, governmental review and approval of results prior to marketing of therapeutic products, adherence to Good Manufacturing Practices, (“GMP”), during production, and compliance with comprehensive post-approval requirements. In the United States, Europe and Canada, these activities are subject to rigorous regulation by the FDA, the EMA, and the Therapeutic Products Directorate (“TPD”), respectively. In addition, the research, manufacturing, distribution, sale, and promotion of pharmaceutical products are also potentially subject to regulation by various regional, national, and local authorities where the products are being developed and marketed.

Our success is ultimately dependent on obtaining marketing approval for drugs currently under development by and with our collaborative partners, and our ability to comply with the regulations in the regions and countries where we conduct clinical trials and market products. Depending upon the circumstances surrounding the clinical evaluation of a product, we may undertake clinical trials, contract clinical trial activities to contract research organizations or rely upon corporate partners for such development. This approach will allow us to make cost effective developmental decisions in a timely fashion. See “*Risk Factors – We rely on third parties for the execution of a significant portion of our regulatory, pharmacovigilance and medical information responsibilities and such third parties may fail to meet their obligations as a result of inadequacies in their systems and processes or execution failure.*”

The principal activities that must be completed after initial drug discovery and synthesis work and before obtaining approval for marketing of a product are as follows:

- pre-clinical studies, which includes pharmacological and efficacy testing in animals, toxicology testing and formulation work based on in vitro results, performed to assess the safety and potential efficacy of the product, and subject to good laboratory practice requirements;

- Phase 1 clinical trials, the initial introduction of the product into human subjects, under which the compound is generally tested for safety, dosage, tolerance, metabolic interaction, distribution, excretion and pharmacodynamics;
- Phase 2 clinical trials involving studies in a limited patient population to: (i) determine the efficacy of the product for specific, targeted indications, (ii) determine optimal dosage, and (iii) identify possible adverse effects and safety risks; and
- Phase 3 clinical trials which are undertaken to further evaluate clinical efficacy of the product and to further test for its safety within an expanded patient population at geographically dispersed clinical study sites in order to support marketing authorization.

Two key factors influencing the rate of progression of clinical trials are the rate at which patients are available to participate in the research project and whether effective treatments are currently available for the disease that the drug is intended to treat.

In the United States, an IND application must be filed and accepted by the FDA before clinical trials may begin. The IND application must contain specified information including the results of the pre-clinical studies or clinical studies completed in other regions at the time of the IND application. The degree of information on the safety and efficacy of the drug must be adequate for the phase of the proposed clinical investigation and allow the FDA to make an informed risk and benefit decision at each stage of investigational drug testing. In addition, since the method of manufacture may affect the safety and efficacy of a drug, information on manufacturing methods and standards and the stability of the drug substance and the dosage form must be presented so that the FDA can ensure that the product that may eventually be sold to the public has the same composition as that determined to be effective and safe in the clinical trials. Production methods and quality control procedures must be in place to ensure a relatively pure compound, essentially free of contamination and uniform with respect to all quality aspects.

In the United States, studies conducted to support approval for product marketing be adequate and well controlled. In general, this means that either a placebo or a product already approved for the treatment of the disease or condition under study must be used as a reference control. Studies must also be conducted in compliance with good clinical practice requirements, and informed consent must be obtained from all study subjects.

The FDA may prevent clinical trials from beginning or may place clinical trials on hold at any point in this process if, among other reasons, it concludes that clinical subjects are being exposed to an unacceptable health risk. Trials may also be prevented from beginning or may be terminated by institutional review boards, who must review and approve all research involving human subjects. Side effects or adverse events that are reported during clinical trials can delay, impede, or prevent marketing authorization.

Upon completion of all clinical studies, the data are analyzed to determine whether the trials successfully demonstrated safety and effectiveness, and whether a product approval application may be submitted. For products regulated as drugs, as opposed to biologics, the results are submitted to the FDA as part of an NDA to obtain approval to commence marketing the product. The NDA must include a substantial amount of data and other information concerning the safety and effectiveness of the compound from laboratory, animal and clinical testing, as well as data and information on manufacturing, product stability, and proposed product labelling. Each domestic and foreign manufacturing establishment, including any contract manufacturers we may decide to use, must be listed in the NDA and must be registered with the FDA. The application will likely not be approved until the FDA conducts a manufacturing inspection, approves the applicable manufacturing process for the drug product, and determines that the facility is in compliance with current GMP requirements. If the manufacturing facilities and processes fail to pass the FDA inspection, we will not receive approval to market these products. We may partner later stage development of our drug candidates with companies that have experience in manufacturing in accordance with GMP requirements.

Under the Prescription Drug User Fee Act, as amended, applicants may be required to pay a substantial fee to the FDA for an NDA and any supplements requiring clinical data thereto, as well as annual fees for commercial manufacturing establishments and for approved products.

Under applicable laws and FDA regulations, each NDA submitted for FDA approval is reviewed for administrative completeness and reviewability within 60 days following submission of the application. If deemed complete, the FDA will file the NDA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. If the FDA refuses to file an application, the FDA will retain 25% of the user fee as a penalty. The FDA has established performance goals for the review of NDAs — six months for priority applications and ten months for regular applications. However, the FDA is not legally required to complete its review within these periods. Moreover, the outcome of the review, even if generally favourable, not uncommonly is not an actual approval but a complete response letter that describes additional work that must be done before the application can be approved. The FDA's review of an application may involve review and recommendations by an independent FDA advisory committee.

Even if the FDA approves a product, it may limit the approved therapeutic uses for the product as described in the product labelling, require that warning statements be included in the product labelling, require that further studies be conducted as a condition of approval (sometimes called Phase 4 studies), impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. Post-market studies may provide additional data on safety and efficacy necessary to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested and approved.

Significant legal and regulatory requirements also apply after FDA approval to market under an NDA. These include, among other things, requirements related to adverse event and other reporting, product advertising and promotion, and ongoing adherence to GMPs, as well as the need to submit appropriate new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labelling or manufacturing process. The FDA also enforces the requirements of the United States *Prescription Drug Marketing Act* which, among other things, imposes various requirements in connection with the distribution of product samples to physicians.

In the United States, the research, manufacturing, distribution, sale, and promotion of drug and biological products are subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the United States Department of Justice and individual United States Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the United States *Medicare-Medicaid Anti-Fraud and Abuse Act*, as amended, the United States *False Claims Act*, as amended, the privacy provisions of the United States *Health Insurance Portability and Accountability Act* and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the United States *Omnibus Budget Reconciliation Act of 1990*, as amended, and the United States *Veterans Health Care Act of 1992*, as amended. If products are made available to authorized users of the United States Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

In the European Union, clinical trial applications must be filed with and approved by the competent authority and ethics committee(s) of each member state where the trial will be conducted prior to initiating the study. The information contained within a clinical trial application is similar to that of an IND to the FDA, although the format of the application is quite different.

Once the clinical trial applications are accepted, clinical studies can commence. Clinical trial regulations are similar to those in the United States with respect to the degree of information required to support each stage of investigational drug testing. However, there are region and national specific differences and approval to conduct clinical trials in one region or country does not guarantee approval in others. Similar to the FDA, European agencies may refuse to approve clinical trials if they conclude that subjects may be exposed to an unacceptable risk. In addition to placebo-controlled trials, the European authorities may recommend a comparator study be completed as part of the development program depending on the indication and availability of current treatments. A comparator study is one where the reference control is a product already approved for the treatment of the disease or condition under study.

Following the completion of clinical studies, and sufficient data has been collected to demonstrate an adequate benefit and risk profile, a MAA is built for submission and review. A medicinal product may only be placed on the market in the EEA, where a marketing authorisation holder is established within the EEA and after one of the following types of authorisations is obtained:

- national authorisation when the marketing authorisation has been issued by the competent authority of a member state, or EEA country, for its own territory; or
- community authorisation, when an authorisation has been granted for the entire community.

Depending on the medicinal product and objectives of the applicant, there are separate and distinct approval processes for obtaining these marketing authorisations.

A national marketing authorisation may be obtained through the submission of an application to the competent authority of the member state where approval is sought. In cases where national authorisations are requested for the same medicinal product in more than one member state and the marketing authorisation holder has received a marketing authorisation in a member state, the applicant would submit an application in the member states concerned using the procedure of mutual recognition. The member states concerned would then recognise the marketing authorisation already granted by the reference member state and authorise the marketing of the product on their national territory. If no marketing authorisation has been granted in the community, the applicant may make use of a decentralised procedure and submit an application in all the member states where it intends to obtain a marketing authorisation at the same time, and choose one of them as reference member state. Based on the assessment report prepared by the reference member state and any comments made by the concerned member state, marketing authorisation should be granted in accordance with the decision taken by the reference member state and concerned member state in this decentralised procedure.

Alternatively, community authorisation, valid throughout the EEA, may be obtained through the submission of an application to the EMA, via the centralised procedure. This process is required for medicinal products which fall within the mandatory scope of the centralised procedure, and discretionary for products that fall under the optional scope, such as vernakalant (IV). Under the centralised procedure, the scientific evaluation of the application is carried out within the Committee for Medicinal Products for Human Use (“CHMP”), and a scientific opinion is prepared. For each application, a Rapporteur and Co-Rapporteur are appointed from amongst the members of the CHMP or CHMP alternate members. This appointment is made on the basis of objective criteria, which ensures the provision of objective scientific opinions and allows the use of the best and available expertise in the EEA on the relevant scientific area. The role of the Rapporteur is to perform the scientific evaluation and to prepare an assessment report to the CHMP according to the timetable agreed for the evaluation procedure. The Rapporteur is supported by a Co-Rapporteur whose responsibility is to conduct a second scientific evaluation and prepare a separate full assessment report or critique of the Rapporteur's report at the discretion of the CHMP.

Following submission of the application to the EMA under the centralised procedure, the application is validated from both a technical and business perspective to ensure the technical components and content of the submission are complete and accurate. The EMA is responsible for ensuring that the opinion of the CHMP is given within 210 days, less any clock-stops for the applicant to provide answers to questions from the CHMP. The CHMP scientific opinion will contain the conclusions on the quality, the safety and the efficacy of the medicinal product and will take into account appropriate benefit and risk scenarios on the populations and conditions of use as documented with clinical data by the applicant. The opinion is sent to the European Commission, or Commission, who, if satisfied with the conclusion, is responsible for drafting a decision to recommend approval of the medicinal product. The Commission will adopt the decision and grant a marketing authorisation after consultation with the member states through the relevant standing committees. Such a marketing authorisation is valid throughout the community and confers the same rights and obligations in each of the member states as a marketing authorisation granted by that member state. Following the granting of marketing authorisation, the product can then be made commercially available in Europe.

Once a medicinal product is granted with a community authorisation, the medicinal product can no longer be the subject of a subsequent national marketing authorisation. In order to maintain coherence, and to preserve the

unity of a single market within the community, a marketing authorisation holder wishing to market another medicinal product with the same active substance already included in a community authorisation must use the centralised procedure.

Similar to the process in the United States, the authorities may limit the approved therapeutic uses for the product as described in the product labelling, require that warning statements be included in the product labelling, require that further studies be conducted as a condition of approval, impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. Post-market studies may provide additional data on safety and efficacy necessary to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested and approved. Significant legal and regulatory requirements also apply after approval to market in Europe. These include, among other things, requirements related to adverse event and other reporting, product advertising and promotion, and ongoing adherence to GMP, as well as the need to submit appropriate variations to approval for certain changes to the approved product, product labelling or manufacturing process.

## **Employees**

As of December 31, 2016, we had approximately 120 employees located in Vancouver, British Columbia, Chadds Ford, Pennsylvania, and various countries in Europe. None of our employees are represented by a collective bargaining agreement and we have never experienced any work stoppage. We consider our relations with our employees to be good. In addition, we view our employees as an important competitive advantage. Thus far, we have been successful in retaining our key employees including members of our management team. See “Risk Factors – We are dependent upon our key personnel to achieve our business objectives.”

## **RISK FACTORS**

*Investing in our securities involves a high degree of risk. You should carefully consider the following risks in addition to the other information included in this annual information form and our historical consolidated financial statements and related notes, before you decide to purchase our common shares. If any of the following risks actually occur, our business, financial condition and results of operations could materially suffer. As a result, the trading price of our common shares could decline and you could lose part or all of your investment. The risks set out below are not the only risks we face; risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business, financial condition and results of operations. You should also refer to information set out in our consolidated financial statements and management’s discussion and analysis for the year ended December 31, 2016.*

***We will have significant additional future capital needs and there are uncertainties as to our ability to raise additional funding.***

We will require significant additional capital resources to expand the commercialization and sales of BRINAVESS<sup>™</sup>, AGGRASTAT<sup>®</sup>, XYDALBA<sup>™</sup>, and ESMOCARD<sup>®</sup> and to further develop vernakalant (IV) in the United States (and elsewhere). Advancing our product candidates, market expansion of our currently marketed products or acquisition and development of any new products or product candidates will require considerable resources and additional access to capital markets. In addition, our future cash requirements may vary materially from those now expected. For example, our future capital requirements may increase if:

- we experience more generic competition for AGGRASTAT<sup>®</sup> from other life sciences companies or in more markets than anticipated;
- we experience delays or unexpected increases in costs in connection with obtaining regulatory approvals or commercializing BRINAVESS<sup>™</sup>, XYDALBA<sup>™</sup>, and ESMOCARD<sup>®</sup> in the various markets where we hope to sell our products;
- we experience unexpected or increased manufacturing or other supply chain costs;

- we experience unexpected or increased costs relating to preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, or other lawsuits, brought by either us or our competition;
- we experience scientific progress sooner than expected in our discovery, research and development projects, if we expand the magnitude and scope of these activities, or if we modify our focus as a result of our discoveries;
- we are required to perform additional pre-clinical studies and clinical trials;
- we consummate suitable business development opportunities;
- we elect to develop, acquire or license new technologies, products or businesses; or
- we are required to conduct pharmacoeconomic studies for reimbursement and/or Phase 4 studies for assessment of real-world use and safety.

