



**CARDIOME PHARMA CORP.**

**ANNUAL INFORMATION FORM**

**FOR THE FISCAL YEAR ENDED DECEMBER 31, 2013**

**MARCH 26, 2014**

## TABLE OF CONTENTS

	<u>Page</u>
REFERENCE INFORMATION .....	2
CAUTION REGARDING FORWARD-LOOKING STATEMENTS.....	2
CORPORATE STRUCTURE .....	5
GENERAL DEVELOPMENT OF THE BUSINESS.....	6
Three Year History .....	6
NARRATIVE DESCRIPTION OF THE BUSINESS.....	8
General.....	8
Our Products and Product Candidates .....	9
Pre-clinical Projects .....	9
Our Products and Product Candidates .....	10
Competition .....	17
Patents and Proprietary Protection.....	18
RISK FACTORS .....	22
DIVIDENDS AND DISTRIBUTIONS.....	38
CAPITAL STRUCTURE .....	38
MARKET FOR SECURITIES .....	39
PRIOR SALES .....	40
ESCROWED SECURITIES.....	41
DIRECTORS AND EXECUTIVE OFFICERS.....	41
CEASE TRADE ORDERS, BANKRUPTCIES, PENALTIES OR SANCTIONS.....	46
CONFLICTS OF INTEREST.....	47
AUDIT COMMITTEE INFORMATION .....	47
LEGAL PROCEEDINGS AND REGULATORY ACTIONS .....	48
INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS.....	48
TRANSFER AGENTS AND REGISTRARS .....	48
MATERIAL CONTRACTS .....	48
INTERESTS OF EXPERTS.....	49
ADDITIONAL INFORMATION.....	49
SCHEDULE “A” AUDIT COMMITTEE MANDATE .....	50

**CARDIOME PHARMA CORP.**

**ANNUAL INFORMATION FORM**

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2013

March 26, 2014

**REFERENCE INFORMATION**

In this annual information form, a reference to the “Corporation”, “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 US dollars, unless otherwise indicated. All references to “Cdn.\$” are to Canadian dollars. On March 26, 2014, the exchange rate for conversion of U.S. dollars into Canadian dollars was U.S.\$1.00 = Cdn.\$1.1143 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, 2013.

**CAUTION REGARDING FORWARD-LOOKING STATEMENTS**

This annual information form contains forward-looking statements or forward-looking information within the meaning of applicable Canadian securities legislation (“forward-looking statements”) that may not be based on historical fact, 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™;
- our plans to develop and commercialize product candidates and the timing of these development programs;
- whether we will receive, and the timing and costs of obtaining, regulatory approvals in the United States, Canada, the European Union and other countries;
- the cost of post-market regulation if we receive necessary regulatory approvals;
- our ability to integrate Correvio LLC (“Correvio”) into our existing business and realize the anticipated benefits of the acquisition;
- 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;
- whether our third party collaborators will maintain their intellectual property rights in the technology we license;

- 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;
- 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 of an effective direct sales and marketing infrastructure for approved products we elect to market and sell directly;
- the rate and degree of market acceptance of our products;
- 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;
- 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 that we already, or hope to, sell our products in, 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”. 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 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; 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; government legislation could adversely impact our ability to obtain product reimbursement and economically price our products; 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 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 the significant amount of confidential information under our control; our success is dependent upon our corporate collaborations with third parties in connection with services we will need for the development of our products; 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, which could have a material adverse effect on our business, financial condition and results of operations and could cause the market value of our securities to decline; we are dependent on two products for a significant portion of our revenues; 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 fiscal periods; our inventory has limited shelf life and may require write-downs; we are exposed to risks relating to the write-down of intangible assets, which comprises of 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; failure to comply with the United States *Foreign Corrupt Practices Act*, 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*, 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 regulation 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; our business depends heavily on the use of information technologies; and other factors as described in detail in this annual information form and our filings with the Securities and Exchange Commission (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 Administrator’s 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 the “Management’s Discussion and Analysis of Financial Condition and Operations” for the fiscal year ended December 31, 2013, filed at or about the same time as this annual information form 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 (“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. All share and per share information in this document gives effect to the share consolidation on a retroactive basis, unless otherwise indicated. Our common shares trade on the Toronto Stock Exchange (“TSX”) under the symbol “COM” and on the NASDAQ Stock Market (“NASDAQ”) under the symbol “CRME”.

Prior to November 18, 2013, we had six wholly-owned subsidiaries: Rhythm-Search Developments Ltd., a company incorporated under the Company Act (British Columbia); Cardiome, Inc. (formerly Paralex, Inc.), a company incorporated under the Delaware General Corporation Law; Artesian Therapeutics, Inc., a company incorporated under the Delaware General Corporation Law; Cardiome International AG (formerly Cardiome Development AG.), a company continued under the laws of Switzerland, Cardiome UK Limited, a company incorporated under the laws of the United Kingdom, and Cardiome Pharma AG, a corporation incorporated under the laws of Germany.

On November 18, 2013, we completed the acquisition of Correvio LLC (“Correvio”), a privately held pharmaceutical company headquartered in Geneva, Switzerland. As a result of this transaction, we acquired or incorporated the following wholly-owned subsidiaries:

<b>Subsidiary Name</b>	<b>Jurisdiction of Incorporation or Organization</b>
Correvio LLC	Delaware, U.S.A.
Murk Acquisition Sub, Inc.	Delaware, U.S.A.
Correvio International S.a.r.l.	Switzerland
Correvio GmbH	Germany
Correvio Italia S.r.l.	Italy
Correvio AB	Sweden
Correvio	France
Correvio Spain S.L.U.	Spain
Correvio Belgium S.p.r.l.	Belgium
Correvio (UK) Ltd.	United Kingdom
Correvio (Australia) Pty Limited	Australia

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 Suite 405, 6190 Agronomy Road, Vancouver, British Columbia, Canada, V6T 1Z3.

## GENERAL DEVELOPMENT OF THE BUSINESS

We are a specialty pharmaceutical company dedicated to the development and commercialization of cardiovascular therapies that will improve the quality of life and health of patients suffering from heart disease. 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 numerous markets outside of the United States.

### Three Year History

#### Collaboration Agreements

In October 2003, we entered into a collaboration and license agreement, referred to as the “North American Vernakalant (IV) Agreement”, with an affiliate of Astellas Pharma US, Inc. (“Astellas”). We granted Astellas an exclusive license to vernakalant (IV) and its related technology to develop, make and sell intravenous or injectable formulations of vernakalant in North America for any and all indications including the treatment of atrial fibrillation and atrial flutter, including a right to sublicense to third parties. In April 2009, we entered into a collaboration and license agreement with Merck & Co., Inc. (“Merck”) for the development and commercialization of vernakalant (the “Collaboration Agreement”). The Collaboration Agreement provided an affiliate of Merck with exclusive global rights to vernakalant (oral) and exclusive rights outside of North America to vernakalant (IV).

In July 2011, Merck acquired the rights for the development and commercialization of vernakalant (IV) in North America from Astellas. All terms, responsibilities and payments that Astellas committed to under the North American Vernakalant (IV) Agreement were assumed by Merck without change.

In March 2012, we announced Merck’s decision to discontinue further development of vernakalant (oral). In September 2012, Merck gave notice to us of its termination of the North American Vernakalant (IV) Agreement and Collaboration Agreement. On April 25, 2013, we entered into a Transition Agreement with Merck (the “Transition Agreement”) to amend and supplement the provisions of the Collaboration Agreements governing their rights and responsibilities in connection with the termination of the Collaboration Agreement and transfer of rights to, and responsibilities for, vernakalant to us. Pursuant to the Transition Agreement, we took responsibility for worldwide sales, marketing, and promotion of vernakalant (IV) on April 25, 2013. Regulatory product rights and product distribution responsibility were transferred to us upon transfer of the marketing authorizations in the relevant countries, subject to the ongoing transfer of certain rights from Merck and its affiliates to us, which has been delayed in some jurisdictions due to routine regulatory requirements and is expected to be completed in the first half of 2014.

In May 2013, we announced the completion of the transfer of sponsorship of the U.S. Investigational NDAs for vernakalant (IV), the transfer of the U.S. NDA for vernakalant (IV), and the transfer of sponsorship of all vernakalant Canadian Clinical Trial Applications from Merck to us. All marketing rights for North America have been returned to us.

On June 21, 2013, the European Commission approved the transfer of the centrally-approved marketing authorization for BRINAVESS™ from Merck to us. We are now the marketing authorization holder for BRINAVESS™ in the member states of the European Union. As a result, royalties on sales and the promotional services fee we previously received from Merck ceased on July 1, 2013 and we began benefiting from all sales of BRINAVESS™ throughout the world.

