



**CARDIOME PHARMA CORP.**

**ANNUAL INFORMATION FORM**

**FOR THE FISCAL YEAR ENDED DECEMBER 31, 2011**

**MARCH 26, 2012**

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**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, 2012, the exchange rate for conversion of U.S. dollars into Canadian dollars was U.S.\$1.00 = Cdn.\$0.9922 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, 2011.

**CAUTION REGARDING FORWARD-LOOKING STATEMENTS**

This annual information form contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 or forward-looking information under applicable Canadian securities legislation 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 plans to develop and commercialize product candidates and the timing of these development programs;
- our collaborative partner and its development programs for our products;
- whether we will receive, and the timing and costs of obtaining, regulatory approvals in the United States, Canada, the European Union and other countries;
- if we receive necessary regulatory approvals, the cost of post-market regulation;
- clinical development of our product candidates, including the results of current and future clinical trials;
- our ability to enrol 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; and
- the manufacturing capacity of third-party manufacturers for our product candidate.

Such 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 the results of the review of the new drug application, or NDA, for vernakalant (iv) by the U.S. Food and Drug Administration, or FDA, will be positive, 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 relationship with our suppliers and service providers will be maintained, assumptions relating to the availability of capital on terms that are favourable to us and assumptions relating the feasibility of future clinical trials.

By their very nature, forward-looking statements or information 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 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 have a history of significant losses and may never achieve or maintain profitability; our success is dependent upon our corporate collaborations with third parties; clinical trials 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 product candidates may not have favourable results in later trials or the commercial setting; difficulties or delays in enrolling patients in our clinical trials; we may not achieve our projected development goals within expected time frames; protection of intellectual property can be unpredictable and costly; some of our products may rely on proprietary technology owned by third parties; we will have additional future capital needs and there are uncertainties as to our ability to raise additional funding; our product candidates are subject to extensive regulation, which can be costly and time-consuming or prevent the receipt of required regulatory approvals; any of our products that receive regulatory approval could be subject to extensive post-market regulation; obtaining regulatory approval in the United States or European Union does not ensure that we will obtain regulatory approval in other countries; if we

successfully develop our products, they may not achieve market acceptance; we do not currently have the marketing expertise to commercialize our products; inability to manage our future growth could impair our business, financial condition and results of operations; acquisitions of companies or technologies may result in disruptions to our business; if milestones are achieved under in-licensing agreements, we will be required to make royalty payments; the life sciences industry is highly competitive; we are subject to risks associated with the use of hazardous materials; our business may be affected by existing legislation and continuing efforts of governmental and third party payors to contain or reduce the costs of healthcare; the use of pharmaceuticals may expose us to product liability claims; we are dependent upon our key personnel to achieve our scientific and business objectives; if we were to lose our “foreign private issuer” status under U.S. securities laws we would likely incur additional expenses to ensure compliance with U.S. securities laws; 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’ 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, 2011, 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 the focus of our business from mining exploration to drug research and development and 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* and effected a four-to-one share consolidation. On May 14, 2003, we amended our articles to create a class of preferred shares, issuable in series, and to create special rights and restrictions for our common shares and our preferred shares. On July 24, 2008, we amended our articles to create the series A preferred shares, or Series A Preferred Shares.

We have five 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 Development AG (formerly Cardiome Development Ltd.), a company continued under the laws of Switzerland; and Cardiome UK Limited, a company incorporated under the laws of the United Kingdom. Our wholly-owned subsidiary Cardiome Research and Development (Barbados), Inc., a company incorporated under the *Companies Act of Barbados*, was continued into Canada under the *Canada Business Corporations Act* on February 28, 2009, and was amalgamated with Cardiome Pharma Corp. on March 1, 2009.

Our head office and principal place of business is located at 6190 Agronomy Road, 6<sup>th</sup> Floor, Vancouver, British Columbia, Canada, V6T 1Z3. The address and the contact numbers of our registered office are as follows: P.O. Box 10424, Pacific Centre, Suite 1300, 777 Dunsmuir Street, Vancouver, British Columbia, Canada, V7Y 1K2; telephone number: (604) 643-7100 and fax number: (604) 643-7900.

## GENERAL DEVELOPMENT OF THE BUSINESS

We are a research-based biopharmaceutical company focused on the discovery, development and commercialization of new therapies that will improve the life and health of patients. We have one product, BRINAVESS™, approved for marketing in Europe and other territories for the rapid conversion of recent onset atrial fibrillation to sinus rhythm in adults. Our lead clinical programs are also focused on the treatment of atrial fibrillation, an arrhythmia (or abnormal rhythm) of the upper chambers of the heart. We also have several pre-clinical projects directed at various therapeutic indications for which we believe there is a high unmet medical need.

### *Merck Collaboration*

In April 2009, we entered into a collaboration and license agreement with Merck & Co., Inc., or Merck, for the development and commercialization of vernakalant. The agreement provides 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 March 2012, we announced that Merck had informed us of its decision to discontinue further development of vernakalant (oral).

Under the terms of the agreement, Merck paid us an initial fee of \$60 million. In addition, we are eligible to receive up to an additional \$200 million in payments, of which we have received \$45 million, based on 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 will receive tiered royalty payments on sales of any approved products and have the potential to receive up to \$340 million in additional milestone payments based on achievement of significant sales thresholds. Merck will be responsible for all future costs associated with the development, manufacturing and commercialization of these candidates.

Merck has granted to us a secured, interest-bearing credit facility of up to \$100 million that we may access in tranches over several years commencing in 2010. In February 2010, we announced that a Merck affiliate had advanced to Cardiome \$25 million under the credit facility. 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, 2016. In January 2012, we received another advance of \$25 million from a Merck affiliate under the credit facility. This second advance must be repaid in full by December 31, 2017.

In July 2009, we received a \$15 million milestone payment as a result of Merck's affiliate filing a Marketing Authorisation Application (MAA) with the European Medicines Agency (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 agreement, we have also shipped and been reimbursed for \$7 million of clinical supplies provided to Merck.

In July 2011, Merck acquired the rights for the development and commercialization of vernakalant (iv) in North America from Astellas.

### *Dutch Auction Tender Offer*

In August 2009, we announced that our Board of Directors authorized management to proceed with a tender offer to purchase for cancellation up to 6,470,588 of our common shares for an aggregate purchase price of up to \$27.5 million. The offer was conducted as a modified "Dutch auction", which enabled shareholders to select a price between \$4.25 per share and \$5.10 per share at which they were willing to tender their common shares to the offer. The purchase price was the lowest price per share between \$4.25 and \$5.10 that enabled us to purchase \$27.5 million of common shares. In October 2009, on expiry of the tender, we purchased for cancellation 6,470,588 of our common shares at a price of \$4.25 per share, for an aggregate purchase price of \$27.5 million. All common shares purchased under the offer were purchased at the same price. The purchased shares represented approximately 9.7% of our outstanding common shares as of October 13, 2009, the date of expiration of the tender offer.