We could potentially seek additional funding through corporate collaborations and licensing arrangements, through public or private equity or debt financing or through other transactions. However, if sales are slow to increase or if capital market conditions in general, or with respect to life sciences companies such as ours, are unfavourable, our ability to obtain significant additional funding on acceptable terms, if at all, will be negatively affected. Additional financing that we may pursue may involve the sale of our common shares or financial instruments that are exchangeable for, or convertible into, our common shares which could result in significant dilution to our shareholders.

If we are unable to obtain financing to fund our operational and strategic business development activities, we may be required to delay, reduce the scope of, or eliminate one or more of our planned development and commercialization activities, which could have a material adverse effect on our business, financial condition and results of operations.

***We have a history of significant losses and a significant accumulated deficit.***

Although we have been involved in the life sciences industry since 1992, we had, prior to the launch of BRINAVESS™ and the acquisition of AGGRASTAT®, only been engaged in research and development. Before Merck, Sharp & Dohme obtained marketing approval for BRINAVESS™ in the European Union, Iceland and Norway in September 2010, and launched BRINAVESS™ in a number of European countries in 2010, none of our product candidates had been approved for marketing or commercialized. Accordingly, we have only recently begun to generate revenue from product sales and have incurred significant operating losses. Net losses for the years ended December 31, 2016 and 2015 were approximately \$19.6 million and \$24.5 million, respectively. At December 31, 2016, our accumulated deficit was \$363.1 million. Our losses in 2016 resulted primarily from SG&A expenses associated with sales and marketing costs required to support the commercialization of BRINAVESS™ and the continued sales of AGGRASTAT® and costs associated with the launch of XYDALBA™ in the fourth quarter of 2016. We cannot assure you that we will generate sufficient revenues in the future or achieve profitable operations.

***We have a history of negative operating cash flow and may continue to experience negative operating cash flow.***

We had negative operating cash flow for the financial years ended December 31, 2016 and December 31, 2015. We anticipate that we will continue to have negative cash flow unless our product sales are able to generate a positive cash flow. To the extent that we have negative operating cash flow in future periods, we may need to allocate a portion of our cash reserves to fund such negative cash flow. We may also be required to raise additional funds through the issuance of equity or debt securities. There can be no assurance that we will be able to generate a positive cash flow from our operations, that additional capital or other types of financing will be available when needed or that these financings will be on terms favourable to us.

***We may not realize the anticipated benefits of past or future acquisitions or product licenses and integration of these acquisitions and any products acquired or licensed may disrupt our business and management.***

As part of our business strategy, we may also continue to acquire additional companies, products or technologies principally related to, or complementary to, our current operations. At any given time, we may be evaluating new acquisitions of companies, products or technologies or may be exploring new licensing opportunities, and may have entered into confidentiality agreements, non-binding letters of intent or may be in the process of conducting due diligence with respect to such opportunities. Any such acquisitions will be accompanied by certain risks including, but not limited to:

- exposure to unknown liabilities of acquired companies and the unknown issues with any associated technologies or research;
- higher than anticipated acquisition costs and expenses;
- the difficulty and expense of integrating operations, systems, and personnel of acquired companies;
- disruption of our ongoing business;
- inability to retain key customers, distributors, vendors and other business partners of the acquired company;
- diversion of management's time and attention; and
- possible dilution to shareholders.

We may not be able to successfully overcome these risks and other problems associated with acquisitions and this may adversely affect our business, financial condition or results of operations.

***If we are unable to make our regularly scheduled payments under the CRG Term Loan, we could have a covenant violation.***

Under the Term Loan Agreement, we are required to make regular quarterly payments. To the extent that we are unable to generate sufficient cash flow to make our regularly scheduled payments, this could result in a breach of the facility, which would require us to repay the entire amount of the CRG Term Loan outstanding. This could have a material adverse effect on our business, financial condition and results of operations.

***We are subject to certain restrictive covenants.***

Restrictive covenants in our Term Loan Agreement impose financial and other restrictions on us. Under our Term Loan Agreement, we must meet specified financial covenants, including carrying a minimum balance of unrestricted cash and cash equivalents or meeting certain annual revenue targets. To the extent that we are not able to satisfy the requirements in our Term Loan Agreement or if we are not in compliance with the specified financial covenants, including meeting certain annual revenue covenants, we may be in breach of the facility which would require us to exercise a cure right by issuing additional common shares in exchange for cash or by borrowing subordinated debt in an amount equal to two times the difference between the minimum required revenue and our revenue for the year or repay outstanding amounts. Exercising the cure right or repaying the entire amount of the CRG Term Loan outstanding could have a material adverse effect on our business, financial condition and results of operations.

***We are dependent on two products for substantially all of our current revenues.***

Sales of a limited number of our products represent substantially all of our current revenues. If the volume or pricing of our products decline in the future, or our cost to manufacture, distribute or market our products increase in the future, our business, financial condition and results of operations could be materially adversely affected and this could cause the market value of our common shares to decline. In addition, if these products were to become subject to any other issues, such as material adverse changes in prescription growth rates, unexpected side effects, regulatory proceedings, material product liability litigation, publicity affecting doctor or patient confidence or pressure from competitive products, the adverse impact on our business, financial condition, results of operations and the market value of our common shares could be significant.

***We are exposed to generic product risk which may result in a decline in sales of AGGRASTAT®.***

AGGRASTAT® is a mature product which faces generic competition and may experience a decline in product sales in several markets. Competition from generic equivalents that would be sold at a price that is less than the price at which we currently sell AGGRASTAT® could have a materially adverse impact on our business, financial condition and operating results. Our efforts to enhance the marketing of AGGRASTAT® through our direct sales force and to expand the indications for which we may market AGGRASTAT® may not be successful in addressing or mitigating the effect of generic competition.

***We have substantial competition in the life sciences industry and with respect to our products.***

The life sciences industry is highly competitive. Many companies, as well as research organizations, currently engage in, or have in the past engaged in, efforts related to the development of products in the same therapeutic areas as we do. Due to the size of the cardiovascular market and the large unmet medical need for products that treat cardiovascular illnesses, a number of the world's largest pharmaceutical companies are developing, or could

potentially develop, products that could compete with ours. GP IIB/IIIa inhibitors that AGGRASTAT® competes with include ReoPro from Eli Lilly and Company and Johnson & Johnson/Centocor, Inc., Angiomax from The Medicines Company, and Integrilin from Merck. Antiarrhythmics that BRINAVESS™ competes with include generic competitors such as flecainide, propafenone, ibutilide and amiodarone. Competitors of dalbavancin include Zyvox from Pfizer, Cubucin from Merck, Tygacil from Pfizer, and generic competitors such as Vancomycin and Targocid.

Many of the companies developing competing technologies and products have significantly greater financial resources and expertise in discovery, research and development, manufacturing, pre-clinical studies and clinical testing, obtaining regulatory approvals, distribution and marketing than we do. Other smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Academic institutions, government agencies and other public and private research organizations may also conduct research, seek patent protection and establish collaborative arrangements for discovery, research, clinical development and marketing of products similar to ours. There is a risk that one or more of our competitors may develop more effective or more affordable products than us and that such competitors will commercialize products that will render our product candidates obsolete. We face competition with respect to product efficacy and safety, ease of use and adaptability to various modes of administration, acceptance by physicians, the timing and scope of regulatory approvals, availability of resources, reimbursement coverage, price and patent positions of others. In addition, these companies and institutions also compete with us in recruiting and retaining qualified personnel. If we fail to develop new products or enhance our existing products in the face of such strong competition, such competition could have a material adverse effect on our business, financial condition or results of operations.

***We are subject to the risks associated with product liability claims, insurance and recalls.***

Our pharmaceutical products have undergone extensive clinical testing and have been approved by the applicable regulatory authorities prior to sale in the European Union and other countries or regions. Certain aspects of our clinical trials, including the design of the trials, the manufacture and storage of clinical trial material, the enrollment, dosing and follow-up of patients, the recording of trial data and the analysis of results, have been, and may in the future be, sponsored and conducted by third-party academic investigators who have not been under our supervision or control. We therefore may not have independently verified or audited the data or clinical trial sites, and may not do so in the future. Despite all reasonable efforts to ensure safety, it is possible that we, our suppliers or our distribution partners may sell products which are defectively manufactured or labeled, contain defective ingredient components or are misused. Our products may also fail to meet patient expectations or produce harmful side effects. Such unexpected quality, safety or efficacy issues may be caused by a number of factors, including manufacturing defects, harmful side effects, physician experience in prescribing our products, failure to adhere to approved labelling, failure to adhere to good clinical practices, good pharmacovigilance practices and good manufacturing practices, or the non-compliance with clinical protocols by us or our academic investigators, the presence of other harmful conditions in a clinical trial, inadequacies of product-related information conveyed to physicians or patients, or other factors or circumstances unique to the patient. Whether or not scientifically justified, such unexpected safety or efficacy concerns can arise and it may lead to product recalls, loss of or delays in market acceptance, market withdrawals, or declining sales, as well as product liability, consumer fraud and/or other claims. Additionally, we may be exposed to product liability claims as a result of the administration of the drug candidates to volunteers and patients in clinical trials. Such liability might result from claims made directly by consumers or by life sciences companies or others selling such products. It is impossible to predict the scope of injury or liability from such defects or unexpected reactions, or the impact on the market for such products of any allegations of these claims, even if unsupported, or the measure of damages which might be imposed as a result of any claims or the cost of defending such claims. Substantial damage awards and/or settlements have been handed down – notably in the United States and other common law jurisdictions – against pharmaceutical companies based on claims for injuries allegedly caused by the use of their products. The expenses of litigation or settlements, or both, in connection with any such injuries or alleged injuries and the amount of any award imposed on us in excess of existing insurance coverage, if any, may have a material adverse impact on us and on the price of our common shares. In addition, we may not be able to avoid significant product liability exposure even if we take appropriate precautions, including maintaining product liability coverage (subject to deductibles and maximum payouts) and obtaining indemnification from partners (subject to the terms of each specific agreement). Any liability that we may have as a result could have a material adverse effect on our business, financial condition and results of operations, to the extent insurance coverage for such liability is not available or that our reputation is negatively affected as a result.

***We rely on third parties for the supply and manufacture of our products, which can be unpredictable in terms of quality, cost and availability.***

All of our products are manufactured by third parties. The production of our products also requires raw materials obtained from third parties, and the sources and quantities of such raw materials are limited. Aside from contractual rights and remedies pertaining to our agreements, there can be no assurance that our manufacturers or raw material providers will supply sufficient quantities of our products, the products supplied will meet our quality standards, or that the products supplied will be on commercially acceptable terms. Any delays or deficiencies in the supply of products will affect the marketing and sales of our products and might expose us to financial costs, penalties, lawsuits, product recalls or reputational harm. If we were to seek alternative sources of supply, we may not be able to find alternative supply arrangements with commercially reasonable terms or at all. Also, we have committed under certain licensing and collaboration arrangements to supply third party distributors with product. If we are unable to fulfill such obligations, we may be in breach of the respective arrangements and may face financial penalties, lawsuits or other claims, weakened negotiating position in future third party agreement negotiations or reputational harm.

In addition, our third-party drug, device and chemical manufacturers are subject to various regulatory inspections, including those conducted by the FDA, to ensure strict compliance with good manufacturing practices and other government mandated quality standards regulations. While we are obligated to audit the performance of our third-party contractors, we do not have complete control over their compliance. We could be adversely impacted if our third-party manufacturers do not comply with these standards and regulations. For non-compliance, the regulatory authority may commence enforcement actions, including public warning letters, costly inspections, fines, injunctions, civil penalties, failure of the government to grant review of submissions or market approval of drugs, or cause delays, suspension or withdrawal of approvals, product seizures or recalls, operating restrictions, facility closures and criminal prosecutions. Any of this will have a material adverse impact on our business, financial condition, and results of operations.

Our third parties may also be unable to produce required amounts of chemical, drug, and/or devices at a price that has been agreed upon, or which is commercially viable.

Our third parties may elect to discontinue manufacturing our products. As a result, we may need to enter into new arrangements with alternative third parties that may be costly. The time that it takes us to find alternative third parties may cause an interruption in supplies and we may not be able to fulfill existing or new product orders, which could subject us to contractual claims or adversely affect our business, financial condition or results of operations.