On September 16, 2013, we announced the completion of the transfer from Merck to us of commercialization responsibility for BRINAVESS™ in the European Union and the responsibility to complete the post-marketing study for BRINAVESS™. We are now supplying BRINAVESS™ under our own trade dress in the European Union.

#### Long-term debt settlement

In January 2012, we received an advance of \$25 million from Merck pursuant to a \$100 million secured, interest-bearing credit facility granted to us under the Collaboration Agreement with Merck. We may, at our option, repay all or a portion of the advance from time to time without premium or penalty. This advance must be repaid in full by December 31, 2017.

In September 2012, Merck gave notice to us of its termination of the Collaboration Agreement. As a result of the notice of termination, Merck did not have an obligation to make further advances to us under the credit facility. Terms of the existing advances made under the credit facility remained the same as prior to the notice of termination of the Collaboration Agreement.

In December 2012, we reached an agreement with Merck to settle our debt obligation. Under the terms of the settlement agreement, we were to pay Merck \$20 million on or before March 31, 2013 to settle our outstanding debt of \$50 million plus accrued interest of \$2 million owed to Merck. The settlement between us and Merck would terminate the credit facility and, upon payment of the \$20 million settlement amount, would release and discharge the collateral security taken in respect of the advances under the line of credit. Interest also ceased to accrue from the effective date of the settlement agreement.

On December 31, 2012, the settlement agreement was amended, which allowed us to pay \$7 million of the \$20 million settlement amount to Merck, settling \$17.5 million of the original outstanding debt obligation of \$50 million and \$0.7 million of accrued interest. We recorded a gain on debt settlement of \$11.2 million in 2012.

On February 28, 2013, the settlement agreement was further amended, allowing us to pay the remaining balance of the settlement amount prior to March 31, 2013. On March 1, 2013, the Company paid the remaining \$13 million of the debt settlement amount to Merck, resulting in an additional gain on debt settlement of \$20.8 million. With this final payment, all outstanding debt obligations are extinguished and Merck has released and discharged the collateral security taken in respect of the advances under the line of credit.

#### Restructuring

On March 19, 2012, we reduced our workforce in response to Merck's decision to discontinue further development of vernakalant (oral). On July 9, 2012, we further reduced our workforce by eliminating positions focused on internal research activities along with certain supporting functions. As a result of the workforce reductions, we exited redundant leased facilities and terminated certain contracts.

#### Management Change

On July 3, 2012, we announced that Chief Executive Officer Doug Janzen has left the Company. Dr. William Hunter, a member of the Company's board of directors, has been appointed Chief Executive officer.

On September 20, 2012, we announced the appointment of Jennifer Archibald as Chief Financial Officer following the resignation of Curtis Sikorsky.

#### Acquisition of Correvio

On November 18, 2013, we completed the acquisition of 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 shares (pro forma ownership of approximately 16.6%) and a deferred cash consideration of \$12.0

million. The deferred cash consideration will be 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.

#### Establishment of European presence

During Q1-2013, we appointed Steen Juul-Möller, M.D., Ph.D./DMSc., FESC as our European Medical Director to oversee our clinical and medical affairs activities. We also began establishing a small, direct sales force in Europe to promote BRINAVESSTM. During Q2-2013, Jürgen Polifka, Ph.D. joined our management team as General Manager, Sales and Marketing Europe to oversee our commercialization activities in Europe. During Q3-2013, we continued to build our direct sales force in Europe as well as the necessary infrastructure to support it, and in Q4-2013, we complemented our coverage through the acquisition of Correvio. Although BRINAVESS<sup>TM</sup> is not currently marketed in all of the European countries, our sales force, following the acquisition of Correvio, now has the capability to cover Germany, Spain, Italy, France, the United Kingdom, Sweden, Norway, Finland, Denmark, the Netherlands and Luxembourg.

#### Share consolidation

On April 3, 2013, our shareholders approved the consolidation of our issued and outstanding common shares on the basis of one (1) post-consolidation common share for every five (5) pre-consolidation common shares. Our common shares began trading on a post-consolidation basis on the NASDAQ and TSX on April 12, 2013. All share and per share information in this document gives effect to the share consolidation on a retroactive basis, unless otherwise indicated.

#### 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 our common shares having an aggregate offer price of up to \$8.9 million in “at the market” distributions effected from time to time pursuant to an At Market Sales Issuance Agreement that we entered into on the same day with MLV & Co. LLC, as agent (the “ATM Offering”). As at the date of this document, we have sold 30,513 of our common shares in the ATM Offering. No sales in the ATM Offering will be made in Canada.

On March 11, 2014, we completed a prospectus offering of 1,500,000 common shares from treasury of Cardiome for gross proceeds of CAD \$15 million and 1,500,000 common shares in a secondary offering from CarCor Investment Holdings LLC, the shareholder from which we purchased Correvio, for gross proceeds of CAD \$15 million, both at CAD \$10.00 per common share, for a combined offering of CAD \$30 million. 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

## NARRATIVE DESCRIPTION OF THE BUSINESS

### General

We are a specialty pharmaceutical company dedicated to the development and commercialization of cardiovascular therapies that will improve the quality of life and health of patients suffering from heart disease. 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<sup>TM</sup> and AGGRASTAT<sup>TM</sup>, which are commercially available in numerous markets outside of the United States.

## 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 atrial fibrillation to sinus rhythm in adults (for non-surgery patients with atrial fibrillation of seven days or less) and for use in post-cardiac surgery patients with atrial fibrillation of three days or less. BRINAVESS™ is recommended as a first-line therapy in the European Society of Cardiology atrial fibrillation guidelines for the cardioversion of recent-onset atrial fibrillation in patients with no, or moderate, structural heart disease.

AGGRASTAT™ (tirofiban HCL) is a reversible GP IIb/IIIa inhibitor (an intravenous anti-platelet drug) for use in Acute Coronary Syndrome (ACS) patients. We acquired the ex-U.S. marketing rights to AGGRASTAT™ as part of the Correvio acquisition. Sales of AGGRASTAT™ were approximately 84% of total revenues in fiscal 2013 (2012 – nil).

Both BRINAVESS™ and AGGRASTAT™ are available commercially outside of the United States either directly through our own sales force in Europe or via our distributor and partner network in other parts of the world. Sales of BRINAVESS™ were 16% of total revenues in fiscal 2013 (2012 – 100%).

## Pre-clinical Projects

We continue to support pre-clinical research and development work externally through academic research collaborations. The focus of the technology is on modulating cellular proteins (ion channels) that gate the movement of ions across the cell membranes to control a variety of essential functions ranging from the contraction of muscles, to the secretion from glands, to responses to foreign bodies and inflammation. The wide variety of such proteins provides a broad area for the development of therapeutics useful in a large number of human disorders.

## Our Strategy

Our core strategy is to create a hospital-based, profitable and sustainable pharmaceutical company through the acquisition, development and commercialization of innovative, cardiovascular products that we believe will help patients, health care providers, and healthcare systems provide safer, more efficacious and cost effective treatments for heart disease. Key elements of our strategy include:

- *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. Priority will be given to later-stage or approved product opportunities that could be sold through our European, in-hospital, cardiology sales force.
- *Successfully obtaining approval for vernakalant worldwide.* We intend to continue to advance the approval and development of vernakalant (IV) in the United States, Canada and elsewhere and vernakalant (oral) worldwide. We intend to pursue a regulatory strategy to further develop both intravenous and oral vernakalant in order to achieve its maximum potential in the treatment of acute and more chronic forms of atrial fibrillation.
- *Successfully commercializing BRINAVESS™ in currently approved countries.* We intend to continue to sell BRINAVESS™ in countries where it is presently approved, marketed and reimbursed. Initially, we intend to focus our sales efforts on promoting BRINAVESS™ product sales in Europe via a fully dedicated direct sales force operating in eight countries in Western Europe. We also intend to seek reimbursement in countries where the product has regulatory approval but has not launched (namely France, Italy, the United Kingdom and Belgium) in order to broaden the commercial opportunity for BRINAVESS™.
- *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 (STEMI – ST-elevated myocardial infarction) intended for primary PCI (percutaneous coronary intervention).” AGGRASTAT™ has already been granted this expanded label in some countries.

- *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, commercial manufacturing, and distribution to external organizations.
- *Continuing to support our pre-clinical programs in ion channel research 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. Whenever possible, we intend to offset the costs of these programs with funding from applicable granting agencies.