### ***Private Placement***

On July 25, 2008, we completed a private placement of 2,272,727 Series A Preferred Shares to CR Intrinsic Investments LLC, or CR Intrinsic, for gross proceeds of \$25 million. Each outstanding Series A Preferred Share was convertible, subject to certain conditions, into one common share of Cardiome. We filed a registration statement on Form F-10 in the United States to register the resale of the underlying common shares by CR Intrinsic. The registration statement was declared effective on November 6, 2008. In October 2009, all of the Series A Preferred Shares were converted into common shares on a one-to-one basis at the option of CR Intrinsic. No Series A Preferred Shares remain outstanding subsequent to the conversion.

### ***Product Candidates***

The following chart summarizes our current product candidates, including the principal disease or indication being targeted, clinical trial status, expected milestones and marketing rights for each program.

<b>Program/ Trial</b>	<b>Indication/ Status</b>	<b>Next Milestone (if applicable)</b>	<b>Marketing Rights</b>
<i>Vernakalant (iv)</i>	<i>Atrial Fibrillation</i>		<i>Merck (Worldwide)</i>
Phase 3 (ACT 1)	Completed		
Phase 3 (ACT 2)	Completed		
Phase 3 (ACT 3)	Completed		
Phase 3 (ACT 4)	Completed		
Phase 3 (AVRO)	Completed		
Phase 3 (Asia Pacific)	Enrolling Patients	Completion of trial	
Phase 3 (ACT 5)	Closed	Trial results	
<i>Vernakalant (oral)</i>	<i>Atrial Fibrillation</i>	<i>Further Development Discontinued</i>	<i>Merck (Worldwide)</i>
Phase 2a Pilot Study	Completed		
Phase 2b Study	Completed		
Phase 1 PK/PD Studies	Multiple studies completed		
<i>Pre-clinical Programs</i>	<i>Various indications</i>	<i>Pre-clinical Studies Ongoing</i>	<i>Cardiome (Global)</i>

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

Atrial fibrillation is the most common cardiac arrhythmia (abnormal heart rhythm), and is the term used to describe an erratic and often rapid heart rate where the electrical activity of the heart's two small upper chambers (atria) is not coordinated, resulting in inefficient pumping of blood and an increased risk of developing a blood clot in the heart, which could lead to stroke. If a blood clot in the atria leaves the heart and becomes lodged in an artery in the brain, a stroke may result. About 15 percent of strokes occur in people with atrial fibrillation. Common symptoms of atrial fibrillation include fast heart rate, palpitations, shortness of breath and weakness.

The risk of atrial fibrillation increases with age. The lifetime risk of developing atrial fibrillation at age 55 has been estimated at 24 percent in men and 22 percent 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.

Vernakalant is a new chemical entity designed to treat atrial fibrillation, with the potential to overcome the limitations of current drugs used 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 was being developed for two potential applications: (a) vernakalant (iv) is being evaluated as an intravenous pharmacological converting agent designed to terminate an atrial fibrillation episode and return the heart to normal rhythm; and (b) vernakalant (oral) was being evaluated as an oral maintenance therapy for the long-term prevention of atrial fibrillation recurrence. Merck has discontinued further development of vernakalant (oral).

Vernakalant (iv) was approved in September 2010 for marketing in European Union, Iceland and Norway, under the trade name BRINAVESS™, for the rapid conversion of recent onset atrial fibrillation to sinus rhythm in adults.

Vernakalant (iv) was approved for marketing in additional countries in 2011.

### ***Vernakalant (iv)***

In December 2006, our former partner, Astellas, filed a NDA for vernakalant (iv) with the FDA. In August 2008, we announced that 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 is approvable. In November 2008, we participated, together with Astellas, in an end of review meeting with the FDA, in respect of the NDA for vernakalant (iv).

In July 2009, Merck's affiliate filed an MAA with the EMA for vernakalant (iv) in the European Union, and we received a \$15 million milestone payment from Merck.

In August 2009, we, together with Astellas, announced that Astellas would undertake a single confirmatory additional Phase 3 clinical trial under a Special Protocol Agreement, or SPA. 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). Under the process prescribed by the SPA, the FDA has agreed that the design and planned analysis of the study adequately address objectives in support of the NDA for vernakalant (iv). ACT 5 began enrollment of recent onset atrial fibrillation patients without a history of heart failure in October 2009.

In June 2010, we announced that the Committee for Medicinal Products for Human Use of the EMA recommended marketing approval 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 post-cardiac surgery patients with atrial fibrillation of three days or less. In September 2010, we announced that vernakalant (iv) received marketing approval under the trade name BRINAVESS™ in the European Union, Iceland and Norway, triggering a \$30 million milestone payment from Merck. Merck has commercially launched BRINAVESS™ in a number of European countries and has planned product launches in the remaining countries for which marketing approval has been obtained.

In August 2010, Merck initiated a 615 patient Phase 3 Asia Pacific study that is expected to support regulatory applications in additional territories for which marketing approval has not yet been attained.

In October 2010, we announced that Astellas had 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, we announced that Merck had acquired the rights for the development and commercialization of vernakalant (iv) in North America. Merck has entered into discussions with the FDA to determine next steps for

the development of vernakalant (iv) in the United States. Merck and the FDA have agreed to close the ACT 5 trial. Results will be analyzed and the two parties are in dialogue regarding future plans for the program.

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

In April 2009, we entered into a collaborative license agreement with Merck for the development and commercialization of vernakalant. The agreement provides that 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 December 2010, we announced that we were advised by Merck that their current review of vernakalant (oral) was complete, and that Merck had informed us of its next steps in clinical development for vernakalant (oral) beginning in 2011.

In November 2011, we announced that Merck recently completed an additional multiple rising-dose Phase 1 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 1 trial assessing the safety and tolerability of vernakalant (oral) when dosed for a more extended period of time at higher exposures.

In March 2012, we announced that Merck had informed us of its decision to discontinue further development of vernakalant (oral).

### ***GED-aPC***

In September 2009, we announced that we had successfully completed multiple cohorts in a Phase 1 study for GED-aPC and that enrollment in the study was completed.

In September 2009, we also announced the decision that future development and commercialization of the GED-aPC technology, currently held in a subsidiary company, would be funded either externally or via a partnership with another life sciences company. Our partnership efforts have not resulted in additional funding for continued development of GED-aPC and, as a result, we have written off the carrying value of the asset in our consolidated financial statements for the year ended December 31, 2011.

### ***Pre-clinical Projects***

We continue to conduct pre-clinical research and development work on our internal early stage assets. Our internal technology focus is on modulating cellular proteins (ion channels) that gate the movement of ions across the cell membrane 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. We consistently evaluate external clinical and pre-clinical candidates to potentially add to our pipeline within the cardiovascular or ion channel realm.

Our lead pre-clinical product candidates leverage our expertise in ion channel and cardiovascular research. In 2012, we expect to continue development of our pre-clinical product candidates.