***We rely on our supply chain and the supply chain of third parties to provide our products, and such supply chains may fail due to inadequacies in their systems and processes, in execution, and for unforeseen reasons.***

We rely on our supply chain and the supply chain of third parties to provide our products (and ingredients or components thereof). These supply chains are complex, and may fail for a variety of reasons, including for example, failure to provide adequate quality control and/or quality assurance in supply chain systems and processes, a lack of coordination between various aspects of the supply chain, failure of logistics providers, and inadequate inventory management and/or order management.

In addition, our supply and the supply chain of third parties who provide our products (and ingredients or components thereof) are global in nature, and hence subject to unforeseen problems, including for example, local regulatory risks, currency fluctuations, natural disasters, and economic, social and/or political instability within a particular country or region. If any such supply chain issues occur, we may not be able to fulfill existing or new product orders, which could subject us to contractual claims or adversely affect our business, financial condition or results of operations.

***We rely on third parties for the execution of a significant portion of our regulatory, pharmacovigilance medical information, and logistical responsibilities and such third parties may fail to meet their obligations as a result of inadequacies in their systems and processes or execution failure.***

We rely on third parties to perform critical services, including preclinical testing, clinical trial management, regulatory, pharmacovigilance, medical information and logistical services.

These third parties may not be available on acceptable terms when needed or, if they are available, may not comply with all regulatory and contractual requirements or may not otherwise perform their services in a timely or acceptable manner. This non-compliance may be due to a number of factors, including inadequacies in third-party

systems and processes or execution failure. We may also experience unexpected cost increases that are beyond our control. As a result, we may need to enter into new arrangements with alternative third parties that may be costly. The time that it takes us to find alternative third parties may cause a delay, extension or termination of our preclinical studies, clinical trials or the commercialization of our product candidates and we may incur significant costs to replicate data that may be lost. These third parties may also have relationships with other commercial entities, some of which may compete with us. In addition, if such third parties fail to perform their obligations in compliance with regulatory requirements and our protocols, our preclinical studies or clinical trials may not meet regulatory requirements or may need to be repeated and our regulatory filings, such as our marketing authorizations or NDS, may not be completed correctly or within the applicable deadlines. As a result of our dependence on third parties, we may face delays or failures outside of our direct control in our efforts to develop and commercialize product candidates.

***We rely on third party distributors in many markets to market and sell our products and such third parties may fail to meet their obligations.***

We rely on third party distributors to market and sell our products in many markets. These distributors may not comply with all regulatory and contractual requirements or may not otherwise perform their services in a timely or acceptable manner. These distributors may not meet the minimum contractual sales requirement or the minimum sales target mutually agreed upon by both parties. The inability to meet minimum sales requirement or sales target may be due to a number of factors, including inadequate resources devoted to sell our products or failure in the distributor's sales efforts. The distributors may be responsible for negotiating reimbursements from third party payers for the cost of our products. If our distributors cannot achieve acceptable profit margins on our products, they may reduce or discontinue the sale of our products. As a result of our dependence on third party distributors, our revenues may not meet expectations and our business, results of operations and financial condition may be adversely affected.

***Government legislation could adversely impact our ability to obtain product reimbursement and economically price our products and may be difficult to interpret or comply with, resulting in additional costs to conduct our business in certain countries.***

In many of the markets we sell to, sales of healthcare products are dependent in part on the availability of reimbursement to the consumer from third party payors, such as government and private insurance plans. Third party payors are increasingly challenging the effectiveness of, and prices charged for, medical products and services, and therefore uncertainty exists as to the reimbursement of existing and newly approved healthcare products. The prices of our products are subject to direct price controls by law and to drug reimbursement programs with varying price control mechanisms.

In addition, as drug costs have increased, there have been more cost containment measures taken by government and third-party private payors, including limitations on both the number of products they list for reimbursements, the conditions under which they will reimburse, and the reimbursement drug prices. For example, we are seeking, but have not yet received reimbursement for BRINAVESS<sup>TM</sup> in several major European markets, including Italy, the United Kingdom and France. There can be no assurance that we will be reimbursed or receive commercially viable pricing. Also, the current conditions and rules relating to the listing submissions to public and private formulary listings may change or become more onerous in the future. If we fail to achieve the listing of our products, it will affect the physicians' decisions regarding the use of our products.

New and existing government legislation in the markets in which we sell or anticipate selling our products may also be difficult to interpret or comply with. Such difficulties may cause slower product introductions in new countries or the termination of sales of our products in existing countries. Violations of any such legislation may lead to financial penalties, product bans or claims brought by regulatory agencies or local or national governments, all of which would have adverse effects on our business, results of operations and financial condition.

***Compulsory licensing and/or generic competition may affect our business in certain countries.***

In a number of countries, governmental authorities and other groups have suggested that companies which manufacture medical products (e.g., pharmaceuticals) should make products available at a low cost. In some cases, governmental authorities have held that where a pharmaceutical company does not do so, its patents might not be enforceable to prevent generic competition. Alternatively, some governmental authorities could require that we grant compulsory licenses to allow competitors to manufacture and sell their own versions of our products, thereby

reducing our sales or the sales of our licensee(s). In all of these situations, the results of our operations in these countries could be adversely affected.

***If we are not able to convince public payors and hospitals to include our products on their approved formulary lists, our revenues may not meet expectations and our business, results of operations and financial condition may be adversely affected.***

Hospitals establish formularies, which are lists of drugs approved for use in the hospital. If a drug is not included on the hospital's formulary, the ability of our distribution partners and key account managers to promote and sell our drugs may be limited or denied. If we fail to secure and maintain formulary inclusion for our drugs on favorable terms or are significantly delayed in doing so, we may have difficulty achieving market acceptance of our drugs and our business, results of operations and financial condition could be materially adversely affected.

***Our hospital customers may be late in their payments and in some cases may not pay monies owed.***

Hospital customers that may purchase our products and product candidates, if approved, generally bill public payors to cover all or a portion of the costs and fees associated with these purchases. Our revenue and financial condition depend on the extent to which our customers are reimbursed for these costs and fees, and the extent to which such payments are made to us according to the timelines required by our contracts or general terms and conditions. Such payments may be delayed or withheld for many reasons, including, but not limited to, regulatory requirements of local and national governments, reimbursement requirements of public payors, the financial condition or access to capital of our customers and public payors or the deterioration of general or local economic conditions. The non-payment or late payment of amounts due from our customers and public payors may impact the timing of receipt of cash, or we may not receive the cash at all which would negatively impact our financial condition. In addition, we may have to increase our allowance for doubtful accounts or write-off accounts receivable, which would also negatively impact our financial position and results of operations. If collectability is not reasonably assured at the time of sale, we may not be able to recognize revenue until cash is collected which would make it difficult to forecast our revenues accurately. We may, as a result, experience significant unanticipated fluctuations in our revenues from period to period. Any failure to achieve anticipated revenues in a period may also cause our stock price to decline.

In addition, many European countries have been severely impacted by the widespread economic recession that began in 2008, the effect of which continued in 2016. Conditions such as a tighter credit environment, declining business and consumer confidence, as well as increased unemployment have contributed to the economic volatility in these regions. As a result of the continued turbulence in Europe, account collection from hospitals in certain regions takes longer now than in the past. Any delay in collection or an inability to collect could have a material adverse effect on our business, financial condition and results of operations.

***Our business may be materially adversely affected by new legislation, new regulatory requirements, and the continuing efforts of governmental and third party payors to contain or reduce the costs of healthcare through various means.***

The government and regulatory authorities in the United States, and in Europe and other markets in which we sell our products may propose and adopt new legislation and regulatory requirements relating to pharmaceutical approval criteria and manufacturing requirements. Such legislation or regulatory requirements, or the failure to comply with such, could adversely impact our operations and could have a material adverse effect on our business, financial condition and results of operations.

In recent years, national, federal, provincial, state, and local officials and legislators have proposed, or are reportedly considering proposing, a variety of price based reforms to the healthcare systems in the European Union, the United States and other countries. Some proposals include measures that would limit or eliminate payments for certain medical procedures and treatments or subject the pricing of pharmaceuticals to government control. Furthermore, in certain foreign markets, the pricing or profitability of healthcare products is subject to government controls and other measures that have been prepared by legislators and government officials. While we cannot predict whether any such legislative or regulatory proposals or reforms will be adopted, the adoption of any such proposals or reforms could adversely affect the commercial viability of our existing and potential products. Significant changes in the healthcare system in the European Union and other countries may have a substantial impact on the manner in which we conduct our business. Such changes could also have a material adverse effect on our business, financial condition and results of operations.

***We rely on proprietary technology, the protection of which can be unpredictable and costly.***

Our success depends in part upon our ability to obtain patent protection or patent licenses for our technology and products. Obtaining such patent protection or patent licenses can be costly and the outcome of any such application for patent protection and patent licenses can be unpredictable.

Our patent portfolio related to vernakalant contains issued United States and European patents (as well as other patents issued worldwide) with composition of matter claims specific to vernakalant and/or claims specific to the use of vernakalant to treat arrhythmia. Our patent portfolio related to tirofiban hydrochloride is much more limited, in that most of our patents related to the compound in a formulation have already expired or will be expiring within the next few years. We will not have any patent protection on tirofiban hydrochloride once all of the patents expire.

It is impossible to anticipate the breadth or degree of protection that patents will afford products developed by us or their underlying technology. Further, countries in which we sell our products may not protect our intellectual property to the same extent as the laws of Europe or the United States, and may lack rules and procedures required for defending our patents. Third parties may attempt to circumvent our patents by means of alternative designs and processes. Third parties may also independently develop similar products, duplicate any of our products not under patent protection, or design around the inventions we claim in any of our existing patents, existing patent applications or future patents or patent applications. There is a risk that any patents issued relating to our products or any patents licensed to us may be successfully challenged or that the practice of our products might infringe the patents of third parties. If the practice of our products infringes the patents of third parties, we may be required to design around such patents, potentially causing increased costs and delays in product development and introduction or precluding us from developing, manufacturing or selling our planned products. In addition, disputes may arise as to the rights to know-how and inventions among our employees and consultants who use intellectual property owned by others for the work performed for our company. The scope and validity of patents which may be obtained by third parties, the extent to which we may wish or need to obtain patent licenses, and the cost and availability of such licenses are currently unknown. If such licenses are obtained, it is likely they would be royalty bearing, which could reduce our income. If licenses cannot be obtained on an economical basis, delays in market introduction of our planned products could occur or introduction could be prevented, in some cases causing the expenditure of substantial funds. If we defend or contest the validity of patents relating to our products or technology or the products or technology of a third party, we could incur substantial legal expenses with no assurance of success.

In certain instances, we may elect not to seek patent protection but instead rely on the protection of our technology through confidentiality agreements or trade secrets. The value of our assets could also be reduced to the extent that third parties are able to obtain patent protection with respect to aspects of our technology or products or that confidential measures we have in place to protect our proprietary technology are breached or become unenforceable. However, third parties may independently develop or obtain similar technology and such third parties may be able to market competing products and obtain regulatory approval through a showing of equivalency to one of our products which has obtained regulatory approval, without being required to undertake the same lengthy and expensive clinical studies that we would have already completed.

Litigation may also be necessary to enforce patents issued or licensed to us or to determine the scope and validity of a third party's proprietary rights. We could incur substantial costs if we are required to defend ourselves in patent suits brought by third parties, if we participate in patent suits brought against or initiated by our corporate collaborators or if we initiate such suits. We may not have the necessary resources to participate in or defend any such activities or litigation. Even if we did have the resources to vigorously pursue our interests in litigation, because of the complexity of the subject matter, it is impossible to predict whether we would prevail in any such action. An adverse outcome in litigation or an interference to determine priority or other proceeding in a court or patent or selling office could subject us to significant liabilities, require disputed rights to be licensed from third parties or require us to cease using certain technology or products, any of which may have a material adverse effect on our business, financial condition and results of operations.

***There may be an unauthorized disclosure of a significant amount of confidential information under our control.***

We maintain and manage personal information obtained from our customers, as well as confidential information relating to our technology, research and development, production, marketing and business operations and those of our customers and collaborators, in various forms. Although we have implemented controls to protect the confidentiality of such information, there can be no assurance that such controls will be effective. Unauthorized

disclosures of such information could subject us to complaints or lawsuits for damages or could otherwise have a negative impact on our business, financial condition, results of operations, reputation and credibility.