## **Our Products and Product Candidates**

We currently have two commercially available pharmaceutical products, BRINAVESS™ and AGGRASTAT™. BRINAVESS™, the intravenous formulation of vernakalant, has been approved in Europe, in some countries in Central and South America, Asia and the Middle East. We hold the global development and commercialisation rights for all indications for vernakalant (IV) and oral on a royalty-free basis, subject to the ongoing transfer of certain rights from Merck and its affiliates to us, which has been delayed in certain jurisdictions due to routine regulatory requirements and is expected to be completed in the first half of 2014. AGGRASTAT™ has been approved in numerous countries worldwide and we hold the global marketing rights outside of the United States. We also have several preclinical stage programs.

In 2013, we began establishing a direct, in-hospital sales force in select European markets in support of BRINAVESS™ and have complemented our coverage through the acquisition of Correvio. Although BRINAVESS™ is not currently marketed in all of the major European countries, our sales force, following the acquisition of Correvio, now has the capability to cover Germany, Spain, Italy, France, the United Kingdom, Sweden, Norway, Finland, Denmark, the Netherlands and Luxembourg. We have partnered with AOP Orphan Pharmaceutical AG (“AOP Orphan”) to commercialize BRINAVESS™ in select European markets where we do not currently operate directly, including Austria and parts of Eastern Europe. We expect that AOP Orphan will support us in obtaining product registrations required for the marketing and sale of BRINAVESS™ in those markets where this is required and will actively call on customers to promote the product. In addition, we entered into commercialization and sales agreements with Tzamal Medical Ltd. (“Tzamal”) in Israel, LifePharma (Z.A.M.) Ltd. in Cyprus, Biospifar S.A. in Colombia and Algorithm S.A.L. (“Algorithm”) in certain Middle Eastern and North African countries. We have also entered into agreements with Oriola Oy in Finland, Nomeco A/S in Denmark and Tamro AB in Sweden for warehousing, consignment and distribution services. Correvio also has a significant distributor network, some of which overlap with our existing network. These distributors include, amongst others, Aspen Global Incorporated, Algorithm and Tzamal.

The following chart summarizes our current products and product candidates, including the principal disease being targeted and the development stage for each program.

	Preclinical	Phase I	Phase II	Phase III	Approved
Atrial Fibrillation	<b>BRINAVESS™ (vernakalant IV)</b>				
	Europe and select countries in Rest of World	[Progress bar: ~95%]			
	Other markets (incl. USA)	[Progress bar: ~75%]			
	<b>Vernakalant (Oral)</b>	[Progress bar: ~45%]			
ACS	<b>AGGRASTAT™ (ex-US)</b>				
Other	<b>External Collaborations</b>	[Progress bar: ~10%]			

Notes:

- (1) In October 2010, the Phase 3, ACT 5 study of vernakalant (IV) was suspended and subsequently terminated in the United States. We have not obtained permission from the FDA to restart the trial.

***Vernakalant for Atrial Fibrillation***

Atrial fibrillation 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 atrial fibrillation.

The risk of developing atrial fibrillation increases with age. The lifetime risk of developing atrial fibrillation 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 new chemical entity designed by Cardiome's scientists to treat atrial fibrillation 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 atrial fibrillation. Its mechanism of action involves the selective blockade of multiple ion channels in the heart that are known to be active during episodes of atrial fibrillation. 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 atrial fibrillation recurrence in patients who have had one or more previous episodes of atrial fibrillation.

*Vernakalant (IV)*

Cardiome has exclusive, global marketing rights to BRINAVESS™, the intravenous formulation of vernakalant, and is responsible for all future development and commercialization of the product, subject to ongoing transfer of certain rights from Merck and its affiliates to us, which has been delayed in certain jurisdictions due to routine regulatory requirements and is expected to be completed in the first half of 2014. Prior to September 2013, global marketing rights to vernakalant (IV) were held by Merck under two collaboration and license agreements.

## *Regulatory Matters*

### North America

In December 2006, our former partner, Astellas, filed a New Drug Application (“NDA”) for vernakalant with the U.S. Food and Drug Administration (“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 atrial fibrillation patients without a history of heart failure in October 2009.

In October 2010, a clinical hold was placed on the ACT 5 study of vernakalant (IV) following a single unexpected serious adverse event of cardiogenic shock experienced by a patient with atrial fibrillation who received vernakalant (IV).

In July 2011, Merck acquired the rights for the development and commercialization of vernakalant (IV) in North America. Merck and the FDA agreed to terminate the ACT 5 study. Merck began discussions with the FDA to determine the next steps for the development of vernakalant (IV) in the United States.

In May 2013, we completed the transfer of sponsorship of the U.S. Investigational New Drugs (“INDs”) for vernakalant (IV) and vernakalant (oral) and the transfer of the NDA for vernakalant (IV) from Merck to us. We intend to continue discussions with the FDA regarding potential development paths for the vernakalant programs in the United States.

### Rest of World (Outside North America)

In July 2009, our former partner Merck submitted a Marketing Authorization Application (“MAA”) to the European Medicines Agency (“EMA”) seeking marketing approval for vernakalant (IV) in the European Union, and as a result of the submission we received a \$15 million milestone payment from Merck.

In June 2010, the Committee for Medicinal Products for Human Use of the EMA recommended marketing approval of vernakalant (IV) for the conversion of recent onset atrial fibrillation to sinus rhythm in adults and in September 2010, vernakalant (IV) received marketing approval under the trade name BRINAVESS™ in the European Union, Iceland and Norway. This milestone triggered a \$30 million milestone payment from Merck. After receipt of marketing approval, Merck began its commercial launch of BRINAVESS™ in a number of European countries.

In June 2013, we announced the decision by the European Commission to allow the transfer of the centrally-approved marketing authorization for BRINAVESS™ from Merck to Cardiome.

### *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 studies (ACT I, ACT II and ACT III) and in an active comparator trial versus intravenous amiodarone. Based on data from 1018 patients in eight Phase 2 and Phase 3 trials, BRINAVESS™ has been approved in the European Union, New Zealand 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:  $\leq 7$  days duration
- For post-cardiac surgery patients:  $\leq 3$  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, and our analysis of the study is ongoing.

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.

#### *Former Collaborations*

##### North America

In October 2003, we entered into a collaboration and license agreement, referred to as the “North American Vernakalant (IV) Agreement”, with an affiliate of Astellas. We granted Astellas an exclusive license to vernakalant (IV) and its related technology to develop, make and sell intravenous or injectable formulations of vernakalant in North America for any and all indications including the treatment of atrial fibrillation and atrial flutter, including a right to sublicense to third parties.

Under the terms of the North American Vernakalant (IV) Agreement, Astellas paid us an up-front payment of \$10 million, invested \$4 million in us at a 25% premium to our then current share price, and agreed to pay us milestone payments of up to \$56 million based on the achievement of specified development and commercialization milestones. In addition, should the product have been approved for use by the applicable regulatory authorities in North America, we would have been entitled to royalty payments of approximately 25% of total North American end-user sales revenue, as well as royalties based on future net sales and sublicense revenue. Following the successful completion of ACT I, in February 2005 we announced the collection of our first milestone payment of \$6 million from Astellas.

In July 2006, we amended our North American Vernakalant (IV) Agreement with Astellas. Under the amended terms of our North American Vernakalant (IV) Agreement, Astellas agreed to fund all of the costs associated with the re-submission of the NDA for vernakalant (IV), including the engagement of external consultants, and Astellas paid to us a \$10 million milestone payment on the re-submission of the NDA for vernakalant (IV) to the FDA. In addition, a \$15 million milestone payment would have been payable on approval of vernakalant (IV) by the FDA.

In October 2010, Astellas suspended patient enrollment in the ACT 5 study of vernakalant (IV) following a single unexpected serious adverse event of cardiogenic shock experienced by a patient with atrial fibrillation who received vernakalant (IV).

In July 2011, Merck acquired the rights for the development and commercialization of vernakalant (IV) in North America from Astellas. All terms, responsibilities and payments that Astellas committed to under the North American Vernakalant (IV) Agreement were assumed by Merck without change.

Merck was responsible for 75% of all the remaining development costs related to seeking regulatory approval in North American markets, and all marketing and commercialization costs for vernakalant (IV) in North America. Under the North American Vernakalant (IV) Agreement we had the right to additional milestone payments with respect to any subsequent drugs developed under the agreement.