## **NARRATIVE DESCRIPTION OF THE BUSINESS**

### **General**

We are a research-based biopharmaceutical company focused on the discovery, development and commercialization of new therapies that will improve the life and health of patients. We have one product, BRINAVESS™, approved for marketing in Europe and other territories for the rapid conversion of recent onset atrial fibrillation to sinus rhythm in adults. Our lead clinical programs are also focused on the treatment of atrial

fibrillation, an arrhythmia (or abnormal rhythm) of the upper chambers of the heart. We have several pre-clinical projects directed at various therapeutic indications for which we believe there is a high unmet medical need.

## **Our Strategy**

Our goal is to create a profitable and sustainable biopharmaceutical company focused on developing new therapies for cardiovascular disease and other therapeutic conditions. Key elements of our strategy include:

- *Supporting our collaborative partner in successfully obtaining approval for vernakalant.* In collaboration with our former partner, Astellas, we have completed three pivotal Phase 3 clinical trials and an open label safety study which formed the basis of the NDA submitted to the FDA by Astellas for vernakalant (iv), and have supported Astellas in conducting the additional Phase 3 clinical trial, named ACT 5, under an SPA. We also completed a Phase 3 European comparator study for vernakalant (iv), the results of which were incorporated by Merck in its filing for marketing approval for vernakalant (iv) in the European Union, Iceland and Norway, which was granted in September 2010. We intend to support our collaborative partner in advancing vernakalant (iv).
- *Continuing to focus on our core expertise in cardiac diseases and ion channel conditions.* By focusing our efforts on our core expertise in cardiac diseases and ion channel research, we have retained employees and external advisors with a strong knowledge and understanding of cardiology. 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.
- *Maintaining capabilities that span pre-clinical and clinical development.* We have the capability to conduct both pre-clinical and clinical development of a product candidate, including late stage trials. This capability allows us to support partnership activities, or develop in-licensed and acquired technologies at any stage of development. We intend to maintain our capabilities in this area.
- *Expanding our product pipeline through in-licensing and/or acquisitions.* We continuously evaluate clinical candidates to potentially add to our clinical pipeline that complement our operational capabilities.
- *Leveraging external resources.* We focus our resources on those activities that we believe add or create the most value. We maintain a core team of scientists and staff with the necessary skill base for our projects, and contract out the specialized work required for our projects, such as pre-clinical toxicology services and commercial manufacturing.

## **Our Product Candidates**

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

Vernakalant is a new chemical entity designed to treat atrial fibrillation, with the potential to overcome the limitations of current drugs used 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 was being developed for two potential applications: (1) vernakalant (iv) is being evaluated as an intravenous pharmacological converting agent designed to terminate an atrial fibrillation episode and return the heart to normal rhythm; and (2) vernakalant (oral) was being evaluated as an oral maintenance therapy for the long-term prevention of atrial fibrillation recurrence. Merck has discontinued development of vernakalant (oral).

Vernakalant (iv) was approved in September 2010 for marketing in European Union, Iceland and Norway, under the trade name BRINAVESS™, 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 post-cardiac surgery patients with atrial fibrillation of three days or less.

### Vernakalant (iv)

Together with our collaboration partner, Merck, who has global marketing rights to vernakalant (iv), we continue to be involved in the development of vernakalant (iv), a product candidate for the treatment of atrial fibrillation. In September 2010, we announced that vernakalant (iv) received marketing approval under the trade name BRINAVESS™ in the European Union, Iceland and Norway, triggering a \$30 million milestone payment from Merck. Merck obtained approval in a number of other countries in 2011. Merck has launched BRINAVESS™ in a number of countries worldwide, and has planned product launches in the remaining countries for which marketing approval has been obtained.

#### *Regulatory Matters*

In December 2006, our former partner, Astellas, filed a NDA for vernakalant (iv) with the FDA. On August 11, 2008, we announced that 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 November 2008, we participated, together with Astellas, in an end of review meeting with the FDA, in respect of the NDA for vernakalant (iv).

In July 2009, a Merck affiliate filed an MAA with the EMA seeking approval for vernakalant (iv) in the European Union, and we received a \$15 million milestone payment from Merck.

In August 2009, we, together with our former partner Astellas, announced that Astellas would undertake a single confirmatory additional Phase 3 clinical trial under an SPA. 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). Under the process prescribed by the SPA, the FDA has agreed that the design and planned analysis of the study adequately address objectives in support of the NDA for vernakalant (iv). ACT 5 began enrollment of recent onset atrial fibrillation patients without a history of heart failure in October 2009.

In June 2010, we announced that 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. In September 2010, we announced that vernakalant (iv) received marketing approval under the trade name BRINAVESS™ in the European Union, Iceland and Norway, triggering a \$30 million milestone payment from Merck. Merck has commercially launched BRINAVESS™ in a number of European countries and has planned product launches in the remaining countries for which marketing approval has been obtained.

In August 2010, Merck initiated a 615 patient Phase 3 Asia Pacific vernakalant (iv) study that is expected to support regulatory applications in additional territories for which marketing approval has not yet been obtained.

In October 2010, we announced that 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, we announced that Merck had acquired the rights for the development and commercialization of vernakalant (iv) in North America. Merck has entered into discussions with the FDA to determine next steps for the development of vernakalant (iv) in the United States. Merck and the FDA have agreed to close the ACT 5 trial. Results will be analyzed and the two parties are in dialogue regarding future plans for the program.

## Clinical Trials

The following table summarizes our recently completed and ongoing trials of vernakalant (iv) for atrial fibrillation:

<b>Trial</b>	<b>Summary</b>	<b>Patients</b>	<b>Initiated</b>	<b>Data Release</b>
ACT 1	Phase 3 Study – Acute treatment of atrial fibrillation	356	3Q03	4Q04
	- Scene 2 – Acute treatment of atrial flutter	60		
ACT 2	Phase 3 Study – Treatment of transient atrial fibrillation following cardiac bypass surgery	190	1Q04	2Q07
ACT 3	Phase 3 Study – Acute treatment of atrial fibrillation and atrial flutter	276	3Q04	3Q05
ACT 4	Open-Label Safety Study – Acute treatment of atrial fibrillation	254	3Q05	n/a
European Comparator (AVRO)	Phase 3 Study – Comparison of safety and efficacy of vernakalant (iv) against amiodarone	254	1Q08	4Q09
ACT 5	Phase 3 Study – Rapid conversion of atrial fibrillation to sinus rhythm	217	4Q09	mid 2012
Phase 3 Asia Pacific Study	Phase 3 Study – Efficacy and safety of vernakalant hydrochloride in patients with atrial fibrillation (Merck)	615	3Q10	2013

In August 2003, we initiated ACT 1, our first Phase 3 clinical trial of vernakalant (iv) for the treatment of atrial fibrillation. This study was a placebo-controlled, double-blinded randomized clinical trial in 416 patients with atrial arrhythmia. The study included three groups of patients, including 237 patients with recent-onset atrial fibrillation (more than three hours but less than seven days), 119 patients with longer-term atrial fibrillation (more than seven days but less than 45 days) and Scene 2, a subgroup of 60 patients with atrial flutter. Atrial flutter represents a small subset of the overall atrial arrhythmia population. The primary endpoint in ACT 1 was conversion of recent-onset atrial fibrillation to normal heart rhythm for a period of at least one minute post-dosing within 90 minutes of the start of dosing. The study was carried out in 45 centres in the United States, Canada and Europe.