***Clinical trials for our product candidates are expensive and time-consuming, and their outcome is uncertain.***

Before we or our partners can obtain regulatory approval for the commercial sale of any product candidate currently under development, we are required to complete extensive clinical trials to demonstrate its safety and efficacy. Clinical trials are very expensive and difficult to design and implement. The clinical trial process is also time-consuming. The ACT 5 trial for vernakalant (IV) was terminated following a single unexpected serious adverse event of cardiogenic shock experienced by a patient in the study and the development program is currently on clinical hold in the United States. If the FDA removes the clinical hold in the United States and allows us to initiate clinical trials, the proposed scope and duration of the vernakalant (IV) clinical program required to obtain regulatory approval must be agreed to by the FDA. Even if we are able to restart the development program, there can be no assurance that the trials will be feasible or successful. Clinical trials, including the post approval safety study for vernakalant (IV), may be subject to significant delays and their outcome may be negatively affected due to various causes, including:

- our inability to find collaboration partners;
- our inability to manufacture or obtain sufficient quantities of materials for use in clinical trials;
- delays in obtaining regulatory approvals to commence a study, or government intervention to suspend or terminate a study;
- delays, suspension, or termination of the clinical trials imposed by the institutional review board or independent ethics board responsible for overseeing the study to protect research subjects at a particular study site;
- delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;
- slower than expected rates of patient recruitment and enrollment;
- uncertain dosing issues;
- inability or unwillingness of medical investigators to follow our clinical protocols;
- variability in the number and types of subjects available for each study and resulting difficulties in identifying and enrolling subjects who meet trial eligibility criteria;
- delays in enrolling patients in the trial;
- scheduling conflicts with participating clinicians and clinical institutions;
- difficulty in maintaining contact with subjects after treatment, which results in incomplete data;
- unforeseen safety issues or side effects;
- lack of efficacy during the clinical trials;
- our reliance on clinical research organizations to conduct clinical trials, which may not conduct those trials with good clinical or laboratory practices; or
- other regulatory delays.

***The results of pre-clinical studies and initial clinical trials are not necessarily predictive of future results, and our current product candidates may not have favourable results in later trials or in the commercial setting.***

Pre-clinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in pre-clinical or animal studies and early clinical trials does not ensure that later large scale efficacy trials will be successful nor does it predict final results. Favourable results in early trials may not be repeated in later trials.

A number of companies in the life sciences industry, including Cardiome, have suffered significant setbacks in advanced clinical trials, even after positive results in earlier trials. Clinical results are frequently susceptible to

varying interpretations that may delay, limit or prevent regulatory approvals. Negative or inconclusive results or adverse medical events during a clinical trial could cause a clinical trial to be delayed, repeated or terminated. In addition, failure to construct appropriate clinical trial protocols could result in the test or control group experiencing a disproportionate number of adverse events and could cause a clinical trial to be repeated or terminated. Additionally, sizing of a trial is based on previous experience of response rates in the control group to vernakalant. Failure to accurately predict event rates may lead to a clinical trial being inadequately powered resulting in an insignificant result. Pre-clinical data and the clinical results we have obtained for vernakalant (IV) and other products may not predict results from studies in larger numbers of subjects drawn from more diverse populations or in a commercial setting, and also may not predict the ability of our products to achieve their intended goals, or to do so safely.

If vernakalant (IV) fails to demonstrate sufficient safety and efficacy in ongoing or future clinical trials, we could experience potentially significant delays in, or be required to abandon development of, our product candidates currently under development.

In October 2010, we announced that patient enrollment in the ACT 5 study of vernakalant (IV) had been suspended and the vernakalant (IV) clinical development program had been placed on clinical hold by the FDA following a single unexpected serious adverse event of cardiogenic shock experienced by a patient with atrial fibrillation who received vernakalant (IV). We are continuing discussions with the FDA regarding the potential path for vernakalant (IV) in the United States; however, we have yet to reach agreement with the FDA. Until such time that we reach a resolution, vernakalant (IV) remains on clinical hold. In the event that we are unable to agree on an executable and mutually acceptable development path, vernakalant (IV) will not receive marketing approval in the United States.

***Our industry is subject to health and safety risks.***

We produce products for human ingestion. While we take substantial precautions such as laboratory and clinical testing, toxicology studies, quality control and assurance testing and controlled production methods, the associated health and safety risks cannot be eliminated. Products produced by us may be found to be, or to contain substances that are harmful to the health of our patients and customers and which, in extreme cases, may cause serious health conditions or death. This sort of finding may expose us to substantial risk of litigation and liability.

Further, we could be forced to discontinue production of certain products, which would harm our profitability. Cardiome maintains product liability insurance coverage; however, there is no guarantee that our current coverage will be sufficient or that we can secure insurance coverage in the future at commercially viable rates or with the appropriate limits and could have a significant adverse effect on our reputation.

***Our approved products may not achieve or maintain expected levels of market acceptance.***

Even if we are able to obtain regulatory approvals for our product candidates, the success of those products is dependent upon achieving and maintaining market acceptance. New product candidates that appear promising in development may fail to reach the market or may have only limited or no commercial success. Levels of market acceptance for our products could be impacted by several factors, many of which are not within our control, including but not limited to:

- safety, efficacy, convenience and cost-effectiveness of our products compared to products of our competitors;
- scope of approved uses and marketing approval;
- timing of market approvals and market entry;
- difficulty in, or excessive costs to, manufacture;
- infringement or alleged infringement of the patents or intellectual property rights of others;
- availability of alternative products from our competitors;
- acceptance of the price of our products; and
- ability to market our products effectively at the retail level.

In addition, the success of any new product will depend on our ability to either successfully build our in-house sales capabilities or to secure new, or to realize the benefits of existing, arrangements with third-party marketing or

distribution partners. Seeking out, evaluating and negotiating marketing or distribution agreements may involve the commitment of substantial time and effort and may not ultimately result in an agreement. In addition, the third-party marketing or distribution partners may not be as successful in promoting our products as we had anticipated. If we are unable to commercialize new products successfully, whether through a failure to achieve market acceptance, a failure to build our own in-house sales capabilities, a failure to secure new marketing partners or to realize the benefits of our arrangements with existing marketing partners, there may be a material adverse effect on our business, financial condition and results of operations and it could cause the market value of our common shares to decline.

In addition, by the time any products are ready to be commercialized, what we believe to be the market for these products may have changed. Our estimates of the number of patients who have received or might have been candidates to use a specific product may not accurately reflect the true market or market prices for such products or the extent to which such products, if successfully developed, will actually be used by patients. Our failure to successfully introduce and market our products that are under development would have a material adverse effect on our business, financial condition, and results of operations.

***We are dependent upon our key personnel to achieve our business objectives.***

As a technology-driven company, intellectual input from key management and personnel is critical to achieve our business objectives. Consequently, our ability to retain these individuals and attract other qualified individuals is critical to our success. The loss of the services of key individuals might significantly delay or prevent achievement of our business objectives. In addition, because of a relative scarcity of individuals with the high degree of education and scientific achievement required for our business, competition among life sciences companies for qualified employees is intense and, as a result, we may not be able to attract and retain such individuals on acceptable terms, or at all. In addition, because we do not maintain “key person” life insurance on any of our officers, employees, or consultants, any delay in replacing such persons, or an inability to replace them with persons of similar expertise, would have a material adverse effect on our business, financial condition, and results of operations.

We also have relationships with scientific collaborators at academic and other institutions, some of whom conduct research at our request or assist us in formulating our research and development strategies. These scientific collaborators are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, even though our collaborators are required to sign confidentiality agreements prior to working with us, they may have arrangements with other companies to assist such other companies in developing technologies that may prove competitive to us.

Incentive provisions for our key executives include the granting of stock options that vest over time, designed to encourage such individuals to stay with us. However, a low share price, whether as a result of disappointing progress in our sales or development programs or as a result of market conditions generally, could render such agreements of little value to our key executives. In such event, our key executives could be susceptible to being hired away by our competitors who could offer a better compensation package. If we are unable to attract and retain key personnel our business, financial conditions and results of operations may be adversely affected.

***We are exposed to concentration of credit risk relating to major distribution relationships and customers in certain geographic regions.***

We have distribution contracts with certain third parties that contribute to a significant portion of our revenue. Due to the concentration of sales and receivables in these certain distributors, the credit risk associated with these accounts are of particular significance to us. If one or several of these distributors fails to fulfill its payment obligations or reduces their business with us, there may be a material adverse effect on our business, financial condition and results of operations.

***Our policies and estimates regarding returns, allowances and chargebacks may reduce revenue in future periods.***

Reserves on sales are calculated based on prior experience and best estimates of the impact in subsequent period in accordance with our established policy. We cannot ensure that the adequacy of the reserves or actual product returns, allowances and chargebacks will not exceed the estimates. Inadequate reserves could have a material adverse effect on our business, financial condition, and results of operations.

***Our inventory has a limited shelf life and may require write-downs.***

We value inventory for accounting purposes at the lower of cost determined on a first-in, first-out basis, and net realizable value. For inventory which has reached its expiration or that is close to expiration and not expected to be sold, we establish the associated reserve to reflect such inventory cost as it is not expected to be recoverable. Even though on a regular basis, management reviews the amount of inventory on hand, reviews the remaining shelf life and estimates the time required to manufacture and sell such inventory, write-down of inventory may still be required. Any write-down could have a material adverse effect on our business, financial condition, and results of operations.

***We are exposed to risks relating to the write-down of intangible assets, which comprises of a significant portion of our total assets.***

A significant amount of our total assets relate to our marketing rights, trade name and patents associated with BRINAVESS™, AGGRASTAT® and XYDALBA™. As of December 31, 2016, the carrying value of our intangible assets was approximately \$24.4 million. In accordance with U.S. generally accepted accounting principles, we are required to review the carrying value of our intangible assets for impairment periodically or when certain triggers occur. In case of events such as generic competition, our inability to manufacture, or our inability to obtain sufficient raw materials, sales of the related product may decline and impairment in the carrying value of the intangible asset may have occurred. Such impairment will result in a write-down of the intangible asset and the write-down is charged to earnings during the period in which the impairment occurs. The write-down of any intangible assets could have a material adverse effect on our business, financial condition, and results of operations.

***We may face exposure to adverse movements in foreign currency exchange rates.***

Our loans and a portion of our revenue are denominated in U.S. dollars. However, our business has expanded internationally and, as a result, a significant portion of our revenues and expenses are denominated in Euros, Canadian dollars and other foreign currencies. A decrease in the value of such foreign currencies relative to the U.S. dollar could result in losses from currency exchange rate fluctuations. To date, we have not hedged against risks associated with foreign exchange rate exposure. We cannot be sure that any hedging techniques we may implement in the future will be successful or that our business, financial condition, and results of operations will not be materially adversely affected by exchange rate fluctuations.

***If we were to lose our foreign private issuer status under United States federal securities laws, we would likely incur additional expenses associated with compliance with the United States securities laws applicable to United States domestic issuers.***

As a foreign private issuer, as defined in Rule 3b-4 under the U.S. Securities Exchange Act of 1934, as amended, we are exempt from certain of the provisions of the United States federal securities laws. For example, the United States proxy rules and the Section 16 reporting and “short swing” profit rules do not apply to foreign private issuers. However, if we were to lose our status as a foreign private issuer, these regulations would immediately apply and we would also be required to commence reporting on forms required of United States companies, such as Forms 10-K, 10-Q and 8-K, rather than the forms currently available to us, such as Forms 40-F and 6-K. Compliance with these additional disclosure and timing requirements under these securities laws would likely result in increased expenses and would require our management to devote substantial time and resources to comply with new regulatory requirements. Further, to the extent that we were to offer or sell our securities outside of the United States, we would have to comply with the more restrictive Regulation S requirements under the U.S. Securities Act of 1933, as amended (the “Securities Act”), that apply to U.S. companies, and we would no longer be able to utilize the multijurisdictional disclosure system forms for registered offerings by Canadian companies in the United States, which could limit our ability to access the capital markets in the future.

***We are subject to risks inherent in foreign operations.***

We intend to continue to pursue international market growth opportunities, such that international sales are likely to continue, at least in the near future, to account for a significant portion of our revenue. We have committed, and intend to commit, significant resources to our international sales and marketing activities. We are subject to a number of risks associated with our international business operations and sales and marketing activities that may increase liability, costs, lengthen sales cycles and require significant management attention. These risks include:

- compliance with the laws of the United States, Canada, Europe and other countries that apply to our international operations, including import and export legislation;

- increased reliance on third parties to establish and maintain foreign operations;
- the complexities and expenses of administering a business abroad;
- complications in compliance with, and unexpected changes in, foreign regulatory requirements;
- instability in economic or political conditions, including inflation, recession and actual or anticipated military conflicts, social upheaval or political uncertainty;
- foreign currency fluctuations;
- foreign exchange controls and cash repatriation restrictions;
- tariffs and other trade barriers;
- difficulties in collecting accounts receivable;
- differing tax structures and related potential adverse tax consequences;
- uncertainties of laws and enforcement relating to the protection of intellectual property or secured technology;
- litigation in foreign court systems;
- unauthorized copying or use of our intellectual property;
- cultural and language differences;
- difficulty in managing a geographically dispersed workforce in compliance with local laws and customs that vary from country to country; and
- other factors, depending upon the country involved.

There can be no assurance that the policies and procedures we implement to address or mitigate these risks will be successful, that our personnel will comply with them or that we will not experience these factors in the future or that they will not have a material adverse effect on our business, results of operations and financial condition.

***There are uncertainties with respect to data protection laws in Europe.***

From 1998 to 2000, “Safe Harbour Privacy Principles” were developed in order to prevent private organizations within the European Union or the United States, which store customer data, from accidentally disclosing or losing customer information. In July 2000, the European Commission decided that U.S. companies complying with these principles and which met European Union requirements would fall under the Safe Harbour Privacy Principles.