In September 2012, Merck gave notice to us of its termination of the North American Vernakalant (IV) Agreement. In May 2013, we announced the completion of the transfer of sponsorship of the U.S. Investigational NDAs for vernakalant (IV), the transfer of the U.S. NDA for vernakalant (IV), and the transfer of sponsorship of all vernakalant Canadian Clinical Trial Applications from Merck to us. All marketing rights for North America have been returned to us.

#### Outside North America

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

Under the terms of the Collaboration Agreement, 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, based on the achievement of certain milestones associated with the development and approval of vernakalant products, and up to \$100 million for milestones associated with approvals in other subsequent indications of both the intravenous and oral formulations. Also, we were eligible to receive tiered royalty payments on sales of any approved products and had the potential to receive up to \$340 million in additional milestone payments based on achievement of significant sales thresholds. Merck was responsible for all costs associated with the development, manufacturing and commercialization of these product candidates.

In July 2009, we received a \$15 million milestone payment as a result of Merck's affiliate filing an MAA with the EMA seeking marketing approval for vernakalant (IV) in the European Union. In September 2010, we received a \$30 million milestone payment from Merck as a result of receiving marketing approval for vernakalant (IV) in the European Union, Iceland and Norway under the trade name BRINAVESS™. Under the Collaboration Agreement, we also shipped and were reimbursed for \$7 million of clinical supplies provided to Merck.

In September 2012, Merck gave notice to us of its termination of the Collaboration Agreement. On April 25, 2013, we entered into a Transition Agreement with Merck (the "Transition Agreement") to amend and supplement the provisions of the Collaboration Agreements governing their rights and responsibilities in connection with the termination of the Collaboration Agreement and transfer of rights to, and responsibilities for, vernakalant to us. Pursuant to the Transition Agreement, we took responsibility for worldwide sales, marketing, and promotion of vernakalant (IV) on April 25, 2013. Regulatory product rights and product distribution responsibility were transferred to us upon transfer of the marketing authorizations in the relevant countries, subject to the ongoing transfer of certain rights from Merck and its affiliates to us, which has been delayed in some jurisdictions due to routine regulatory requirements and is expected to be completed in the first half of 2014.

On June 21, 2013, the European Commission approved the transfer of the centrally-approved marketing authorization for BRINAVESS™ from Merck to us. We are now the marketing authorization holder for BRINAVESS™ in the member states of the European Union. As a result, royalties on sales and the promotional services fee we previously received from Merck ceased on July 1, 2013 and we began benefiting from all sales of BRINAVESS™ throughout the world.

On September 16, 2013, we announced the completion of the transfer from Merck to us of commercialization responsibility for BRINAVESS™ in the European Union and the responsibility to complete the post-marketing study for BRINAVESS™. We are now supplying BRINAVESS™ under our own trade dress in the European Union.

As part of the Collaboration Agreement, Merck granted us a secured, interest-bearing credit facility of up to \$100 million accessible in tranches over several years commencing in 2010. In February 2010, we received an advance of \$25 million from a Merck affiliate under the credit facility. In January 2012, we received another advance of \$25 million from a Merck affiliate under the credit facility. In December 2012, we reached an agreement with Merck to settle our debt obligation. In 2013, we paid Merck \$20 million to settle our outstanding debt of \$50 million plus accrued interest of \$2 million owed to Merck. The settlement between us and Merck terminated the credit facility, extinguished all outstanding debt obligations, and released and discharged the collateral security taken in respect of the advances under the line of credit.

### Vernakalant (oral)

Vernakalant (oral) is being developed as an oral maintenance therapy for the long-term prevention of atrial fibrillation recurrence. In July and September 2006, we announced positive top line results for the sequential 300 mg and 600 mg dosing groups, respectively, from the Phase 2a pilot study of vernakalant (oral). In July 2008, we announced positive clinical results from the Phase 2b clinical study of vernakalant (oral) to further evaluate the safety and tolerability, pharmacokinetics and efficacy of vernakalant (oral).

In April 2009, we entered into the Collaboration Agreement with Merck for the development and commercialization of vernakalant. The agreement provided an affiliate of Merck with exclusive global rights to vernakalant (oral) and exclusive rights outside of the United States, Canada and Mexico to vernakalant (IV).

In November 2011, Merck completed an additional multiple rising-dose Phase I study to explore the safety, tolerability, pharmacokinetics and pharmacodynamics of higher doses of vernakalant (oral) than previously studied in healthy subjects and that in this study, vernakalant (oral) was well-tolerated at increased exposures. We also announced that Merck had scheduled, to start in late 2011, an additional Phase I trial assessing the safety and tolerability of vernakalant (oral) when dosed for a more extended period of time at higher exposures.

In March 2012, Merck informed us of its decision to discontinue further development of vernakalant (oral). In September 2012, we announced that Merck would return the global marketing and development rights for vernakalant (oral) to us in connection with Merck's termination of the Collaboration Agreement. In May 2013, we completed the transfer of sponsorship of the IND for vernakalant (oral) from Merck to us.

### *Clinical Trials*

In an oral dosing study in humans completed in December 2002, vernakalant was shown to have significant oral bioavailability, suggesting that it could also be used for long-term oral therapy. Based on these results, we conducted a series of Phase 1 clinical studies to evaluate vernakalant (oral) as a candidate for further clinical development as an oral maintenance therapy for the long-term prevention of atrial fibrillation recurrence. In August 2005, we announced the successful completion of the Phase 1 studies required to advance clinical testing of vernakalant (oral) into a Phase 2 study.

In July and September 2006, we announced positive top-line results from a Phase 2A pilot trial evaluating 300 mg and 600 mg dosing groups, of vernakalant (oral). For the 300 mg dosing group, 61% (33 of 54) of patients receiving vernakalant (oral) completed the study in normal heart rhythm, as compared to 43% (24 of 56) of all patients receiving placebo. For the 600 mg dosing group, 61% (30 of 49) of patients receiving vernakalant (oral) completed the study in normal heart rhythm, as compared to 43% (24 of 56) of all patients receiving placebo.

A Kaplan-Meier analysis of the results demonstrated a statistically significant efficacy difference between the 300 mg dosing group and the placebo group ( $p=0.048$ ). The difference between the 600 mg dosing group and the placebo group trended toward but did not reach statistical significance ( $p=0.060$ ). A combined analysis of all drug group patients relative to the placebo group also demonstrated a statistically significant difference ( $p=0.028$ ).

The safety data for both dosing groups suggests that vernakalant (oral) appears well-tolerated over the one-month dosing period within the target population. During the 28 days of oral dosing, serious adverse events occurred in 8% of all placebo patients, 10% of patients in the 300 mg dosing group, and 11% of patients in the 600

mg dosing group. Potentially drug-related serious adverse events occurred in 1% of all placebo patients, 4% of patients in the 300 mg dosing group and 5% of patients in the 600 mg dosing group. There were no cases of drug-related “Torsades de Pointes” (an uncommon type of ventricular arrhythmia).

In early 2007, we initiated a Phase 2b clinical study of vernakalant (oral) to further evaluate the safety and tolerability, pharmacokinetics and efficacy of vernakalant (oral) in up to 90 days of oral dosing in patients at risk of recurrent atrial fibrillation. The study included four dosing groups, three of which received the active drug and one that received placebo. Patients received a 150 mg, 300 mg or 500 mg dose of vernakalant (oral) or placebo twice per day. After the first three days, patients still in atrial fibrillation were electrically cardioverted. Successfully cardioverted patients continued to receive vernakalant (oral) or placebo for the remainder of the 90-day trial and were monitored throughout the dosing period. A total of 735 patients were randomized in the study, of which 605 were successfully cardioverted to sinus rhythm and entered the maintenance phase and therefore were evaluated for efficacy.

In March 2008, we announced positive interim analysis results from the Phase 2b trial. In July 2008, we announced final clinical results from the Phase 2b trial. The final results demonstrated that the 500 mg dosing group significantly reduced the rate of atrial fibrillation relapse as compared to the placebo group (two-sided log rank,  $p=0.0221$ ). The median time to recurrence of atrial fibrillation was greater than 90 days for the 500 mg dosing group, compared to 27 days for the placebo group. Of the patients in the 500 mg dosing group ( $n=150$ ), 51% completed the study in normal heart rhythm compared to 37% of patients receiving placebo ( $n=160$ ). Both the 150 mg ( $n=147$ ) and 300 mg ( $n=148$ ) dosing groups also trended toward efficacy in preventing relapse to atrial fibrillation, but were not statistically significant when compared with the placebo group. These results provide evidence of a clear dose response, with 500 mg dose taken twice per day proving to be the effective dose to prevent the recurrence of atrial fibrillation in this trial.