In December 2004 and February 2005, we announced top-line results from our ACT 1 trial, and we presented the full trial report in May 2005 at the Heart Rhythm Society Meetings in New Orleans. In patients with recent-onset atrial fibrillation, 52% of those receiving vernakalant (iv) converted to normal heart rhythm, as compared to 4% of placebo patients ( $p < 0.001$ ). In those recent-onset atrial fibrillation patients dosed with vernakalant (iv) who converted to normal heart rhythm, the median time to conversion was 11 minutes from the initiation of dosing. Of the 75 patients who converted to normal heart rhythm within 90 minutes of the initiation of dosing, 74 (99%) of them remained in normal rhythm for at least 24 hours. In the longer-term atrial fibrillation population, 8% of patients who were dosed with vernakalant (iv) had their atrial fibrillation converted to normal heart rhythm, as compared to 0% of placebo patients.

The top-line ACT 1 study data suggests that vernakalant (iv) is also well-tolerated in the targeted patient population. In the 30-day interval following drug administration, serious adverse events occurred in 18% of placebo patients and 13% of vernakalant (iv) patients. Potentially drug-related serious adverse events occurred in 0% of placebo patients and 1.4% of patients receiving vernakalant (iv). There were no cases of drug-related “Torsades de Pointes”, a well-characterized ventricular tachycardia, which is an occasional side effect of many current anti-arrhythmia drugs. No patients needed to discontinue the ACT 1 study due to vernakalant (iv).

Scene 2 study data suggests that vernakalant (iv) is ineffective in converting atrial flutter patients to normal heart rhythm. In the 30-day interval following treatment administration, serious adverse events occurred in 27% of placebo patients and 18% of vernakalant (iv) patients. Potentially serious adverse drug-related events occurred in zero placebo patients and in two patients receiving vernakalant (iv).

In July 2004, Astellas initiated the ACT 3 study in patients with atrial arrhythmia. There were 276 patients evaluated in the ACT 3 study. ACT 3 was essentially a replica of ACT 1 with similar patient population and endpoints. The primary efficacy endpoint of the ACT 3 trial was the conversion of atrial fibrillation to normal heart rhythm in recent-onset atrial fibrillation patients. The study also included the analysis of patients with longer-term atrial fibrillation and patients with atrial flutter.

In September 2005, we announced top-line results from ACT 3. The study achieved its primary endpoint, showing that of the 170 patients with recent-onset atrial fibrillation, 51% of those receiving an intravenous dose of vernakalant (iv) converted to normal heart rhythm, as compared to 4% of placebo patients ( $p < 0.0001$ ). These percentages are similar to those reported in ACT 1.

The ACT 3 study data suggests that vernakalant (iv) was generally well-tolerated in the targeted patient population. In the 30-day interval following drug administration, serious adverse events occurred in 13% of all placebo patients and 10% of all patients dosed with vernakalant (iv). Potentially drug-related serious adverse events occurred in 1% of placebo patients and 2% of patients receiving vernakalant (iv). There were no cases of drug-related “Torsades de Pointes”.

In the overall atrial fibrillation study population (more than three hours and less than forty five days), 41% of patients who were dosed with vernakalant (iv) experienced termination of atrial fibrillation, as compared to 4% of placebo patients ( $p < 0.0001$ ). In the longer-term atrial fibrillation population (more than seven days but less than forty five days), 9% of patients who were dosed with vernakalant (iv) had their atrial fibrillation terminated, as compared to 3% of placebo patients. In the atrial flutter population (nine subjects received placebo and 14 received vernakalant (iv)), 7% of those who were dosed with vernakalant (iv) experienced conversion to normal heart rhythm, as compared to 0% of placebo patients.

In the recent-onset atrial fibrillation patients dosed with intravenous vernakalant (iv) who converted to normal heart rhythm within 90 minutes, the median time to conversion was eight minutes from the initiation of dosing. This result also compared well with ACT 1 study data.

In June 2007, we announced results from the completed ACT 2 trial. The trial evaluated the efficacy and safety of vernakalant (iv) for the treatment of patients who developed atrial fibrillation or atrial flutter between 24 hours and 7 days following coronary artery bypass graft (CABG) or valve replacement surgery. In the atrial fibrillation population, 47% of patients dosed with vernakalant (iv) experienced conversion to normal heart rhythm within 90 minutes, as compared to 14% of placebo patients, a statistically significant difference ( $p = 0.0001$ ). The ACT 2 study data suggests that vernakalant (iv) was well-tolerated in the studied patient population. In the 30-day interval following drug administration, serious adverse events occurred in 9% of all patients dosed with vernakalant (iv) and 11% of all placebo patients. Potentially drug-related serious adverse events occurred in 2% of patients who received vernakalant (iv) and 0% of placebo patients. There were no cases of drug-related “Torsades de Pointes”.

The study achieved its primary endpoint in the combined atrial fibrillation and atrial flutter groups, showing that 45% of patients receiving vernakalant (iv) converted to normal heart rhythm within 90 minutes, as compared to 15% of placebo patients within the same time period ( $p = 0.0002$ ). Of the ten patients in the atrial flutter population, no patients in the vernakalant (iv) group and one patient in the placebo group converted to normal heart rhythm. A total of 190 patients were randomized in the study, of which 161 received treatment. In the patients treated with vernakalant (iv) who converted to normal heart rhythm within 90 minutes, the median time to conversion was 12 minutes from the initiation of dosing.

The ACT 4 trial was an open-label safety study to gather additional safety data in atrial fibrillation patients to supplement ACT 1 and ACT 3 pivotal results for the NDA submission for vernakalant (iv). The ACT 4 trial has been completed, and data from this trial was included in the NDA submission to the FDA for vernakalant (iv).

ACT 1 and ACT 3 are the two trials which formed the basis of the NDA submission for vernakalant (iv) to the FDA which Astellas re-filed with the FDA in December 2006. The re-submitted NDA for vernakalant (iv) included additional safety and efficacy data from ACT 2 and ACT 4. Efficacy data from the ACT 2 trial for vernakalant (iv) was submitted at the request of the FDA in September 2007.

In October 2009, Astellas initiated the ACT 5 trial. This 450 patient trial had been designed to measure the safety and efficacy of vernakalant (iv) in patients with recent-onset atrial fibrillation (more than 3 hours but less than 7 days) across approximately 100 centres focused in North America. The study excluded patients with evidence or history of congestive heart failure. Further, the study had been designed to evaluate the influence of CYP2D6 genotype status on the pharmacokinetics and pharmacodynamics of vernakalant and its metabolites, and also allowed for an exploratory analysis of safety and healthcare resource utilization between vernakalant (iv) and electrocardioversion. In October 2010, we announced that Astellas suspended patient enrolment in the ACT 5 study following a single unexpected serious adverse event of cardiogenic shock experienced by a patient with atrial fibrillation who received vernakalant (iv). Merck and the FDA have agreed to close the ACT 5 trial.