In October 2015, the Court of Justice for the European Union nullified the Safe Harbor Privacy Principles. In early 2016, German authorities initiated legal proceedings against several companies that were still transferring personal data to the United States under the now invalidated Safe Harbor Privacy Principles. On February 29, 2016, the European Commission unveiled new legal texts which, if approved, would create the EU–U.S. Privacy Shield, which will impose stronger obligations on companies in the United States to protect the personal data of Europeans and stronger monitoring and enforcement by the U.S. Department of Commerce and Federal Trade Commission. These new legal texts are still subject to public comment, and have not been enacted.

Cardiome is headquartered in Vancouver, Canada, and has offices in many European countries, as well as an office in the United States. Given the uncertainty associated with the current legal environment for data protection in Europe, it is possible that, despite best efforts, we or any of our third-party distributors, suppliers, manufacturers or regulatory service providers might run afoul of currently developing laws associated with data privacy in Europe. Violations of such laws might subject us to lawsuits, fines, penalties or injunctions that could negatively affect our business, financial condition or results of operations.

***Failure to comply with the FCPA, as well as the anti-bribery laws of the nations in which we conduct business (such as the United Kingdom’s Bribery Act or the CFPOA, could subject us to penalties and other adverse consequences.***

Our business is subject to the FCPA which generally prohibits companies and company employees from engaging in bribery or other prohibited payments to foreign officials for the purpose of obtaining or retaining business. The

FCPA also requires companies to maintain accurate books and records and internal controls, including at foreign-controlled subsidiaries. In addition, we are subject to other anti-bribery laws of the nations in which we conduct business that apply similar prohibitions as the FCPA (e.g. the United Kingdom's Bribery Act, the CFPOA and the Organization for Economic Co-operation and Development Anti-Bribery Convention). Our employees or other agents may, without our knowledge and despite our efforts, engage in prohibited conduct under our policies and procedures and the FCPA or other anti-bribery laws that we may be subject to for which we may be held responsible. If our employees or other agents are found to have engaged in such practices, we could suffer severe penalties and other consequences that may have a material adverse effect on our business, financial condition and results of operations.

***Legislative actions, potential new accounting pronouncements, and higher insurance costs are likely to impact our future financial position or results of operations.***

Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with greater frequency and are expected to occur in the future. Compliance with changing regulations of corporate governance and public disclosure may result in additional expenses. All of these uncertainties are leading generally toward increasing insurance costs, which may adversely affect our business, results of operations and our ability to purchase any such insurance, at acceptable rates or at all, in the future.

***Our product candidates are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays, or prevent the receipt of the required approvals to commercialize products.***

The pre-clinical and clinical trials of any products developed by us or our future collaborative partners, if any, and the manufacturing, labelling, sale, distribution, export or import, marketing, advertising and promotion of any of those products are subject to regulation by federal, provincial, state and local governmental authorities. Our product candidates are principally regulated in the United States by the FDA, in Canada by the TPD, in the European Union by the EMA, and by other similar regulatory authorities in other jurisdictions. Government regulation substantially increases the cost and risk of researching, developing, manufacturing and selling products. Following several widely publicized issues in recent years, the FDA and similar regulatory authorities in other jurisdictions have become increasingly focused on product safety. This development has led to requests for more clinical trial data, for the inclusion of a significantly higher number of patients in clinical trials and for more detailed analysis of trial results. Consequently, the process of obtaining regulatory approvals, particularly from the FDA, has become more costly, time consuming and challenging than in the past. Any product developed by us or our future collaborative partners, if any, must receive all relevant regulatory approvals or clearances from the applicable regulatory authorities before it may be marketed and sold in a particular country.

In connection with our pre-clinical studies and clinical trials for vernakalant (IV) and other product candidates, we are required to adhere to extensive regulations established by the applicable regulatory authorities. In general, these regulatory authorities and the regulatory process require us to conduct extensive pre-clinical studies and clinical trials of each of our product candidates in order to establish its safety and efficacy. These pre-clinical studies and clinical trials can take many years, are highly uncertain, and require the expenditure of substantial resources. We, or our future collaborative partner, if any, must obtain and maintain regulatory authorization to conduct clinical trials. Our pre-clinical research is subject to good laboratory practice and other requirements, and our clinical research is subject to good clinical practice and other requirements. Failure to adhere to these requirements could invalidate our data. In addition, the relevant regulatory authority or independent review board may modify, suspend or terminate a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the benefits.

In addition to the risk of unfavourable results of our research, because the data obtained from our pre-clinical and clinical activities are susceptible to varying interpretations, our successful completion of the regulatory process is uncertain. We may encounter delays, such as refusals from regulatory authorities to accept our marketing applications for review. We may have limits imposed on us, or clinical trials or our product candidates. Unfavourable results from our clinical data may require us to limit the indications sought in connection with the product candidate or otherwise limit our ability to obtain the regulatory approval required from the applicable regulatory authorities to commercialize our product candidates. In addition, delays or rejections may be encountered based upon changes in regulatory policy or views during the period of product marketing, product development or the period of review of any application for regulatory approval or clearance for a product. Delays in obtaining regulatory approvals would adversely affect the marketing of any products developed by us, impose significant additional costs on us, diminish any competitive advantages that we may otherwise have attained and adversely

affect our ability to receive royalties and generate revenues and profits. Accordingly, despite our expenditures and investment of time and effort, we may be unable to receive required regulatory approvals for product candidates developed by us.

We are also subject to numerous federal, provincial, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, the environment and the use and disposal of hazardous substances used in connection with our discovery, research and development work. Although we have not yet been required to expend identifiable additional resources to comply with these regulations, the extent of government regulations may change in a manner which could have an adverse effect on the discovery, development, production, manufacturing, sales, marketing and distribution of our products, and we may be required to incur significant additional costs to comply with future laws or regulations. We cannot predict whether or not regulatory approvals will be obtained for the products we develop or, in the case of products that have been approved in one or more jurisdictions, that those products will be approved in other jurisdictions as well. Compounds developed by us, alone or with other parties, may not prove to be safe and effective in clinical trials and may not meet all of the applicable regulatory requirements needed to receive marketing approval.

Administering any of our product candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our product candidates and could result in the applicable regulatory authorities denying approval of our product candidates for any or all of the targeted indications. If regulatory approval for a product is granted, the approval will be limited to those disease states and conditions for which the product is demonstrated through clinical trials to be safe and effective, and any approval granted may be too narrow to be commercially viable.

***Any of our product candidates that receive regulatory approval could be subject to extensive post-market obligations that can affect sales, marketing and profitability.***

With respect to any drug candidates for which we obtain regulatory approval, we will be subject to post-marketing regulatory obligations, including the requirements by the FDA, TPD, EMA and similar agencies in other jurisdictions to maintain records regarding product safety and to report to regulatory authorities serious or unexpected adverse events. Any post-approval commitments required by the regulatory agencies as a condition of approval, such as registration studies, may not be feasible. The occurrence of unanticipated serious adverse events or other safety problems could cause the governing agencies to impose significant restrictions on the indicated uses for which the product may be marketed, impose other restrictions on the distribution or sale of the product or require potentially costly post-approval studies. In addition, post-market discovery of previously unknown safety problems or increased severity or significance of a pre-existing safety signal could result in withdrawal of the product from the market and product recalls. Compliance with extensive post-marketing record keeping and reporting requirements requires a significant commitment of time and funds, which may limit our ability to successfully commercialize approved products.

In addition, manufacturing of approved drug products must comply with extensive regulations governing current good manufacturing practices. Manufacturers and their facilities are subject to continual review and periodic inspections. Failure to comply with good manufacturing practices requirements could result in a suspension of manufacturing, product recalls or even withdrawals from the market. As we will be dependent on third parties for manufacturing, we will have limited ability to ensure that any entity manufacturing products on our behalf is doing so in compliance with applicable good manufacturing practices requirements. Failure or delay by any manufacturer of our products to comply with good manufacturing practices regulations or to satisfy regulatory inspections could have a material adverse effect on us, including potentially preventing us from being able to supply products for clinical trials or commercial sales. In addition, manufacturers may need to obtain approval from regulatory authorities for product, manufacturing, or labelling changes, which requires time and money to obtain and can cause delays in product availability. We are also required to comply with good distribution practices such as maintenance of storage and shipping conditions, as well as security of products, in order to ensure product quality determined by good manufacturing practices is maintained throughout the distribution network. In addition, we are subject to regulations governing the import and export of our products.

Sales and marketing of pharmaceutical products are subject to extensive federal and state laws governing on-label and off-label advertising, scientific/educational grants, gifts, consulting and pricing. Sales, marketing and pricing activities are also potentially subject to federal and state consumer protection and unfair competition laws. Compliance with extensive regulatory requirements requires training and monitoring of the sales force, which imposes a substantial cost on us and our collaborators. To the extent our products are marketed by our collaborators,

our ability to ensure their compliance with applicable regulations will be limited. In addition, we are subject to regulations governing the design, testing, control, manufacturing, distribution, labeling, quality assurance, packaging, storage, shipping, import and export of our products and product candidates. Failure to comply with applicable legal and regulatory requirements may result in negative consequences to us, including but not limited to:

- issuance of warning letters by the FDA or other regulatory authorities;
- fines and other civil penalties;
- criminal prosecutions;
- injunctions, suspensions or revocations of marketing licenses;
- suspension of any ongoing clinical trials;
- suspension of manufacturing;
- delays in commercialization;
- refusal by the FDA or other regulators to approve pending applications or supplements to approved applications filed by us or our collaborators;
- refusals to permit products to be imported or exported to or from the United States, Europe or Canada;
- restrictions on operations, including costly new manufacturing requirements; and
- product recalls or seizures.

In the future, the regulatory climate might change due to changes in the FDA and other regulatory authorities' staffing, policies or regulations and such changes could impose additional post-marketing obligations or restrictions and related costs. While it is impossible to predict future legislative or administrative action, if we are not able to maintain regulatory compliance, we will not be able to market our drugs and our business could suffer.

***Obtaining regulatory approval in the European Union does not ensure we will obtain regulatory approval in other countries.***

We aim to obtain regulatory approval for our drug candidates in the United States and the European Union, as well as in other countries. To obtain regulatory approval to market any FDA or EMA approved products outside of the United States or European Union, as the case may be, we must comply with numerous and varying regulatory requirements in other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA or EMA approval. The regulatory approval process in other countries may include all of the risks associated with FDA or EMA approval as well as additional, presently unanticipated risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects associated with regulatory approval in the United States or the European Union, including the risk that our product candidates may not be approved for all indications requested or that such approval may be subject to limitations on the indicated uses for which the product may be marketed. In addition, any approved products will be subject to post-marketing regulations related to manufacturing standards, facility and product inspections, labelling and possibly sales and marketing.

Failure to comply with applicable regulatory requirements in other countries can result in, among other things, warning letters, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, refusal of the government to renew marketing applications or criminal prosecution.

***Our business depends heavily on the use of information technologies.***

Several key areas of our business depend on the use of information technologies, including sales and marketing, production, manufacturing and logistics, as well as clinical and regulatory matters. Despite our best efforts to prevent such behaviour, third parties may nonetheless attempt to hack into our systems and obtain data relating to our pre-clinical studies, clinical trials, patients using our products or our proprietary information on BRINAVESS<sup>™</sup>, AGGRASTAT<sup>®</sup>, XYDALBA<sup>™</sup> or any of our other products. If we fail to maintain or protect our information

systems and data integrity effectively, we could lose existing customers, have difficulty attracting new customers, have problems in determining product cost estimates and establishing appropriate pricing, have difficulty preventing, detecting, and controlling fraud, have disputes with customers, physicians, and other health care professionals, have regulatory sanctions or penalties imposed, have increases in operating expenses, incur expenses or lose revenues as a result of a data privacy breach, or suffer other adverse consequences. While we have invested in the protection of data and information technology, there can be no assurance that our efforts, or those of our third-party collaborators, if any, or manufacturers, to implement adequate security and quality measures for data processing would be sufficient to protect against data deterioration or loss in the event of a system malfunction, or to prevent data from being stolen or corrupted in the event of a security breach. Any such loss or breach could have a material adverse effect on our business, operating results and financial condition.

## **DIVIDENDS AND DISTRIBUTIONS**

We have never declared or paid any dividends on our common shares. Subject to the discretion of our board of directors to declare a dividend, we expect that, for the foreseeable future, to retain our future earnings, if any, to finance our commercial activities and further research and the expansion of our business. The payment of future dividends, if any, will be subject to the discretion of our board of directors and will depend upon, among other things, conditions then existing including earnings, financial conditions, cash on hand, financial requirements to fund our commercial activities, development and growth, and other factors that our board of directors may consider appropriate in the circumstances.

## **CAPITAL STRUCTURE**

Our authorized share capital consists of an unlimited number of common shares and an unlimited number of preferred shares, issuable in series, of which, Series A Preferred Shares have been assigned special rights and restrictions. As of March 27, 2017, we had 31,913,172 common shares and no preferred shares of any series issued and outstanding. In addition, as of March 27, 2017, there were 2,986,197 common shares issuable upon the exercise of outstanding stock options at a weighted-average exercise price of Cdn.\$5.25 per common share and 1,002,950 common shares reserved for future grant or issuance under our 2014 Incentive Stock Option Plan (the "Incentive Stock Option Plan"). There are also 124,852 common shares issuable upon the vesting of restricted share units ("RSUs") of the Company.