There was no significant difference in the incidence of serious adverse events between treatment groups. Potentially drug-related serious adverse events occurred in 0.5% of placebo patients, 1.1% of patients in the 150 mg dosing group, 0.5% of patients in the 300 mg dosing group and 0.5% of patients in the 500 mg dosing group. There were no cases of “Torsades de Pointes”. There were four deaths in the study, all unrelated to vernakalant (oral), with two such patients in the placebo group, one patient in the 150 mg dosing group and one patient in the 300 mg dosing group. There were no deaths in the 500 mg dosing group.

### **AGGRASTAT™ for Acute Coronary Syndrome**

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 or 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™ is administered intravenously, and has been on the market for many years with an excellent safety and efficacy profile.

### **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 compliance, commercial manufacturing, and distribution to external organizations. In addition, we support our pre-clinical programs in ion channel research 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.”*

## **Employees**

As of the date of this annual information, we have approximately 75 employees located in Vancouver, British Columbia, Chester, 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.”*

## **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 BRINAVESS™ and AGGRASTAT™ 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™, 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™ 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™ 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™”* 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.

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. However, we may have royalty obligations if any of our other assets are commercialized. See *“Risk Factors – We rely on proprietary technology, the protection of which can be unpredictable and costly.”*

## **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.

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 PDUFA, as amended, applicants must pay a substantial fee to the FDA for an NDA and any supplements 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 usually reviewed for administrative completeness and reviewability within 45 to 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 and these performance goals have not been strictly adhered to over the past few years. Moreover, the outcome of the review, even if generally favourable, typically is not an actual approval but an action 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 Marketing Authorization Application (“MAA”) is built for submission and review. A medicinal product may only be placed on the market in the European Economic Area (“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 currently underway for vernakalant (IV), 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.

## 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, including 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 12 months ended December 31, 2013.*

**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 our business, in particular the further development of our product candidates, vernakalant (IV) in the United States (and elsewhere) and vernakalant (oral) worldwide. 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™ 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 for BRINAVESS™ in the various markets where we hope to sell our products;
- 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 experience setbacks in our progress with pre-clinical studies and clinical trials are delayed;
- we are required to perform additional pre-clinical studies and clinical trials; or
- we elect to develop, acquire or license new technologies, products or businesses.

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 sufficient capital is not available, we may be required to delay our business expansion or our research and development projects, either of which could have a material adverse effect on our business, financial condition, prospects or 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 have, prior to the launch of BRINAVESS™ and the acquisition of AGGRASTAT™, only been engaged in research and development. Before Merck 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. Excluding the gain on settlement of debt, net losses for the 12-month periods ended December 31, 2013 and 2012 were approximately \$16.1 million and \$29.5 million, respectively. As of December 31, 2013, our accumulated deficit was \$300.7 million. Our losses have resulted in large part from the significant research and development expenditures we have made in seeking to identify and validate new drug targets and compounds that could become marketed drugs. Although we will seek a new collaboration partner for the further research, development, testing and approval of vernakalant (IV) and vernakalant (oral), we anticipate that we will continue to incur these types of expenses in connection with our collaboration. We cannot assure you that we will generate sufficient revenues in the future or achieve profitable operations.

**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.**

On November 18, 2013, we announced that we completed the acquisition of Correvio and its pharmaceutical product AGGRASTAT™ in order to obtain the ability to market and sell AGGRASTAT™ outside of the United States, as well as for the business infrastructure provided by Correvio. We may not be able to fully realize the anticipated future benefits and synergies of the acquisition on a timely basis or at all. The acquisition involves challenges and risks, including risks that the transaction does not advance our business strategy or that we will not realize a satisfactory return. In addition, the seller's indemnification of us for misrepresentations in representations, breaches of covenants or certain tax matters is capped at the actual consideration paid by us (or \$1 million in some cases). The potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, revenue recognition or other accounting practices, taxes, corporate governance and internal controls, regulatory compliance, employee, customer or partner disputes or issues and other legal and financial contingencies could decrease or eliminate the anticipated benefits and synergies of the Correvio acquisition and could negatively affect our future business and financial results.

The overall success of the Correvio acquisition will depend, in part, on our ability to realize the anticipated benefits and synergies from combining and integrating the Correvio business into our existing business including our ability to successfully manage the sales force acquired in the Correvio transaction. Integration of Correvio and AGGRASTAT™ requires significant management attention and expansion of our staff in marketing, sales and general and administrative functions. We may have difficulties in the integration of the acquired company's departments, systems, including accounting, human resource and other administrative systems, technologies, books and records, and procedures, as well as in maintaining uniform standards, controls, including internal control over financial reporting required by Canadian securities laws, the Sarbanes-Oxley Act of 2002, and

related procedures and policies. If we cannot integrate the acquisition successfully, it could have a material adverse impact on our business, financial condition and results of operations.

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. 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.

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

AGGRASTAT™ is a mature product which is beginning to face 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, Integrilin from Merck & Co., Inc., and MediCure Inc. Antiarrhythmics that BRINAVERS™ competes with include generic competitors such as flecainide, propafenone, ibutilide and amiodarone.

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 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. However, 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, failure to adhere to good manufacturing practices, non-compliance with clinical protocols or 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. Although our shareholders would not have personal liability for such damages, 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 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, 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 and chemical manufacturers are subject to various regulatory inspections, including those conducted by the FDA, to ensure strict compliance with GMP 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.

**Government legislation could adversely impact our ability to obtain product reimbursement and economically price our products.**

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 UK and France. There can be no assurance that we will be reimbursed. 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.

**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 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, 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 HCI contains a number of issued patents in the United States and worldwide, although a large number of these patents have expired or will be expiring within the next few years. There can be no assurance that we will be able to renew these patents. We intend to file, when appropriate, additional patent applications with respect to inventions. However, because the patent positions of life sciences companies are highly uncertain and involve complex legal and factual questions, it is uncertain that any patents will be issued or that, if issued, they will be of commercial value.

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 we may sell to 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 the 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.

**Our success is dependent upon our corporate collaborations with third parties in connection with services we will need for the development of our products.**

The success of our business is largely dependent on our ability to enter into corporate collaborations regarding the development, clinical testing, and regulatory approval of our product candidates currently under development. We have in the past relied on Astellas and Merck for the co-development and commercialization of vernakalant (IV) and vernakalant (oral) but the collaborations ended in July 2011 and September 2012, respectively. We are currently seeking corporate collaboration or partnership opportunities for the continuing development of vernakalant (IV) in North America and vernakalant (oral) generally. We cannot assure you that we will be able to establish any such corporate collaborations or partnerships on favourable terms, or at all, or that we will successfully manage such relations. Even if we are successful in establishing such relationships, these collaborations may not result in the successful development of our product candidates or the generation of revenue. Management of these relationships will require significant time and effort from our management team and effective allocation of our resources. As well, any collaboration agreements will subject us to the risk that certain decisions, such as the establishment of budgets, development and promotion strategies and specific tasks, are under the control of our collaboration partners, and that deadlocks, failures in the development or differing priorities may adversely affect the activities conducted through the collaboration arrangements. Any conflicts that we may have with our future partners during the course of these agreements or at the time of their renewal or renegotiation may negatively affect the marketing of certain of our products and may cause a decline in our revenues and affect our results of operations.

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

Before we 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. If we find a collaboration partner for the development of vernakalant (oral), the clinical trials are expected to continue for several years, although costs associated with vernakalant (oral) may well be shared with our collaboration partner. The Phase 3 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 we obtain permission from the FDA to restart the trial, the proposed scope and duration of the vernakalant (IV) clinical trials required to obtain regulatory approval for vernakalant (IV) 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 successful. The timing of the commencement, continuation and

completion of clinical trials, including the PASS, may be subject to significant delays relating 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 have suffered significant setbacks in advanced clinical trials, even after positive results in earlier trials, including Cardiome. 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. Pre-clinical data and the clinical results we have obtained for vernakalant (IV), vernakalant (oral) 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.

We will be required to demonstrate through larger-scale clinical trials that vernakalant (oral) is safe and effective for use in a diverse population before we can seek regulatory approvals for its commercial sale. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical and post-approval trials. If vernakalant (IV) or vernakalant (oral) fail 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 Phase 3, ACT 5 study of vernakalant (IV) had been suspended and the vernakalant (IV) clinical development program 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). Although the trial's independent Data Safety Monitoring Board reviewed the case and recommended the trial continue, the FDA has requested that full data regarding this event be provided for their review prior to determining what steps, if any, are needed to restart the study. After the transfer of rights from Astellas to Merck, Merck terminated the ACT 5 study. We intend to continue discussions with the FDA regarding the potential path for vernakalant (IV) in the United States. However, if the FDA does not permit us to restart the development program, we may not be able to obtain approval to market vernakalant (IV) in the United States. We have yet to reach agreement with the FDA on an appropriate development path forward in the United States and 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.