In December 2009, we announced positive results from the Phase 3 European comparator (AVRO) study for vernakalant (iv). This 254 patient study was a prospective, active-controlled, double-blinded randomized clinical trial that compared the safety and efficacy of vernakalant (iv) against amiodarone as a treatment for the acute conversion of atrial fibrillation in patients. The study met its primary endpoint, achieving statistical significance in demonstrating the superiority of vernakalant (iv) over amiodarone in the conversion of atrial fibrillation to sinus rhythm within 90 minutes of the start of drug administration. The data suggests that vernakalant (iv) was well-tolerated in the study population, and that there were no vernakalant-related deaths or cases of “Torsades de Pointes”. In May 2010, we announced final results from the Phase 3 European comparator (AVRO) study, which showed that vernakalant (iv) was superior to amiodarone injection in converting patients’ heart rate from atrial fibrillation to sinus rhythm within 90 minutes of the start of administration. The results of the study were presented at Heart Rhythm 2010, the annual meeting of the Heart Rhythm Society.

In August 2010, Merck initiated a 615 patient Phase 3 Asia Pacific study that is expected to support regulatory applications in additional territories for which marketing approval has not yet been obtained.

#### *North American Vernakalant Collaboration*

In October 2003, we entered into a collaboration and license agreement, referred to as the “North American Vernakalant (iv) Agreement, with Astellas (renamed after the merger of Fujisawa Pharmaceutical Co. Ltd. and Yamanouchi Pharmaceutical Co., Ltd.), a U.S. affiliate of Astellas Pharma Inc., a leading pharmaceutical company headquartered in Japan. 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 our 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 the then share price, and agreed to pay us milestone payments of up to \$54 million based on achievement of specified development and commercialization milestones. In addition, if the product is approved for use by the applicable regulatory authorities in North America, we are entitled to royalty payments which are expected to average approximately 25% of total North America end-user sales revenue, as well as royalties based on future net sales and sublicense revenue. Following the successful completion of ACT 1, 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 terms of our amended 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 is payable on approval of vernakalant (iv) by the FDA.

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

Merck is 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 our amended North American Vernakalant (iv) Agreement we have the right to additional milestone payments with respect to any subsequent drugs developed under the agreement. The North American Vernakalant (iv) Agreement has an indefinite term but can be terminated entirely, or on a country by country basis, by either party if certain development or commercialization milestones are not met.

All development activities related to regulatory approval in North American markets are jointly managed by Merck and us until the termination of our agreement with Merck. Merck is responsible for the development plan, NDA application and registration for vernakalant (iv), along with the sales, marketing and distribution of vernakalant (iv). Merck is responsible for the commercial manufacturing of vernakalant (iv).

#### *Merck Collaboration*

In April 2009, we entered into a collaboration and license agreement with Merck for the development and commercialization of vernakalant. The agreement provides 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 agreement, Merck paid us an initial fee of \$60 million. In addition, we are eligible to receive up to an additional \$200 million in payments, of which we have received \$45 million to date, based on 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 will receive tiered royalty payments on sales of any approved products and have the potential to receive up to \$340 million in additional milestone payments based on achievement of significant sales thresholds. Merck will be responsible for all future costs associated with the development, manufacturing and commercialization of these candidates.

Merck has granted us a secured, interest-bearing credit facility of up to \$100 million that we may access 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. We may, at our option, repay all or a portion of the advance from time to time without premium or penalty. This first advance must be repaid in full by December 31, 2016. In January 2012, we received another advance of \$25 million from a Merck affiliate under the credit facility. This second advance must be repaid in full by December 31, 2017.

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 BRINAVESSTM. Under the agreement, we have also shipped and been reimbursed for \$7 million of clinical supplies provided to Merck.

#### *Vernakalant (oral)*

Vernakalant (oral) was being evaluated 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 December 2005, we announced the initiation of a Phase 2a pilot study of vernakalant (oral) for the prevention of recurrence of atrial fibrillation. In July and September 2006, we announced positive top-line results for the 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 November 2011, we announced that Merck recently completed an additional multiple rising-dose Phase 1 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 1 trial assessing the safety and tolerability of vernakalant (oral) when dosed for a more extended period of time at higher

exposures. In March 2012, we announced that Merck had informed us of its decision to discontinue further development of vernakalant (oral).

### *Clinical Trials*

In an oral dosing study in humans completed in December 2002, vernakalant was shown to have significant oral bioavailability, suggesting 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 December 2005, we announced the initiation of a Phase 2a pilot study of vernakalant (oral) for the prevention of recurrence of atrial fibrillation. The double-blind, placebo-controlled, randomized, dose-ranging study was designed to measure the safety and tolerability, pharmacokinetics and preliminary efficacy of vernakalant (oral) in up to 28 days of oral dosing in patients at risk of recurrent atrial fibrillation.

In July and September 2006, we announced positive top-line results for the 300 mg and 600 mg dosing groups, respectively, from the Phase 2a pilot study 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 ( $p=0.028$ ).

For the entire study, a total of 171 patients were successfully cardioverted after the initial three days of dosing and continued in the study, of which 159 reached an endpoint of the study (completion of dosing or relapse to atrial fibrillation). The remainder of the patients were discontinued from the study for reasons unrelated to atrial fibrillation.

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".

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 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 placebo (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 placebo. These results provide evidence of a clear dose response, with 500 mg b.i.d. 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), comprising two 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.

### Market Opportunity

Atrial fibrillation is the most common cardiac arrhythmia (abnormal heart rhythm). It has been estimated that 5.5 million patients each year are treated for atrial fibrillation in the seven leading industrialized nations. Atrial fibrillation is the term used to describe an erratic and often rapid heart rate where the beat of the heart’s two small upper chambers (the atria) is not coordinated with the two lower chambers (the ventricles). It commonly leads to symptoms of heart palpitations, shortness of breath and weakness, and blood clots may form. If a blood clot in the atria leaves the heart and becomes lodged in an artery in the brain, a stroke results. It has been estimated that about 15 percent of strokes occur in people with atrial fibrillation. The risk of atrial fibrillation increases with age.

### Intellectual Property

Our patent portfolio related to vernakalant contains two issued U.S. patents and one issued European patent with composition of matter claims specific to vernakalant and/or with claims specific to the use of vernakalant to treat arrhythmia, and we are pursuing similar claims in other jurisdictions worldwide. In addition to the foregoing specific composition of matter protection, we also have nineteen issued U.S. patents, eight pending U.S. applications and numerous issued patents and pending applications in other jurisdictions worldwide more generally related to vernakalant and analogs thereof, including, but not limited to, composition of matter, various therapeutic uses, manufacturing methods and formulations thereof.