All of our common shares are of the same class and, once issued, rank equally as to entitlement to dividends (if, as and when declared by the board of directors), voting powers (one vote per common share) and participation in assets upon dissolution, liquidation or winding-up. No common shares have been issued subject to call or assessment. Our common shares contain no pre-emptive or conversion rights and have no provisions for redemption or purchase for cancellation, surrender, or sinking or purchase funds. Provisions as to the modification, amendment or variation of such rights or provisions are contained in our articles and by-laws and in the CBCA.

We may issue our preferred shares from time to time in one or more series. The terms of each series of preferred shares, including the number of shares, the designation, rights, preferences, privileges, priorities, restrictions, conditions and limitations, will be determined at the time of creation of each such series by our board of directors, without shareholder approval, provided that all preferred shares will rank equally within their class as to dividends and distributions in the event of our dissolution, liquidation or winding-up.

Our by-laws provide that at any meeting of our shareholders a quorum shall be shareholders present in person or represented by proxy holding shares representing not less than 20% of the votes entitled to be cast at the meeting. If there is only one shareholder, the quorum is one person present and being, or representing by proxy, such shareholder. The listing standards of the NASDAQ, require a quorum for shareholder meetings to be not less than 33⅓% of a corporation's outstanding voting shares. As a foreign private issuer and because our quorum requirements are consistent with generally accepted business practices in Canada, our country of domicile, we have been exempted from the NASDAQ quorum requirement.

## MARKET FOR SECURITIES

Our common shares are listed on the TSX in Canada (trading symbol: “COM”) and on the NASDAQ in the United States (trading symbol: “CRME”).

The following table sets forth, for the periods indicated, the reported high and low prices (in Canadian dollars) and volume of our common shares traded on the TSX:

<u>Month</u>	<u>High</u>	<u>Low</u>	<u>Close</u>	<u>Total Monthly Volume</u>
January 2016	11.00	6.78	9.25	56,320
February 2016	9.11	6.25	6.95	53,944
March 2016	6.97	4.75	5.38	127,002
April 2016	6.68	5.43	5.54	83,098
May 2016	8.15	5.32	6.16	150,044
June 2016	7.35	6.02	6.65	90,870
July 2016	7.15	3.96	4.08	341,658
August 2016	4.36	3.80	3.82	283,566
September 2016	4.21	3.60	4.10	159,407
October 2016	4.20	3.65	3.70	702,486
November 2016	4.10	3.25	3.55	206,733
December 2016	4.09	3.42	3.75	191,405

## PRIOR SALES

There were no common shares issued upon the exercise of options granted under our Incentive Stock Option Plan during the year ended December 31, 2016.

The following table sets forth information in respect of our common shares that we issued upon the vesting of RSUs granted under our 2014 Restricted Share Unit Plan during the year ended December 31, 2016:

<u>Vesting Date</u>	<u>Number of Common Shares</u>
January 13, 2016	500
February 24, 2016	500
June 22, 2016	33,859
August 11, 2016	833
September 14, 2016	500
November 8, 2016	9,324
December 18, 2016	4,166
<b><u>Total</u></b>	<b><u>49,682</u></b>

The following table sets forth information in respect of options to acquire our common shares that we granted under our Incentive Stock Option Plan during the year ended December 31, 2016:

<u>Grant Date</u>	<u>Number of Options</u>	<u>Grant Price</u>
June 21, 2016	475,000	Cdn.\$6.15
June 21, 2016	75,000	\$4.84
August 11, 2016	25,000	Cdn.\$4.01
August 11, 2016	42,500	\$3.08
<b><u>Total</u></b>	<b><u>617,500</u></b>	

The following table sets forth information in respect of the RSUs that we granted under our 2014 Restricted Share Unit Plan during the year ended December 31, 2016:

<u>Grant Date</u>	<u>Number of RSUs</u>
January 13, 2016	3,000
June 22, 2016	31,282
July 4, 2016	500
August 11, 2016	11,000
August 30, 2016	2,000
September 1, 2016	500
November 8, 2016	2,500
<b><u>Total</u></b>	<b><u>50,782</u></b>

The following table sets forth information in respect of our common shares that we issued during the year ended December 31, 2016:

<u>Issuance Date</u>	<u>Number of Common Shares</u>	<u>Issue Price</u>
January 12, 2016	48,856	nil <sup>(1)</sup>
January 19, 2016	20,000	\$5.33 <sup>(2)</sup>
January 22, 2016	20,000	\$5.16 <sup>(2)</sup>
January 26, 2016	20,000	\$5.21 <sup>(2)</sup>
January 28, 2016	20,000	\$5.21 <sup>(2)</sup>
February 1, 2016	20,000	\$5.21 <sup>(2)</sup>
February 4, 2016	20,000	\$5.21 <sup>(2)</sup>
February 8, 2016	20,000	\$5.36 <sup>(2)</sup>
February 10, 2016	20,000	\$5.37 <sup>(2)</sup>
July 29, 2016	11,500,000	\$3.00 <sup>(3)</sup>
<b><u>Total</u></b>	<b><u>11,708,856</u></b>	

<sup>(1)</sup> Common shares were issued to LPC as a commitment fee. No proceeds were received for these shares.

<sup>(2)</sup> Common shares were sold pursuant to the Purchase Agreement.

<sup>(3)</sup> Common shares were sold pursuant to the Offering.

No other common shares, preferred shares, debt securities or warrants, or securities exchangeable or convertible into common shares, preferred shares, debt securities or warrants have been issued during the year ended December 31, 2016.

## DIRECTORS AND EXECUTIVE OFFICERS

The following sets forth the names and province or state and country of residence of our directors and executive officers, the offices held by them in the Corporation, their current principal occupations, all as of the date hereof, their principal occupations during the last five years and the month and year in which they became directors or officers. The term of each director expires on the date of our next annual meeting.

<u>Name, Province/State and Country of Residence and Present Position with the Corporation</u>	<u>Date Became a Director/Officer</u>	<u>Principal Occupation Last Five Years</u>
Richard M. Glickman <sup>(1)(2)(3)</sup> British Columbia, Canada Director	December 11, 2006	February 2017 to present – CEO, Aurinia Pharmaceuticals; July 2007 to January 2017 – Retired
W. James O’Shea <sup>(2)(3)</sup> Massachusetts, United States Director	June 17, 2014	September 2007 to present – Retired

<b><u>Name, Province/State and Country of Residence and Present Position with the Corporation</u></b>	<b><u>Date Became a Director/Officer</u></b>	<b><u>Principal Occupation Last Five Years</u></b>
Arthur H. Willms <sup>(1)(3)</sup> British Columbia, Canada Director	June 22, 2015	January 2009 to present – Retired
Mark H. Corrigan <sup>(1)(2)(4)</sup> Massachusetts, United States Director	June 22, 2015	July 2014 to July 2016 – Chairman of the Board, Epirus Pharmaceuticals; January 2010 to June 2014 – President and CEO, Zalicus Inc.
Robert J. Meyer <sup>(4)</sup> Virginia, United States Director	September 25, 2015	March 2013 to present – Director for Translational and Regulatory Sciences at the University of Virginia School of Medicine; January 2008 to January 2013 – VP of Global Regulatory Strategy, Policy, and Safety at Merck, Sharpe and Dohme
William L. Hunter British Columbia, Canada President and Chief Executive Officer, Director	June 11, 2007	July 2012 to present – President and Chief Executive Officer, Cardiome Pharma Corp.; 1997 to October 2011 – President and Chief Executive Officer, Angiotech Pharmaceuticals, Inc. (“Angiotech”)
Jennifer Archibald British Columbia, Canada Chief Financial Officer	September 20, 2012	September 2012 to present – Chief Financial Officer, Cardiome Pharma Corp.; September 2006 to September 2012 – Director of Finance, Cardiome Pharma Corp.
Sheila M. Grant British Columbia, Canada Chief Operating Officer	August 1, 2003	March 2013 to present – Chief Operating Officer, Cardiome Pharma Corp.; April 2005 to March 2013 – Vice President of Product Development – vernakalant, Cardiome Pharma Corp.
David D. McMasters Washington, United States General Counsel	January 1, 2015	November 2012 to present – General Counsel, Cardiome Pharma Corp.; 2000 to July 2011 – General Counsel, Angiotech
David C. Dean British Columbia, Canada VP, Investor Relations and Business Development	June 22, 2015	June 2015 to present – VP, Investor Relations and Business Development, Cardiome Pharma Corp.; January 2013 to June 2015 – Director and Research Analyst, Cormark Securities Inc.; January 2012 to January 2013 – Institutional Equity Sales, Cantor Fitzgerald Canada; January 2010 to January 2012 – VP Institutional Equity Sales, Versant Partners Inc.

<b>Name, Province/State and Country of Residence and Present Position with the Corporation</b>	<b>Date Became a Director/Officer</b>	<b>Principal Occupation Last Five Years</b>
Hugues Sachot St. Gregoire, France SVP, Sales	June 22, 2015	March 2013 to present – SVP, Sales, Cardiome Pharma Corp.; September 2007 to February 2013 – VP, Commercial, Angiotech

- (1) Member of the Compensation Committee. Dr. Glickman is the Chair of this Committee.
- (2) Member of the Corporate Governance and Nomination Committee. Dr. Corrigan is the Chair of this Committee.
- (3) Member of the Audit Committee. Mr. Willms is the Chair of this Committee.
- (4) Member of the Special Committee. Dr. Corrigan is the Chair of this Committee.

As of March 27, 2017, our directors and executive officers beneficially owned, or exercised control of or direction over, directly or indirectly, in the aggregate 706,821 (2%) of our outstanding common shares.

### **Directors and Executive Officers**

The following are short biographies of our directors and executive officers:

**Richard M. Glickman, L.L.D. (Hon), Director.** Dr. Glickman was a co-founder and Executive Chairman of Aurinia Pharmaceuticals, or Aurinia, and currently serves as the Chairman of the Board for Aurinia. Dr. Glickman was a co-founder, Chairman and Chief Executive Officer of Aspreva Pharmaceuticals, or Aspreva. Prior to establishing Aspreva, Dr. Glickman was the co-founder and Chief Executive Officer of StressGen Biotechnologies Corporation. Since 2000, Dr. Glickman has served as the Chairman of the Board of Vigil Health Solutions Inc., a healthcare services company and more recently, as Chairman of the Board of Essa Pharmaceuticals Inc. Dr. Glickman was also the founder and a director of Ontario Molecular Diagnostics, a diagnostic facility that evolved into the largest molecular diagnostic laboratories in Canada. He co-founded Probtect Corporation, a rational drug design and molecular genetics firm, where he established and introduced the first licensed DNA-based forensic and paternity testing services in Canada. He has served on numerous biotechnology boards including roles as Chairman of Life Sciences B.C. (formerly the British Columbia Biotechnology Alliance), Director of the Canadian Genetic Disease Network and a member of the federal government’s National Biotechnology Advisory Committee. Dr. Glickman currently serves as a member of the British Columbia Innovation Council and a Director for the Vancouver Aquarium. Dr. Glickman received the Ernst & Young Entrepreneur of the Year 2004 Award for the Pacific Region Life Sciences Group and has received both Canada’s and British Columbia’s Top 40 under 40 Award for Entrepreneurs and has been the recipient of 2006 BC Biotech Leadership Award. Dr. Glickman has served on the audit committees of other publicly listed companies.

**W. James O’Shea, Chairman.** Mr. O’Shea was President and Chief Operating Officer of Sepracor Inc., or Sepracor, from October 1999 to March 2007 where he was responsible for successfully building that organization’s commercial infrastructure. From April to August 2007, Mr. O’Shea served as Sepracor’s Vice Chairman. Prior to Sepracor, Mr. O’Shea was Senior Vice President of Sales and Marketing and Medical Affairs for Zeneca Pharmaceuticals, a business unit of Astra Zeneca Plc, a publicly held biopharmaceutical company. Mr. O’Shea is past Chairman of the National Pharmaceutical Council and is also a board member of BTG Plc, Prostrakan Group Plc, Ocular Therapeutics and Trevi Therapeutics. Mr. O’Shea has served on the audit committees of other publicly listed companies.

**Arthur H. Willms, Director.** Mr. Willms currently participates on several boards, including the Board of Directors of: Naikun Wind Energy Group Inc.; 2010 Games Operating Trust; and Pacific Autism Family Centre Foundation. He was previously the President and Chief Operating Officer of Westcoast Energy Inc. Mr. Willms has

a B.A. in Mathematics and an M.A. in Economics and has served on numerous audit committees of major corporation entities.

**Mark H. Corrigan, M.D., Director.** Dr. Corrigan was the Chairman of the Board of Directors at Epirus Biopharmaceuticals, Inc. until July 2016, and was a former Board member of Cubist Pharmaceuticals, Inc. He was formerly the Chief Executive Officer of Zalicus Inc., prior to its merger with Epirus Biopharmaceuticals Inc., and prior to that was the executive vice president of R&D at Sepracor Inc. Prior to Sepracor Inc., he spent 10 years with Pharmacia & Upjohn, where he served most recently as Group Vice President of Global Clinical Research and Experimental Medicine.