#### **Our approved products may not achieve or maintain expected levels of market acceptance, which could have a material adverse effect on our business, financial condition and results of operations and could cause the market value of our securities to decline.**

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 securities 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 on two products for substantially all of our current revenues. If the volume or price of these products decline or the costs of related manufacturing, distribution or marketing increase, it could have a material adverse effect on our business, financial condition and results of operations and could cause the market value of our securities to decline.**

Sales of a limited number of our products represent substantially all of our current revenues. If the volume or pricing of our existing significant products decline in the future, or our cost to manufacture, distribute our existing significant products increase in the future, our market our business, financial condition and results of operations could be materially adversely affected and this could cause the market value of our securities 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 securities could be significant.

**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.

In addition, many European countries have been severely impacted by the widespread economic recession that began in 2008, the effect of which continues in 2014. 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 policies and estimates regarding returns, allowances and chargebacks may reduce revenue in future fiscal 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. In particular, our limited direct sales experience with BRINAVESS™ may limit our ability to establish appropriate reserves. Inadequate reserves could have a material adverse effect on our business, financial condition, and results of operations.

**Our inventory has 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 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 rights related to BRINAVESS™ as well as the AGGRASTAT™ and our associated licenses. As of December 31, 2013, the carrying value of our intangible asset relating to BRINAVESS™ and AGGRASTAT™ were approximately US\$1.3 million and US\$17.3 million, respectively. In accordance with U.S. GAAP, 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 income 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 business has expanded internationally and as a result, a significant portion of our revenues, expenses, current assets and current liabilities are preliminary denominated in Euros, Canadian dollars and other foreign currencies but our financial statements are expressed in U.S. dollars. A decrease in the value of such foreign currencies relative to the U.S. dollar could result in losses in revenues 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 Exchange Act, 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 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.

**Failure to comply with the United States Foreign Corrupt Practices Act (“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 (“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 OECD 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 Japan and 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 regulation 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, EMA and similar agencies in other jurisdictions to maintain records regarding product safety and to report to regulatory authorities serious or unexpected adverse events. 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 GMP. Manufacturers and their facilities are subject to continual review and periodic inspections. Failure to comply with GMP 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 GMP requirements. Failure or delay by any manufacturer of our products to comply with GMP 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 GMP 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™, AGGRASTAT™, vernakalant (oral) 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 26, 2014, we had 16,520,072 common shares and no preferred shares of any series issued and outstanding. In addition, as of March 26, 2014, there were 1,140,912 common shares issuable upon the exercise of outstanding stock options at a weighted-average exercise price of Cdn.\$4.44 per common share and 219,088 common shares reserved for future grant or issuance under our stock option plan.

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 33 ⅓% 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 NASDAQ in the United States (trading symbol: CRME). Our common shares began trading post 5 to 1 consolidation on April 12, 2013. All prices and trading volume have been adjusted retroactively to reflect the effects of share consolidation.

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

<u>Month</u>	<u>High</u>	<u>Low</u>	<u>Close</u>	<u>Average Daily Volume</u>
January 2013	2.55	1.98	2.40	20,665
February 2013	2.70	1.95	2.10	19,144
March 2013	2.45	1.63	1.90	8,390
April 2013	2.50	1.78	2.18	6,574
May 2013	2.27	1.89	2.10	11,886
June 2013	2.15	1.83	2.04	8,992
July 2013	2.35	2.02	2.29	3,485
August 2013	2.34	2.05	2.14	6,508
September 2013	4.12	2.15	3.66	19,515
October 2013	5.75	3.51	4.55	28,719
November 2013	7.50	3.77	6.75	35,163
December 2013	7.35	6.25	6.70	11,977
January 2014	8.43	6.57	7.96	10,936
February 2014	12.02	7.33	10.75	91,452
March 1-25, 2014 <sup>(1)</sup>	11.23	8.52	9.61	82,068

Notes:

(1) March 25, 2014 was the last trading day prior to the date of this annual information form

The following table sets forth, for the periods indicated, the reported high and low prices (in United States dollars) and volume traded on NASDAQ.

<u>Month</u>	<u>High</u>	<u>Low</u>	<u>Close</u>	<u>Average Daily Volume</u>
January 2013	2.55	1.90	2.40	88,708
February 2013	2.68	1.95	2.00	135,342
March 2013	2.44	1.58	1.80	109,910
April 2013	2.50	1.61	2.17	72,090
May 2013	2.27	1.85	2.00	51,400
June 2013	2.11	1.80	1.95	19,469
July 2013	2.26	1.92	2.20	26,026
August 2013	2.26	1.90	2.11	32,200
September 2013	4.05	2.05	3.54	188,764
October 2013	5.60	3.41	4.35	221,288
November 2013	7.15	3.58	6.29	200,071
December 2013	6.95	5.87	6.23	60,483
January 2014	7.75	6.08	7.14	106,550
February 2014	11.00	6.61	9.70	251,930
March 1-25, 2014 <sup>(1)</sup>	10.13	7.55	8.57	200,325

Notes:

(1) March 25, 2014 was the last trading day prior to the date of this annual information form

#### PRIOR SALES

The following table sets forth information in respect of our common shares that we issued upon the exercise of options granted under our incentive stock option plan during the last completed financial year:

<u>Exercise Date</u>	<u>Number of Shares</u>	<u>Exercise Price</u>
December 5, 2013	2,750	<u>Cdn.\$1.70</u>
December 16, 2013	2,442	<u>Cdn.\$1.70</u>
December 17, 2013	1,154 <sup>(1)</sup>	<u>Cdn.\$1.70</u>
February 7, 2014	31,282 <sup>(2)</sup>	<u>Cdn.\$1.70</u>
<b><u>Total</u></b>	<b><u>37,628</u></b>	

- (1) Common shares issued upon cashless exercise of 1,518 options.  
(2) Common shares issued upon cashless exercise of 40,000 options.

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 previous twelve month period.

<u>Grant Date</u>	<u>Number of Options</u>	<u>Grant Price</u>
March 21, 2013	288,000	<u>Cdn.\$1.65</u>
November 20, 2013	257,000	<u>Cdn.\$5.10</u>
<b><u>Total</u></b>	<b><u>545,000</u></b>	

The following table sets forth information in respect of our common shares that we issued during the last completed financial year.

<u>Issuance Date</u>	<u>Number of Common Shares</u>	<u>Issue Price</u>
November 18, 2013 .....	2,481,596	\$3.88 <sup>(1)</sup>
February 18, 2014 .....	30, 513	\$9.78 <sup>(2)</sup>
March 11, 2014 .....	1,500,000	Cdn.\$10.00 <sup>(3)</sup>
<b><u>Total</u></b> .....	<b><u>4,012,109</u></b>	

- 
- (1) Common shares were issued to the seller as partial consideration for the acquisition of Correvio on November 18, 2013.
  - (2) Common shares were sold in at the market distributions pursuant to Cardiome’s prospectus supplement dated February 18, 2014. The stated issue price represents the average issue price of the common shares sold during the day.
  - (3) Common shares were issued pursuant to an underwritten offering in connection with Cardiome’s short form prospectus dated March 5, 2014.

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 twelve month period preceding the date of this document.

#### **ESCROWED SECURITIES**

To our knowledge, none of our securities are held in escrow.

#### **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.

<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>
Robert W. Rieder British Columbia, Canada Chairman of the Board of Directors <sup>(1)</sup>	April 21, 1997	September 2010 to present – Chief Executive Officer, ESSA Pharma Inc.; August 2009 to September 2010 – Executive Chairman, Cardiome Pharma Corp.; March 2007 to August 2009 – Chairman, Cardiome Pharma Corp.; March 2006 to March 2007– Vice Chairman, Cardiome Pharma Corp.; April 1998 to August 2009 – Chief Executive Officer, Cardiome Pharma Corp.