On December 14, 2004, we completed a reorganization of certain intellectual property rights related to vernakalant and related technology between us and our wholly-owned subsidiary in Barbados. On February 28, 2009, our wholly-owned subsidiary in Barbados was continued into Canada under the *Canada Business Corporations Act* and was amalgamated with Cardiome Pharma Corp. on March 1, 2009. We continue to own this intellectual property.

### **GED-aPC**

We entered, through our wholly-owned subsidiary Cardiome Development AG, into an exclusive in-licensing agreement with Eli Lilly and Company (“Lilly”) on April 30, 2007, whereby we have been granted exclusive worldwide rights to GED-aPC for all indications. GED-aPC is an engineered analog of recombinant human activated Protein C (aPC) with enhanced cytoprotective, anti-inflammatory, anti-thrombotic and strong-binding to endothelial protein C receptor properties, and has broad potential across multiple indications. We will not fund the clinical development of GED-aPC in the future and have written off the carrying value of the asset in our consolidated financial statements for the year ended December 31, 2011.

### **Pre-clinical Projects**

We continue to conduct pre-clinical research and development work on our internal early stage assets. Our internal technology focus is on modulating cellular proteins (ion channels) that gate the movement of ions across the cell membrane 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 lead pre-clinical product candidates leverage our expertise in ion channel and cardiovascular research. In 2012, we expect to continue development work on our pre-clinical product candidates.

We continuously evaluate external clinical and pre-clinical candidates to potentially add to our pipeline that complement our operational capabilities.

### **Licenses and Collaborative Research Agreements**

An important aspect of our product development strategy is the establishment of collaborations with pharmaceutical companies and research centers with resources and expertise vital to our programs and commercial objectives, such as our collaboration with Merck.

### **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. Companies including, but not limited to, Boston Scientific, Johnson & Johnson, Medtronic, Pfizer, Sanofi-Aventis, Astra Zeneca, Glaxo SmithKline, ARYx, Boehringer, Gilead, Xention and Bayer all have products in development or in the market that could potentially compete with our vernakalant product candidates.

### **Patents and Proprietary Protection**

We consider our patent portfolio as one of the key value contributors to our business. Therefore, we devote a substantial amount of resources each year 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. For known compounds, claims directed to novel composition and/or use will be made in the patent application. 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 is commercialized.

## 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, or 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 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.

U.S. law requires that 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 U.S. *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 U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice and individual U.S. 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 U.S. *Medicare-Medicaid Anti-Fraud and Abuse Act*, as amended, the U.S. *False Claims Act*, as amended, the privacy provisions of the U.S. *Health Insurance Portability and Accountability Act* and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. *Omnibus Budget Reconciliation Act of 1990*, as amended, and the U.S. *Veterans Health Care Act of 1992*, as amended. If products are made available to authorized users of the U.S. 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, an MAA is built for submission and review. A medicinal product may only be placed on the market in the European Economic Area, or 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, or 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.

## **Human Resources**

As of December 31, 2011, we employed or retained 92 persons, 58 of whom hold advanced degrees in science or business, including 26 who hold Ph.D. or M.D. degrees. Following Merck's decision to discontinue further development of vernakalant (oral) we reduced our workforce. As of March 20, 2012, we employed or retained 54 persons, 33 of which hold advanced degrees in science or business, including 16 who hold Ph.D. or M.D. degrees.

## Facilities

Our principal office and main laboratory are located at 6190 Agronomy Road, Vancouver, British Columbia, V6T 1Z3, Canada. We entered into a lease agreement effective September 2003, as amended effective May 2005, June 2007 and April 2008, pursuant to which we leased the 5<sup>th</sup> and the 6<sup>th</sup> floors of the building, as well as parts of the 3<sup>rd</sup> and 4<sup>th</sup> floors. The term of this lease expires in March 2014. In November 2010, we entered into a new lease for certain of our principal office and laboratory facilities for a period of 10 years, effective March 2011, for a total of 62,801 square feet. Effective April 2009, June 2009 and May 2010, we sub-leased certain floor space located on the 3<sup>rd</sup> and 4<sup>th</sup> floors. Our lease agreements consist of customary scheduled rent increases, escalation clauses and renewal options. As of March 26, 2012, our basic lease payments approximate \$1.7 million per annum.

## Reorganization

On February 28, 2009, our wholly-owned subsidiary Cardiome Research and Development (Barbados), Inc., a company incorporated under the Companies Act of Barbados, was continued into Canada under the *Canada Business Corporations Act*, and was amalgamated with Cardiome Pharma Corp. on March 1, 2009.

## RISK FACTORS

*Investing in our securities involves a high degree of risk. You should carefully consider carefully 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. 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, 2011.*

### **We have a history of significant losses and a significant accumulated deficit and we may never achieve or maintain profitability.**

Although we have been involved in the life sciences industry since 1992, we have, prior to the launch of BRINAVESS<sup>TM</sup>, only been engaged in research and development. Before Merck obtained marketing approval for BRINAVESS<sup>TM</sup> in the European Union, Iceland and Norway in September 2010, and launched BRINAVESS<sup>TM</sup> in a number of European countries in 2011, none of our drug 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. 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 our collaboration partner, Merck, will continue to be responsible for future expenses related to research, development, testing and approval of vernakalant (iv), we anticipate that we will continue to incur these types of expenses in connection with our collaboration with Merck in obtaining approval for vernakalant (iv) in North America, as well as research and development of any future products. We expect these expenses to result in continuing operating losses in the near future.

Although we have received milestone payments under the terms of our collaborative agreements with Merck and Astellas, we cannot assure you that we will receive additional milestone payments from our collaborative partner in the future. Our ability to significantly increase revenues or achieve profitable operations is largely dependent upon Merck's ability to develop and commercialize the vernakalant products and we cannot assure you that Merck will be able to successfully develop and commercialize these products. For example, the amount of royalty payments we receive from the sale of BRINAVESS<sup>TM</sup> will depend on the ability of Merck to successfully commercialize BRINAVESS<sup>TM</sup> and, as a consequence, we cannot assure you that we will generate sufficient revenues from royalty payments from the sale of BRINAVESS<sup>TM</sup> to significantly increase revenues or achieve profitable operations.

If we, together with our collaborative partner, are unable to develop, obtain regulatory approval for our product candidates currently under development or are unable to successfully commercialize BRINAVESS™ or any other product candidates in respect of which we obtain marketing approval, we will not be able to significantly increase revenues or achieve profitable operations. It takes many years and significant financial resources to successfully develop a pre-clinical or early clinical compound into a marketed drug.

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

The success of our business is largely dependent on our ability to enter into corporate collaborations regarding the development, clinical testing, regulatory approval and commercialization of our product candidates currently under development. Merck is responsible for the co-development and commercialization of vernakalant (iv) in North America pursuant to our North American Vernakalant (iv) Agreement. Merck is responsible for all future development and commercialization of vernakalant (iv) outside of North America.