**Robert J. Meyer, M.D., Director.** Dr. Meyer is currently a Director at the Virginia Center for Translational and Regulatory Sciences at the University of Virginia School of Medicine, but has held senior roles at Merck Research Laboratories from 2007 to 2013, most recently as Vice President, Global Regulatory Strategy, Policy and Safety, as well as at the FDA from 1999 to 2007 where Dr. Meyer served as Director of the Division of Pulmonary and Allergy Drug Products and then Director of the Office of Drug Evaluation II in the Center for Drug Evaluation and Research.

**William Hunter, M.D., President and Chief Executive Officer & Director.** Dr. Hunter has been a member of Cardiome's Board of Directors since 2007 and became the Company's President and CEO in July 2012. Prior to Cardiome, Dr. Hunter co-founded Angiotech in 1992 and assumed the position of Chief Executive Officer in 1997 when Angiotech was a venture-stage, private, pre-clinical company with less than 50 employees. He led Angiotech through three rounds of private equity financing, the Company's IPO and listing on the TSX and the NASDAQ, over \$1 billion in equity and debt financings, a debt restructuring and eight separate corporate acquisitions. During that time, Angiotech grew to become a profitable, diversified, healthcare company with over 1,400 employees, several thousand commercially available products, 12 facilities in five countries and worldwide annual revenues exceeding \$250 million. Dr. Hunter has over 200 patents and patent applications to his name and products in which he was an inventor or co-inventor include the TAXUS<sup>®</sup> Drug-Eluting Coronary Stent, the Zilver PTX Peripheral Drug-Eluting Stent, the Quill barbed wound closure device and the 5-FU Anti-Infective Catheter; combined these products have been used in over 6 million patients and recorded revenues of over \$12 billion worldwide. Dr. Hunter currently serves as a director of Epirus Pharmaceuticals Inc. (NASDAQ: EPRS) and Rex Bionics Plc, and selected awards he has received include the 2006 Principal Award from the Manning Foundation (one of Canada's highest awards for innovation); BC Innovation Council's Cecil Green Award for Science and Technology Entrepreneurship; Entrepreneur of the Year from the Canadian Venture Capital and Private Equity Association; and Canada's 40 Under 40. Dr. Hunter served as a practicing physician in British Columbia for five years.

**Jennifer Archibald, CPA, CA, Chief Financial Officer.** Ms. Archibald is Cardiome's Chief Financial Officer, with responsibility for overseeing Cardiome's financial operations. She joined Cardiome in 2006 and served as Cardiome's Director of Finance until her appointment as Chief Financial Officer in September 2012. Ms. Archibald has extensive accounting and finance experience, dealing with the complexities of both public and private corporations. Prior to joining Cardiome, Ms. Archibald managed the accounting operations at the corporate office of The Jim Pattison Group. Ms. Archibald began her career as a corporate auditor with KPMG LLP. She is a Chartered Professional Accountant and earned a Bachelor of Commerce degree from the University of British Columbia.

**Sheila M. Grant, MBA, Chief Operating Officer.** Ms. Grant is Cardiome's Chief Operating Officer. Ms. Grant was most recently Cardiome's Vice President of Product Development, with responsibility for the overall management of the vernakalant (IV) program. She has overseen the development of vernakalant from its initial pre-clinical studies through to commercialization. Ms. Grant's past roles at Cardiome have included Vice President, Commercial Affairs and Director of Business & Clinical Development. Prior to joining Cardiome, Ms. Grant acted as business consultant to De Novo Enzyme Corporation and Coopers & Lybrand. Ms. Grant also worked in research and development, production, and quality assurance with Schering Agrochemicals U.K., Wellcome Biotechnologies U.K. and Serono Diagnostics U.K.. Ms. Grant holds an MBA degree from Simon Fraser University.

**David D. McMasters, JD, General Counsel.** Mr. McMasters is Cardiome's General Counsel, and oversees all legal affairs of the Company. Mr. McMasters was formerly General Counsel to Angiotech for 11 years, and, prior to that, was the Managing Partner of a mid-sized intellectual property law firm (Seed Law Group).

**David C. Dean, Vice President, Investor Relations and Business Development.** Mr. Dean has 15 years of capital markets experience as a top ranked industry analyst focused exclusively on the Canadian healthcare sector, most recently as a Director and Research Analyst at one of Canada's leading independent investment banks. Mr. Dean attained a M.Sc. from the University of Ottawa with a focus on Cardiac Physiology as well as an MBA (Finance) from Queens University.

**Hugues Sachot, Senior Vice President, Sales.** Mr. Sachot is Cardiome's Senior Vice President of Sales and leads the commercial organization in all direct market and distributor sales worldwide. He was previously Vice President of Commercial at Angiotech.

### **CEASE TRADE ORDERS, BANKRUPTCIES, PENALTIES OR SANCTIONS**

To the best of our knowledge, no director or executive officer or any shareholder holding a sufficient number of our common shares to materially affect the control of the Corporation:

- (a) is, as at the date of this annual information form, or has been, within the ten years before, a director or executive officer of any company (including the Corporation), that while that person was acting in that capacity,
  - (i) was the subject of a cease trade or similar order or an order that denied the relevant company access to any exemption under securities legislation, for a period of more than 30 consecutive days,
  - (ii) was subject to a cease trade or similar order or an order that denied the relevant company access to any exemption under securities legislation, for a period of more than 30 consecutive days that was issued after the director or executive officer ceased to be a director or an executive officer and which resulted from an event that occurred while that person was acting in the capacity as director or executive officer, or
  - (iii) 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, or
- (b) has, within the 10 years before the date of this annual information form, become bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency, or become subject to or instituted any proceedings, arrangement or compromise with creditors, or had a receiver, receiver manager or trustee appointed to hold the assets of the director or executive officer or shareholder,

except in respect of the following companies:

- Angiotech and each of the following subsidiaries: 0741693 B.C. Ltd. and Angiotech International Holdings Corp. (the "Angiotech Canadian Subsidiaries") and Angiotech Pharmaceuticals (US), Inc., American Medical Instruments Holdings Inc., NeuColl Inc., Angiotech BioCoatings Corp., Afmedica Inc., Quill Medical Inc., Angiotech America Inc., Angiotech Florida Holdings Inc., B.G. Sulzle Inc., Surgical Specialties Corporation, Angiotech Delaware Inc., Medical Device Technologies Inc., Manan Medical Products Inc. and Surgical Specialties Puerto Rico Inc. (the "Angiotech U.S. Subsidiaries"). On January 28, 2011, Angiotech, the Angiotech Canadian Subsidiaries and the Angiotech U.S. Subsidiaries voluntarily filed a petition under the CCAA in the Supreme Court of British Columbia to implement a proposed recapitalization transaction. On January 31, 2011, the Angiotech U.S. Subsidiaries filed a voluntary petition under Chapter 15 of Title 11 of the United States Code to obtain recognition and enforcement in the United States for certain relief granted in the CCAA proceedings, and to obtain assistance of the United States

courts to the Supreme Court of British Columbia in effectuating the proposed recapitalization. Dr. Hunter was the president and chief executive officer and a director of Angiotech until October 2011, and Mr. McMasters was General Counsel of Angiotech until July 2011. Mr. Willms was a director of Angiotech until May 2011.

To the best of our knowledge, none of our directors or executive officers or any shareholder holding a sufficient number of our common shares to materially affect the control of the Corporation have been subject to:

- (a) 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
- (b) any other penalties or sanctions imposed by a court or regulatory body that would likely be considered important to a reasonable investor in making an investment decision.

### **CONFLICTS OF INTEREST**

To the knowledge of Cardiome, and other than as disclosed herein, there are no known existing or potential material conflicts of interest among Cardiome, its directors and officers or a subsidiary of Cardiome and any director or officer of Cardiome or of a subsidiary of Cardiome, or other members of management as a result of their outside business interests, except that certain of the directors or officers may serve as directors and officers of other companies, and therefore it is possible that a conflict may arise between their duties to Cardiome and their duties as a director or officer of such other companies. See “Risk Factors – We are dependent upon our key personnel to achieve our business objectives” in this annual information form.

The directors of Cardiome are required by law to act honestly and in good faith with a view to the best interests of Cardiome and to disclose any interests that they may have in any material contract or material transaction. If a conflict of interest arises at a meeting of the Board of Directors of the Cardiome, any director in a conflict is required to disclose his or her interest and abstain from voting on such matter. The directors and officers of Cardiome are aware of the existence of laws governing accountability of directors and officers for corporate opportunity and requiring disclosures by directors of conflicts of interest in respect of Cardiome and are required to comply with such laws in respect of any directors’ and officers’ conflicts of interest or in respect of any breaches of duty by any of its directors or officers.

### **AUDIT COMMITTEE INFORMATION**

#### **Audit Committee Mandate**

The mandate of the Audit Committee is attached as Schedule “A”.

#### **Composition and Relevant Education and Experience**

The Audit Committee is comprised of three independent directors: Arthur H. Willms, Richard M. Glickman and W. James O’Shea. A description of the experience of each Audit Committee member that is relevant to the performance of his or her responsibilities as an Audit Committee member may be found above under the heading “Directors and Executive Officers” in this annual information form.

Under the SEC rules implementing the *Sarbanes-Oxley Act of 2002*, Canadian issuers filing reports in the United States must disclose whether their audit committees have at least one “audit committee financial expert”. The Board has determined that Mr. Willms qualifies as an audit committee financial expert under such rules. In addition, all members of the Audit Committee are considered financially literate under applicable Canadian and U.S. laws and we provide continuing education to all Audit Committee members. On a regular basis, the Audit Committee performs and reviews a self-assessment.

## Auditor Independence

Our Audit Committee has concluded that KPMG LLP, our independent registered chartered accountant, is independent under applicable rules and guidelines and, in particular, that KPMG LLP is free from conflicts of interest that could impair its objectivity in conducting the audit of our financial statements. The Audit Committee is required to approve all audit and non-audit related services performed by KPMG LLP, and KPMG LLP is not permitted to perform services for us prohibited for an independent auditor under applicable Canadian and United States laws, including the Securities Act, and the rules and regulations adopted thereunder by the SEC and the Public Company Accounting Oversight Board (United States).

## Auditor's Fees

The following table sets out the fees billed to us by KPMG LLP for professional services for the years ended December 31, 2016 and December 31, 2015.

	December 31, 2016	December 31, 2015
Audit Fees <sup>(1)</sup>	Cdn.\$574,500	Cdn.\$583,300
Audit-Related Fees <sup>(2)</sup>	Cdn.\$45,200	Nil
Tax Fees <sup>(3)</sup>	Nil	Cdn.\$42,200
All Other Fees	Nil	Nil

- (1) Audit fees consist of fees for the audit and interim reviews of our consolidated financial statements or services that are normally provided in connection with statutory and regulatory filings or engagements.
- (2) Audit-related fees are fees for assurance and related services reasonably related to the performance of the audit or review of our consolidated financial statements that are not reported under "Audit Fees".
- (3) Tax fees include tax compliance, tax planning, tax advice and various taxation matters.

## LEGAL PROCEEDINGS AND REGULATORY ACTIONS

There are no outstanding material legal proceedings or regulatory actions to which we are a party, nor, to our knowledge, are any material legal proceedings or regulatory actions contemplated.

## INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS

None of our directors, executive officers, person or company, beneficially owning or exercising control or direction over, directly or indirectly, more than 10% of our common shares, or any associate or affiliate of the foregoing, has had any material interest, direct or indirect, in any transaction within the three most recently completed financial years or during the current financial year prior to the date of this annual information form that has materially affected us or is reasonably expected to materially affect us.

## TRANSFER AGENTS AND REGISTRARS

Our co-transfer agents and co-registrars for our common shares are Computershare Investor Services Inc. located at its principal offices in Vancouver, British Columbia and Toronto, Ontario and Computershare Trust Company, N.A. located at its principal offices in Golden, Colorado.

## MATERIAL CONTRACTS

We are party to the following material contracts as defined in National Instrument 51-102 - Continuous Disclosure Obligations:

- 1) Term Loan Agreement between Cardiome Pharma Corp. and CRG entered into on June 13, 2016 described in the section titled “General Development of the Business” in this annual information form.
- 2) License Agreement by and between Correvio International Sarl and Durata Therapeutics International B.V. (Allergan) entered into on May 5, 2016 described in the section titled “General Development of the Business” in this annual information form.
- 3) Supply Agreement by and between Correvio International Sarl and Durata Therapeutics International B.V. (Allergan) entered into on May 5, 2016. The Supply Agreement was entered into in conjunction with the License Agreement by and between Correvio International Sarl and Durata Therapeutics International B.V. (Allergan) entered into on May 5, 2016 described in the section titled “General Development of the Business” in this annual information form.
- 4) Exclusive License and Supply Agreement by and between Cardiome Pharma Corp., Correvio International Sarl and SteadyMed entered into on June 28, 2015 described in the section titled “General Development of the Business” in this annual information form.
- 5) Registration Rights Agreement by and between Cardiome Pharma Corp. and CarCor Investment Holdings LLC (“CarCor”) entered into on November 18, 2013 in connection with the acquisition of Correvio described in the section titled “General Development of the Business” in this annual information form.
- 6) Stock and Asset Purchase Agreement by and among Cardiome Pharma Corp., Cardiome International AG, Murk Acquisition Sub, Inc., Correvio, and CarCor entered into on November 18, 2013 in connection with the acquisition of Correvio described in the section titled “General Development of the Business” in this annual information form.