<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>
Harold H. Shlevin <sup>(2)(3)</sup> Georgia, United States Director	October 14, 2004	Oct 2012 to present – Chief Operating Officer, Galectin Therapeutics Inc.; Nov 2009 to Sept 2012 – Head of Advanced Technology Development Center – Biosciences and Start-Up Company Catalyst, Georgia Institute of Technology, Enterprise Innovation Institute; October 2008 to November 2009 – Head of Operations and Commercial Development, Altea Therapeutics Corporation; June 2006 to July 2008 – President and Chief Executive Officer, Tikvah Therapeutics Inc.
Peter W. Roberts <sup>(2)(3)</sup> British Columbia, Canada Director	September 18, 2005	July 2009 to present – Member of the Board of Directors and Audit Committee of the Canadian Public Accountability Board; April 2008 to April 2011 – Member of the Board of Directors and Chair of the Audit Committee of WebTech Wireless Inc.; December 2005 to January 2010 – Member of the Risk Oversight and Governance Board, Canadian Institute of Chartered Accountants; June 2006 to July 2007 – President, Institute of Chartered Accountants of British Columbia; November 1998 to March 2004 (retired March 2004) – Chief Financial Officer and Corporate Secretary of Sierra Wireless, Inc.
Richard M. Glickman <sup>(2)(3)(4)</sup> British Columbia, Canada Director	December 11, 2006	July 2007 to present – Retired; January 2002 to July 2007 – Co-founder, Chairman and Chief Executive Officer, Aspreva Pharmaceuticals Corporation
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.
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.

<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>
Karim Lalji British Columbia, Canada Chief Commercial Officer	September 14, 2006	October 2012 to present – Chief Commercial Officer, Cardiome Pharma Corp.; February 2007 to October 2012 – Senior Vice President, Commercial Affairs, Cardiome Pharma Corp.; September 2006 to February 2007 – Senior Vice President, Commercial Affairs, Cardiome Pharma Corp. (part-time)
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.; August 2003 to April 2005 – Vice President, Commercial Affairs, Cardiome Pharma Corp.

- 
- (1) Mr. Rieder retired from the position of our Chief Executive Officer in August 2009, a position he held since 1998, and assumed the role as Executive Chairman of the Board effective August 2009. Mr. Rieder resigned as Executive Chairman in September 2010 and became Chairman of the Board.
  - (2) Member of the Governance, Nominating, and Compensation Committee. Dr. Shlevin is the Chair of this Committee.
  - (3) Member of the Audit Committee. Mr. Roberts is the Chair of the Audit Committee.
  - (4) Lead Independent Director.

As of March 26, 2014, our directors and executive officers owned, or exercised control of or direction over, directly or indirectly, in the aggregate 3.8% of our outstanding common shares.

### **Directors and Executive Officers**

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

**Robert W. Rieder, MBA, Chairman.** Mr. Rieder is Cardiome’s Chairman of the Board of Directors and has also previously served as Cardiome’s Vice-Chairman. He served as Cardiome’s Chief Executive Officer from joining Cardiome in April 1998 until August 2009. Mr. Rieder was appointed Chairman of the Board in March 2007 and assumed the role of Executive Chairman in August 2009. Mr. Rieder has extensive experience in venture capital and in operational management. Prior to joining Cardiome, Mr. Rieder was Vice-President at MDS Ventures Pacific Inc., the Vancouver-based affiliate of MDS Capital Corp., and has served as a director for nine public and private technology companies. Mr. Rieder has also acted as Chief Operating Officer for DBA Telecom Inc., CEO for Synapse Technologies Inc. and was non-executive chairman of the board of directors of Akela Pharma Inc. Mr. Rieder is currently the Chief Executive Officer of ESSA Pharma Inc. Mr. Rieder received his MBA from the University of Western Ontario.

**Harold H. Shlevin, Ph.D., Director.** Dr. Shlevin is Chief Operating Officer of Galectin Therapeutics Inc. a public biopharmaceutical company (NASDAQ:GALT) applying its leadership in galectin science and drug development to create new therapies for fibrotic disease and cancer. Dr. Shlevin is responsible for all operational aspects of the company, including amongst others, financial management, regulatory affairs and quality assurance,

business development and commercial development. Previously he led the Georgia Institute of Technology's Advanced Technology Development Center as manager of bioscience commercialization efforts. In this general faculty role, Dr. Shlevin assisted faculty in identifying technology worthy of commercialization, catalyzed formation of new start-up bioscience companies, and mentored new company management. He is also a member of the board of directors of NeurOp, Inc., a biopharmaceutical company developing new therapies to treat central nervous system diseases. He was previously Head of Operations for Altea Therapeutics Corporation, an advanced drug delivery company focused on the delivery of therapeutic levels of water-soluble biotherapeutics and small drugs through the skin. At Altea, he was responsible for pharmaceutical research and development, clinical research, regulatory affairs, engineering, clinical and commercial manufacturing, quality assurance, information technology, facility operations and finance. Prior to this, Dr. Shlevin was a founder and the President and Chief Executive Officer of Tikvah Therapeutics, Inc., a pharmaceutical enterprise focused on late-stage development of neuroscience therapeutics. He was previously the Global Senior Vice President, and a member of the boards of Solvay Pharmaceutical, SA, Solvay Pharmaceuticals Inc. and CEO and President of Solvay Pharmaceuticals, Inc. (USA). He was also Chairman of the Board of Solvay's subsidiary Unimed Pharmaceuticals, Inc., and a member of the board of Solvay Draka, a specialty plastic company with medical device products. He has also held senior executive positions at Bausch & Lomb Pharmaceuticals, CIBA Vision Ophthalmics, CIBA-Geigy Pharmaceuticals (now Novartis) and G.D. Searle Pharmaceuticals. Dr. Shlevin has over twenty-five years of diverse healthcare business-related and global management experience. His direct skills and experience span functions from R&D through commercial operations, including many international roles. Dr. Shlevin earned a BA from Boston University, a MS and PhD in psychology from the University of Rochester Medical School and completed post-doctoral training in pharmacology at Mayo Clinic. Dr. Shlevin's experience related to his responsibilities as an audit committee member include his tenure as CEO of Solvay and as Senior Vice President where he was regularly involved in assessments and analysis of financial statements and projections and acquisitions of companies and of products as well as his tenure in business development positions at CIBA-Geigy and CIBA Vision Corporation. Dr. Shlevin has also taken courses in financial strategies.

**Peter W. Roberts, FCA, CPA (Illinois), ICD.D, Director.** Mr. Roberts retired as Chief Financial Officer and Corporate Secretary of Sierra Wireless, Inc. (NASDAQ: SWIR / TSX: SW) in March 2004. He served in this role from January 1999 until retirement, and was responsible for taking the company public on the Toronto Stock Exchange in May 1999 and a follow-on financing on NASDAQ in May 2000. Prior to joining Sierra Wireless, Inc., Mr. Roberts held senior financial roles over a fifteen-year period with Service Corporation IJK plc, The Loewen Group Inc., The Overwaitea and Save-On Foods Chain and Sydney Development Corporation. Mr. Roberts resigned as a member of the board of directors of WebTech Wireless Inc. in April, 2011. Mr. Roberts is a graduate of Touche Ross, and practiced a decade in public accounting. He holds professional accounting designations in Canada, the United States, and the United Kingdom. Mr. Roberts completed his term as President of the Institute of Chartered Accountants of British Columbia in 2007 and completed his term as Chair of the Risk Oversight and Governance Board of the Canadian Institute of Chartered Accountants in 2010. Mr. Roberts is currently a member of the board of directors of the Canadian Public Accountability Board. Mr. Roberts is a graduate of the Institute of Corporate Directors.

**Richard M. Glickman, L.L.D. (Hon), Lead Independent Director.** 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. 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 Probtex 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.

**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 Pharmaceuticals 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 3 rounds of private equity financing, the Company's IPO and listing on the Toronto Stock Exchange and NASDAQ, over \$1B in equity and debt financings, a debt restructuring and 8 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 5 countries and worldwide annual revenues exceeding \$250M. 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® 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 a director of Zalicus Inc (NASDAQ: ZLCS) and Union Medtech 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 5 years.

**Jennifer Archibald, CA, Chief Financial Officer.** Ms. Archibald is Cardiome's Chief Financial Officer, with responsibility for overseeing our 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 performing audit, tax and accounting work. She is a Chartered Accountant and earned a Bachelor of Commerce Degree from the University of British Columbia.