Our success is highly dependent upon the performance of Merck and any future corporate collaborators. The amount and timing of resources to be devoted to activities by Merck and future corporate collaborators, if any, are not within our direct control and, as a result, we cannot assure you that Merck, or any future corporate collaborators, will commit sufficient resources to our research and development projects or the commercialization of our product candidates. Merck, or any future corporate collaborators, might not perform its obligations as expected and might pursue existing or other development-stage products or alternative technologies in preference to those being developed in collaboration with us, or may terminate particular development programs, or the agreement governing such development programs. If any such agreement was terminated, we would have to find one or more new collaborators to undertake the research and development and/or commercialization of our product candidates and we cannot assure you that we would be able to find such new collaborators on favourable terms, or at all. If we were unable to find a new collaborator for the research and development and/or commercialization of our product candidates, we may have to undertake such activities ourselves, which could have a material adverse effect on our business, financial condition, prospects and results of operations.

In addition, if Merck, or any future collaborators, fails to comply with applicable regulatory requirements, the FDA, the EMA, the TPD or other authorities could take enforcement action that could jeopardize our ability to develop and commercialize our product candidates. Despite our best efforts to limit them, disputes may arise with respect to ownership of technology developed under any such corporate collaborations.

**We are primarily a pharmaceutical development business and are subject to all of the risks of a pharmaceutical development business.**

We are primarily a pharmaceutical development business and are subject to all of the risks associated with a pharmaceutical development business. As a result, our business must be evaluated in light of the problems, delays, uncertainties and complications encountered in connection with establishing a pharmaceutical development business.

Apart from BRINAVESS™, which has been launched in a number of countries, all of our proposed products are currently in the research and development and registration stage. We have not generated any revenues from product sales except BRINAVESS™, nor do we expect to generate any significant product sales over the next year. Apart from BRINAVESS™, which has been approved for sale in a number of countries internationally, none of our product candidates have received regulatory approval for commercial sale from any jurisdiction. Substantial pre-clinical safety and toxicology work and clinical development testing for our product candidates remain ongoing. The single confirmatory additional Phase 3 clinical trial under the SPA has been closed by Merck and the development of vernakalant (oral) has been discontinued. There is a possibility that none of our drug candidates that are currently under development will be found to be safe and effective, that we will be unable to receive necessary regulatory approvals in order to commercialize them, or that we will obtain regulatory approvals that are too narrow to be commercially viable.

Any failure to successfully develop and obtain regulatory approval for products that are currently under development would have a material adverse effect on our business, financial condition and 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. 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). Merck and the FDA have agreed to close the ACT 5 trial. Results will be analyzed and the two parties are in dialogue regarding future plans for the program.

The timing of the commencement, continuation and completion of clinical trials may be subject to significant delays relating to various causes, including:

- our inability to manufacture or obtain sufficient quantities of materials for use in clinical trials;
- delays arising from our collaborative partnerships;
- 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 due to 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;
- 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. 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) and other products may not predict results from studies in larger numbers of subjects drawn from more diverse populations or in the commercial setting, and also may not predict the ability of our products to achieve their intended goals, or to do so safely.

Although vernakalant (iv) has been approved for marketing in certain Europe countries and other territories, we may be required to do additional trials in other jurisdictions in order to obtain approval to market vernakalant (iv) in countries located in other jurisdictions. 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) fails to demonstrate sufficient safety and efficacy in ongoing or future clinical trials, we could experience potentially significant delays in, or be required to abandon development of, our product candidates currently under development.

**If we encounter difficulties enrolling patients in our clinical trials, our clinical trials could be delayed or otherwise adversely affected.**

Clinical trials for our product candidates require that we identify and enroll a large number of patients with atrial fibrillation and other cardiovascular dysfunctions. We may not be able to enroll a sufficient number of patients to complete our clinical trials in a timely manner. Patient enrollment is a function of many factors including:

- design of the protocol;
- the size of the patient population;
- eligibility criteria for the study in question;
- perceived risks and benefits of the drug under study;
- availability of competing therapies;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- availability of clinical trial sites.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing clinical trials. Any delay or termination of ongoing trials will have an adverse effect on our ability to develop and market our products and could have a material adverse effect on our business financial condition and results of operations.

**We or our partners have ongoing and/or planned clinical trials for our product candidates. Our share price could decline significantly if those clinical results are not favourable or are perceived negatively.**

Subject to obtaining permission from the FDA to restart the vernakalant (iv) development program for the United States market, we expect that additional trials and studies may be required to obtain approval. The results of such trials may not be favourable or viewed favourably by us or third parties, including investors, equity research analysts and potential collaborators. Share prices for life sciences companies have declined significantly in certain instances where clinical results were not favourable, were perceived negatively or otherwise did not meet expectations. Unfavourable results or negative perceptions regarding the results of clinical trials for any of our product candidates currently under development could cause our share price to decline significantly.

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

We set goals for, and make public statements regarding timing, of the accomplishment of objectives material to our success, such as the commencement and completion of clinical trials, anticipated regulatory approval dates, and time of product launch. The actual timing of these events can vary dramatically due to factors within and

beyond our control such as delays or failures in our clinical trials, the uncertainties inherent in the regulatory approval process, and delays in achieving product development, manufacturing or marketing milestones necessary to commercialize our products. We cannot assure you that our clinical trials will be completed, that we will make regulatory submissions or receive regulatory approvals as planned, or that we will be able to adhere to our current schedule for the scale-up of manufacturing and launch of any of our products. Any failure to achieve one or more of these milestones as planned would have a material adverse effect on our business, financial condition and results of operations.

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

Our success will depend 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 application for patent protection and patent licenses can be unpredictable.

Our patent portfolio related to vernakalant contains two issued U.S. patents and one issued European patent with composition of matter claims specific to vernakalant and/or claims specific to the use of vernakalant to treat arrhythmia and we are pursuing similar claims in other jurisdictions worldwide. In addition to the foregoing specific composition of matter protection, we also have nineteen issued U.S. patents, eight pending U.S. applications and numerous issued patents and pending applications in other jurisdictions worldwide more generally related to vernakalant, including, but not limited to, composition of matter, various therapeutic uses, manufacturing methods and formulations thereof. We have no assurance that any patents from these applications will ever be issued.

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. Third parties may attempt to circumvent our patents by means of alternative designs and processes. Further, third parties may 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 also a risk that any patents issued relating to our vernakalant products or any patents licensed to us may be successfully challenged or that the practice of our vernakalant products might infringe the patents of third parties. If the practice of our vernakalant 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. 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 if 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 or license 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 at this point 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 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.

**Some of our products may rely on licenses of proprietary technology owned by third parties and we may not be able to maintain these licenses on favourable terms.**

The manufacture and sale of some of the products we hope to develop may involve the use of processes, products, or information, the rights to which are owned by third parties. Such licenses frequently provide for limited periods of exclusivity that may be extended only with the consent of the licensor. If licenses or other rights related to the use of such processes, products or information are crucial for marketing purposes, and we are not able to obtain them on favourable terms, or at all, the commercial value of our products will be significantly impaired. If we experience delays in developing our products and extensions are not granted on any or all of such licenses, our ability to realize the benefits of our efforts may be limited.