#### **INTERESTS OF EXPERTS**

Our auditor is KPMG LLP, Chartered Professional Accountants, P.O. Box 10426, 777 Dunsmuir Street, Vancouver, British Columbia, V7Y 1K3. KPMG LLP has audited our consolidated financial statements as at December 31, 2016 and 2015, and for each of the years in the two-year period ended December 31, 2016 as set forth in their report. KPMG LLP confirmed that they are independent within the meaning of the relevant rules and related interpretations prescribed by the relevant professional bodies in Canada and any applicable legislation or regulations and that they are independent accountants with respect to the Company under all relevant U.S. professional and regulatory standards.

#### **ADDITIONAL INFORMATION**

Additional information relating to us may be found on SEDAR at [www.sedar.com](http://www.sedar.com) or on EDGAR at [www.sec.gov](http://www.sec.gov).

#### **Executive Compensation**

Additional information, including directors’ and officers’ remuneration and indebtedness, principal holders of our securities, options to purchase securities and interests of insiders in material transactions, if applicable, is contained in the information circular for our annual meeting held on June 21, 2016.

#### **Additional Financial Information**

Additional financial information is provided in our consolidated financial statements and Management’s Discussion and Analysis of Financial Condition and Results of Operations for the financial year ended December 31, 2016.

**SCHEDULE “A”  
AUDIT COMMITTEE MANDATE**

**Date of Adoption: May 11, 2016**

**Purpose**

The audit committee (the “Committee”) of Cardiome Pharma Corp. (the “Corporation”) was established by the Board of Directors (“Board”) to assist the Board in fulfilling its responsibilities for oversight of the following:

- the Corporation’s systems of internal and disclosure controls;
- the Corporation’s financial reporting process, including the Corporation’s financial statements and other financial information provided by the Corporation to its shareholders, the public and others in accordance with applicable securities and corporate legislation and the Corporation’s Disclosure Policy;
- the Corporation’s compliance with financial, accounting, legal and regulatory requirements including the Corporation’s Code of Business Conduct and Ethics;
- the appointment, compensation, independence, oversight, communication with , performance and change of the Corporation’s independent external auditors (the “Auditors”);
- the Corporation’s process for identification of the principal risks of the Corporation’s business and ensuring that an appropriate process is in place to manage risks across the enterprise; and
- the fulfillment of the other responsibilities set forth in this mandate

**Organization, Membership and Reporting**

1. The Committee shall consist of three or more directors who are “independent” as defined by applicable law, regulations, guidelines and policies.
2. All members of the Committee shall be “financially literate” and at least one member of the Committee shall be a “financial expert”. “Financially literate” and “financial expert” will have the respective meanings set out in applicable law, regulations, guidelines and policies.
3. Appointments and replacements to the Committee will be made by the Board and will be reviewed on an annual basis. The Board will provide for continuity of membership, while at the same time allowing fresh perspectives to be added. Each member of the Committee will automatically cease to be a member if he or she ceases to be independent.
4. The chairman of the Committee (the “Chairman”) will be appointed by a vote of the Board on an annual basis.
5. The Committee will report to the Board, at the next scheduled meeting of the Board, the proceedings of the Committee and any recommendations made by the Committee.
6. The Committee shall meet from time to time, as it deems necessary, but at least four times per year. Special meetings of the Committee will be authorized at the request of any member of the Committee or at the request of the Auditors. The Auditors will be informed about, and can attend, meetings of the Committee as deemed appropriate by the Chairman. Provision will be made to meet privately with external auditors on a quarterly basis and to meet privately with management at least once per annum.

## **Organization, Membership and Reporting (continued)**

7. The Committee shall maintain written minutes of its meetings, which minutes shall be filed in the corporate minute book.

## **Authority and Responsibilities**

### **External Audit:**

1. The Auditors will report directly to the Committee. The Committee is responsible for overseeing the work of the Auditors and will communicate directly with the Auditors as required.
2. The Committee will review the basis and amount of the Auditors' fees and pre-approve all auditing services and permitted non-audit services.
3. The Committee will consider whether the Auditors should be re-appointed and make recommendations to the Board. At least on an annual basis, the Committee will evaluate the qualifications, performance and independence of the Auditors and the senior audit partners having primary responsibility for the audit, including considering whether the Auditors' quality controls are adequate.
4. The Committee will pre-approve the appointment of the Auditors for all accounting services, internal control related services and permitted non-audit services to be provided to the Corporation. The Committee may establish policies and procedures, from time to time, pre-approving the appointment of the Auditors for certain non-audit services. In addition, the Committee may delegate to one or more members the authority to pre-approve the appointment of the Auditors for any non-audit service to the extent permitted by applicable law, provided that any pre-approvals granted pursuant to such delegation will be reported to the full Committee at its next scheduled meeting.
5. The Committee will receive from the Auditors a formal written statement delineating all relationships between the Auditors and the Corporation and will actively engaging in a dialogue with the Auditors with respect to any disclosed relationships or services that may impact the objectivity and independence of the Auditors.
6. The Committee will confirm that the rotation of the lead audit partner or the audit partner responsible for reviewing the audit (the concurring partner), for the Corporation's Auditors complies with the requirements of the Canadian and US regulatory authorities
7. The Committee will review, based upon the recommendation of the Auditors and management, the scope and plan of the work to be done by the Auditors for each fiscal year.
8. The Committee will review and approve the Corporation's hiring of partners, employees, former partners and former employees of the present and former Auditors of the Corporation.

## **Authority and Responsibilities (continued)**

### **Financial Statements:**

1. The Committee will review and discuss with management and the Auditors the Corporation's interim financial statements, management discussion and analysis ("MD&A") and the interim earnings press release prior to submission to shareholders, any governmental body, any stock exchange or disclosure to the public. On behalf of the Board, the Committee will approve the interim financial statements, MD&A and interim earnings press release and sign a resolution to that effect.
2. The Committee will review and discuss with management and the Auditors the Corporation's annual audited financial statements, management discussion and analysis ("MD&A") and the annual earnings press release prior to submission to shareholders, any governmental body, any stock exchange or disclosure to the public. The Committee will recommend to the Board approval of the annual audited financial statements, MD&A and annual earnings press release and sign a resolution to that effect.
3. The Committee will review and discuss with management and the Auditors, the results of the external audit and any changes in accounting practices or policies and the financial statements impact thereof. In addition, the Committee will review any accruals, provisions, or estimates that have a significant effect upon the financial statements as well as other sensitive matters such as disclosure of related party transactions.
4. The Committee will issue any necessary reports required of the Committee to be included in the Corporation's annual proxy statement. The Committee will review and recommend to the Board the approval of all documents filed with securities regulatory authorities.
5. In addition, the Committee will review other financial statements, information and documents that require the approval of the Board. These will include financial statements in prospectus and other offering memoranda and financial statements required by regulatory authorities. The Committee will sign a resolution to the effect that such financial statements, information or documents that are being presented to the Board are satisfactory, and recommend their approval.

### **Periodic and Annual Reviews:**

1. The Committee will review and discuss with management all material off-balance sheet transactions, arrangements, obligations (including contingent obligations) and other relationships of the Corporation with unconsolidated entities or persons that may have a material current or future effect on financial condition, changes in financial condition, results of operation, liquidity or capital resources.
2. The Committee will discuss with management the application of the Corporation's accounting policies that are in accordance with U.S. generally accepted accounting principles and their consistency from period to period.

## **Authority and Responsibilities (continued)**

### **Periodic and Annual Reviews (continued):**

3. The Committee will periodically review with each of management and the Auditors any significant disagreements between management and the Auditors in connection with the preparation of the financial statements and any difficulties encountered during the course of the audit or review (including any restrictions on the scope of work or access to required information).
4. The Committee will review with management and the Auditors any legal matters, tax assessments, correspondence with regulators or governmental agencies or published reports that raise material issues regarding the Corporation's financial statements or accounting policies and the manner in which these matters have been disclosed in public filings, if applicable.
5. The Committee will approve all related party transactions.
6. The Committee will review the Corporation's Treasury Investment Policy annually.
7. The Committee will review with management and the Auditors the sufficiency and quality of the financial and accounting personnel of the Corporation.
8. The Committee will review the policies and practices of the Corporation regarding the regular examination of officers' expenses and perquisites, including the use of the assets of the Corporation.
9. The Committee will review and reassess the adequacy of this mandate annually.

### **Internal Controls and Disclosure:**

1. The Committee will review the Corporation's systems of and compliance with internal financial controls
2. The Committee will review and discuss with management and the Auditors any major issue as to the adequacy and effectiveness of internal controls over the accounting and financial reporting systems of the Corporation, either directly, or through the Auditors or other advisors and obtain and review a report from the Auditors, at least annually, regarding same; and the Committee will review and discuss with management and the Auditors any special steps adopted in light of material internal control deficiencies and the adequacy of disclosures about changes in internal controls over financial reporting.
3. The Committee will establish procedures for the receipt, retention and treatment of complaints received by the Corporation regarding accounting, internal accounting controls or auditing matters and for the confidential, anonymous submission by employees of the Corporation of concerns regarding questionable accounting or auditing matters.
4. The Committee will be satisfied that adequate procedures are in place for the review of the Corporation's public disclosure of financial information extracted or derived from the Corporation's financial statements and periodically assess the adequacy of those procedures.

## **Authority and Responsibilities (continued)**

### **Risk Management and Compliance:**

1. The Committee will ensure that the business of the Corporation is conducted in compliance with applicable laws and regulations and according to the highest ethical standards.
2. The Committee will review management's fraud risk assessment on an annual basis.
3. The Committee will discuss with management the Corporation's guidelines and policies governing the Corporation's process of risk assessment and risk management.

The Committee has the authority, to the extent it deems necessary or appropriate, to retain independent legal, accounting or other advisors. The Corporation will provide appropriate funding, as determined by the Committee, for payment of compensation to the independent auditor for the purpose of rendering or issuing an audit report and to any advisors employed by the Committee.

	Q1	Q2	Q3	Q4
<b>Audit Committee Purpose</b>				
Review audit committee mandate	X			
Conduct special investigations	*	*	*	*
<b>Audit Committee Composition and Meetings</b>				
Assess independence and financial literacy of Committee members		X		
Establish number and timing of meetings				X
Committee chair to establish meeting agendas	X	X	X	X
Maintain minutes and report to Board	X	X	X	X
Private sessions with auditors	X	X	X	X
Perform self-assessment of Committee and members			X	
Prepare report of Committee effectiveness to Board				X
<b>Audit Committee Responsibilities and Duties</b>				
<b>External Auditor</b>				
Recommend appointment of Auditors				X
Review audit plan			X	
Approve audit and non-audit fees in advance	X	X	X	X
Review performance of Auditors	X			
Review independence letter and discuss auditor independence				X
Review reports from Auditors' on their own internal control procedures			X	
Review audit partner rotation		X		
<b>Financial Statements</b>				
Review quarterly financial statements, MD&A and earnings press release and approve on behalf of the Board	X	X	X	
Review interim financial reports and Auditors' findings	X	X	X	
Review annual financial statements, MD&A, earnings release and recommend approval to Board				X
Review audit report				X
Review regulatory reports				X
Prepare reports to be included in annual meeting materials		X		

	Q1	Q2	Q3	Q4
<b>Periodic and Annual Reviews</b>				
Review material off-balance sheet transactions, arrangements, obligations and contingent obligations	X	X	X	X
Discuss appropriateness of accounting principles, critical accounting policies and management's judgments and estimates without management present	X	X	X	X
Consider and approve, if necessary, significant changes to accounting policies and financial disclosure practices	X	X	X	X
Review any significant disagreements between management and Auditors	X	X	X	X
Review any difficulties encountered during the review or audit	X	X	X	X
Review legal matters with legal counsel	*	*	*	*
Review Corporation's Treasury Investment Policy				X
Review with management and Auditors the sufficiency and quality of financial and accounting personnel	*	*	*	*
Review and approve related party transactions	*	*	*	*
Review policies and practices regarding examination of officers' expenses and perquisites			X	
Review and approve hiring of partners, employees, former partners and employees of the present and former Auditors	*	*	*	*
<b>Internal Controls and Disclosure</b>				
Review adequacy of internal control structure and system with management and Auditors	X		X	
Discuss any whistleblowing activity	X	X	X	X
Review adequacy of procedures for review of public disclosure of financial information			X	
Review disclosure of audit committee information required in the management information circular	X			
<b>Risk Management</b>				
Discuss with management the Corporation's guidelines and policies governing the Corporation's process of risk assessment and risk management				X
Review management's fraud risk assessment annually				X

\* As needed

X Recommended timing