**Karim Lalji, Chief Commercial Officer.** Karim Lalji is Cardiome's Chief Commercial Officer. Mr. Lalji has significant experience in pharmaceutical business strategy, product commercialization and marketing, Mr. Lalji was previously Vice President of Business Strategy and New Product Commercialization at Sepracor, Inc. At Sepracor, Inc., he was responsible for the commercial success of their pipeline of drug candidates, including identifying which products to take into development and ensuring that the development program and marketing strategy resulted in successful product launches. One of the key achievements for Mr. Lalji at Sepracor, Inc. was his leadership in the development and launch of Lunesta (eszopiclone) for the treatment of insomnia. Mr. Lalji's earlier experience includes ten years with Merck & Company, where he led several successful product launches His launch experience at Merck included CRIVAN (indinavir) which was the key drug of the first triple-cocktail therapy for treatment of HIV/AIDS and FOSAMAX Once Weekly for the treatment of osteoporosis. Mr. Lalji also has cardiovascular experience from Merck & Company as the Director of Business Strategy for the cholesterol reducers and hypertension/heart failure franchises. Mr. Lalji is currently a member of the Board of Overseers at the Beth Israel Deaconess Hospital Medical Center in Boston, Massachusetts, an academic teaching hospital for Harvard Medical School. Mr. Lalji holds a Bachelor's Degree in Business Administration from Simon Fraser University and a Science Masters in Health Policy and Management from Harvard University. He was awarded the Wilinsky Prize for Academic Excellence while at Harvard.

**Sheila M. Grant, MBA, Chief Operating Officer.** Ms. Grant is Cardiome's Chief Operating Officer. Ms. Grant was most recently Cardiome's VP of Product Development, with responsibility for the overall management of the vernakalant IV and oral programs. 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. respectively. Ms. Grant holds an MBA degree from Simon Fraser University.

## 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 an event that resulted, after the director or executive officer ceased to be a director or executive officer, in the company being 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, or
  - (iii) or within a year of that person ceasing to act in that capacity, became bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency or was subject to or instituted any proceedings, arrangement or compromise with creditors or had a receiver, receiver manager or trustee appointed to hold its assets, 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:

- Akela Pharma, Inc., or Akela. Mr. Rieder is a director of Akela. Due to the late filing of its financial statements, management's discussion and analysis and annual information form for the year ended December 31, 2009, Akela applied to the British Columbia Securities Commission for a management cease trade order covering Mr. Rieder. The management cease trade order was granted on April 6, 2010 and revoked on June 29, 2010 following the filing of all required records. The management cease trade order did not affect trading in the securities of Akela generally.
- Angiotech Pharmaceuticals Inc., or 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.

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”*.

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: Peter W. Roberts, Richard M. Glickman and Harold H. Shlevin. A description of the education and 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.”

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 Peter W. Roberts 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.

### **Pre-Approval of Non-Audit Services**

All audit and non-audit services performed by our auditors for the financial year ended December 31, 2013 were pre-approved by our Audit Committee. It is our policy that all audit and non-audit services performed by our auditors will continue to be pre-approved by our Audit Committee.

### External Auditor Service Fees (By Category)

The following table sets out the fees billed to us by KPMG LLP for professional services for the financial years ended December 31, 2013 and December 31, 2012. During 2013 and 2012, KPMG LLP was our only external auditor.

	December 31, 2013	December 31, 2012
Audit Fees <sup>(1)</sup>	Cdn.\$330,500	Cdn.\$235,000
Audit-Related Fees <sup>(2)</sup>	Nil	Nil
Tax Fees <sup>(3)</sup>	Cdn.\$80,279	Cdn.\$60,500
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 or shareholders, owning or exercising control or direction over more 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 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 have not, during our financial year ended December 31, 2013, entered into any material contracts and do not have any material contracts entered into prior to our financial year ended December 31, 2013 but still in effect, other than contracts in the ordinary course of business, except for the following:

- (1) Registration rights agreement entered into on November 18, 2013 in connection with the acquisition of Correvio described in the section titled “General Development of the Business”.
- (2) Stock and asset purchase agreement entered into on November 18, 2013 in connection with the acquisition of Correvio described in the section titled “General Development of the Business”.

- (3) Transition agreement entered into on April 25, 2013 with Merck described in the section titled “Narrative Description of the Business”.

#### **INTERESTS OF EXPERTS**

Our auditor is KPMG LLP, Chartered Accountants, P.O. Box 10426, 777 Dunsmuir Street, Vancouver, British Columbia, V7Y 1K3. KPMG LLP has reported on our fiscal 2013 and 2012 audited consolidated financial statements, which have been filed with the securities regulatory authorities. KPMG LLP are the auditors of the Company and have confirmed that they are independent with respect to the Company within the meaning of the Rules of Professional Conduct of the Institute of Chartered Accountants of British Columbia and 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 also 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 28, 2013.

#### **Additional Financial Information**

Additional financial information is provided in our consolidated financial statements and management’s discussion and analysis for the financial year ended December 31, 2013.

**SCHEDULE “A”  
AUDIT COMMITTEE MANDATE**

**Date of Adoption: May 12, 2006**

**Purpose**

The audit committee (the “Committee”) of Cardiome Pharma Corp. (the “Corporation”) is responsible for ensuring accounting integrity and solvency. The Committee is also responsible for ensuring the appropriateness of insurance, investment of liquid funds, information security, contracts, and liability. The Committee will assist the board of directors of the Corporation (the “Board”) in fulfilling its oversight responsibilities by:

- reviewing the integrity of the consolidated financial statements of the Corporation;
- appointing (subject to shareholder ratification if required), determine funding for, and oversee the independent auditor and reviewing the independent auditor’s qualifications and independence;
- reviewing the performance of the Corporation’s independent auditors;
- reviewing the timely compliance by the Corporation with all legal and regulatory requirements for audit and related financial functions of the Corporation;
- reviewing financial information contained in public filings of the Corporation prior to filing;
- reviewing earnings announcements of the Corporation prior to release to the public;
- reviewing the Corporation’s systems of and compliance with internal financial controls;
- reviewing the Corporation’s auditing, accounting and financial reporting processes;
- dealing with all complaints regarding accounting, internal accounting controls and auditing matters; and
- dealing with any issues that result from the reviews set forth above.

**Membership and Reporting**

1. The Committee will be comprised of independent directors and will have a minimum of three members. All members of the Committee must have a working familiarity with basic finance and accounting practices and be able to read and understand financial statements.
2. 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 an independent director.
3. The chairman of the Committee (the “Chairman”) will be appointed by a vote of the Board on an annual basis.
4. 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.
5. At least one member of the Committee will be a “financial expert”, as such term is defined by applicable legislation.
6. The external auditor will report directly to the Committee.

## Terms of Reference

1. The Committee is responsible for overseeing the work of the external auditor and will communicate directly with the external auditors as required.
2. The Committee will meet as required, but at least once quarterly (to review the quarterly financial statements, management discussion and analysis (“MD&A”) and the related press release before such documents are presented to the Board or filed with regulatory authorities, as the case may be). Special meetings of the Committee will be authorized at the request of any member of the Committee or at the request of the Corporation’s external auditors. The external auditors will be informed about, and can attend, meetings of the Committee as deemed appropriate by the Chairman of the Committee. 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.
3. The Committee will review, with the external 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 review and approve interim financial statements, MD&A and the related press release on behalf of the Board and sign a resolution to that effect.
5. In addition, the Committee will review other financial statements, information and documents that require the approval of the Board. These will include year-end audited statements, year-end MD&A, statements in prospectus and other offering memoranda and 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.
6. The Committee will review and discuss with management and the independent auditor 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 external auditors or other advisors and obtain and review a report from the independent auditor, at least annually, regarding same; and the Committee will review and discuss with management and the independent auditor any special steps adopted in light of material internal control deficiencies and the adequacy of disclosures about changes in internal controls over financial reporting.
7. 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.
8. The Committee will review the basis and amount of the external auditors’ fees and pre-approve all auditing services and permitted non-audit services.
9. The Committee will consider whether the external 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 external auditor and the senior audit partners having primary responsibility for the audit, including considering whether the auditor’s quality controls are adequate.
10. The Committee will pre-approve the appointment of the external auditor 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 external auditor 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 external auditor 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.

11. The Committee will review and approve the Corporation's hiring of partners, employees, former partners and former employees of the present and former external auditor of the Corporation.
12. 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.
13. The Committee will review and reassess the adequacy of this mandate annually.
14. 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.
15. 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.
16. The Committee will approve all related party transactions.
17. The Committee will discuss with management and the independent auditor any correspondence with regulators or governmental agencies and any published reports that raise material issues regarding the Corporation's financial statements or accounting policies.
18. The Committee will receive from the independent auditor a formal written statement delineating all relationships between the independent auditor and the Corporation and will actively engaging in a dialogue with the independent auditor with respect to any disclosed relationships or services that may impact the objectivity and independence of the independent auditor.

Annual Review and Approval: March 14, 2013