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

We will require substantial additional capital resources to further develop product candidates currently under development, obtain regulatory approvals and ultimately to commercialize such product candidates. We believe that our current capital resources, including our anticipated milestone payments and anticipated revenues from Merck under the terms of our collaboration and license agreements, should be sufficient to fund our operations as currently anticipated for at least the next 24 months. However, advancing our other product candidates, market expansion of our current products or development of any new product candidates through to commercialization 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 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 experience delays or unexpected increased costs in connection with obtaining regulatory approvals;
- we are required to perform additional pre-clinical studies and clinical trials;
- we experience unexpected or increased costs relating to preparing, filing, prosecuting, maintaining, defending and enforcing patent claims; or
- we elect to develop, acquire or license new technologies and products.

We could potentially seek additional funding through corporate collaborations and licensing arrangements or through public or private equity or debt financing. However, if our research and development activities do not show positive progress, or if capital market conditions in general, or with respect to life sciences or development stage companies such as ours in particular, are unfavourable, our ability to obtain 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. Alternatively, we may choose to further access the line of credit currently available to us under the collaboration and license agreement with Merck. In February 2010, we drew down \$25 million under the Merck line of credit and in January 2012, we received an additional \$25 million.

If sufficient capital is not available, we may be required to delay, reduce the scope of, eliminate or divest of one or more of our research or development projects, any of which could have a material adverse effect on our business, financial condition, prospects or results of operations.

**We have been advanced funds under our credit facility with Merck and we must repay such funds when they become due and payable.**

Under our credit facility with Merck, a Merck affiliate advanced to us \$25 million in February 2010 and another \$25 million in January 2012. We are required to pay quarterly interest payments on the funds advanced to us under the credit facility. The first advance must be repaid in full by December 31, 2016 and the second advance must be repaid in full by December 31, 2017. Our ability to repay our indebtedness to Merck under the credit facility when such amounts are due and payable will depend upon our available capital resources at such time. If we do not have sufficient capital resources to make such payments, we may need to seek additional funding through public or private equity or debt financing, or we may be required to divert capital that would otherwise have been used for research or development projects, which could adversely affect our business, financial condition, prospects and 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.**

The pre-clinical and clinical trials of any products developed by us or our collaborative partners 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 focussed 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 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 guidelines 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 collaborative partner, 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 and lead to other adverse consequences.

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, as we experienced with Astellas' submission to the FDA of the NDA for vernakalant (iv), the delay by the FDA in providing us with an action letter by the January 19, 2008 PDUFA date, the approvable action letter subsequently received from the FDA in August 2008 requiring us to provide additional information and safety data, and the single confirmatory additional Phase 3 clinical trial, named ACT 5, required under an SPA with the FDA. We may have limits imposed on us, or our product candidates, or fail to obtain the regulatory approval required from the applicable regulatory authorities to commercialize our product candidates. In October 2010, we announced that Astellas has suspended patient enrollment in the Phase 3, ACT 5 study following a single unexpected serious adverse event of cardiogenic shock experienced by a patient with atrial fibrillation who received vernakalant (iv). There is no guarantee that the FDA will allow us to re-start the clinical development program for

vernakalant (iv) in the United States. In addition, delays or rejections may be encountered based upon changes in regulatory policy during the period of 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, including BRINAVESS™, 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 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.

Sales and marketing of pharmaceutical products in the United States are subject to extensive federal and state laws governing on-label and off-label advertising, scientific/educational grants, gifts, consulting and pricing. Advertising and promotion of approved drugs must comply with the U.S. *Federal Food, Drug, and Cosmetic Act*, as amended, the U.S. *Anti-Kickback Statute*, as amended, provisions of the U.S. *Social Security Act*, as amended,

similar state laws, and the U.S. *False Claims Act*, as amended. The distribution of product samples to physicians in the United States must comply with the requirements of the U.S. *Prescription Drug Marketing Act*, as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. *Omnibus Budget Reconciliation Act of 1990*, as amended and the U.S. *Veteran's Health Care Act of 1992*, as amended. If products are made available to authorized users of the U.S. Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. 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. 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;
- 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 FDA 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 United States or European Union does not ensure we will obtain regulatory approval in other countries.**

We and our collaborative partner 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 and our collaborative partner 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 and 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 and criminal prosecution.

**If we do successfully develop our products, they may not achieve market acceptance and we may not be able to sell them.**

Because of the competitive and dynamic nature of the drug development industry, there is a risk that BRINAVESS<sup>TM</sup> or any other candidates in respect of which we obtain marketing approval in the future:

- will not be economical to market, reimbursable by third party payors, or marketable at prices that will allow us to achieve profitability;
- will not be successfully marketed or achieve market acceptance;
- will not be preferable to existing or newly developed products marketed by competitors;
- will infringe proprietary rights held by third parties now or in the future that would preclude us from marketing any such product; or
- will not be subject to patent protection.

The degree of market acceptance of BRINAVESS<sup>TM</sup> or other products developed by us and our collaborative partners, if any, will depend on a number of factors, including the establishment and demonstration in the medical community of the clinical efficacy and safety of our products and their potential advantage over alternative treatment methods, and similar acceptance by public and private third party payors. We cannot assure you that physicians, patients, the medical community in general or payors will accept and utilize or reimburse any products we and our collaborative partner developed or may in the future develop.

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 do not currently have the marketing expertise needed to commercialize our products.**

We have limited resources to market BRINAVESS<sup>TM</sup> or any other potential products. Marketing of new products presents greater risks than are posed by the continued marketing of proven products. Under our collaborative agreement with Merck, we have licensed to Merck the rights to market vernakalant (iv) in all jurisdictions with the exception of North America. Similarly, pursuant to our North American Vernakalant (iv) Agreement with Merck, we have licensed to Merck the rights to market vernakalant (iv) in North America if and when it is approved for marketing by the applicable regulatory authorities. If either of our agreements with Merck are terminated for any reason, we would need to find a new collaborative partner or undertake this marketing on our own. Furthermore, we have no similar arrangement for any other product candidates. Accordingly, if we are able to commercialize any of our other product candidates, we would either have to develop a marketing capability (including a sales force) or attempt to enter into a joint venture, license, or other arrangement with third parties to provide the financial and other resources needed to market such products. We do not currently employ any full-time sales personnel and have limited experience in hiring and managing such personnel. Our ability to develop our own marketing capability is untested. Our ability to negotiate favourable terms in connection with additional arrangements to market our product candidates, if and when approved, through joint venture, license or other arrangements is unknown at this time.

While our collaborative agreements with Merck provide that Merck is responsible for the commercial manufacture of vernakalant (iv), we have no experience manufacturing commercial quantities of products and do not

currently have the resources to manufacture commercially any additional products that we may develop. Accordingly, if we were able to develop any additional products with commercial potential, we would either be required to develop the facilities to manufacture such products independently, or secure a contract manufacturer or enter into another arrangement with third parties to manufacture such products. If we are unable to develop such capabilities or enter into any such arrangement on favourable terms, we may be unable to compete effectively in the marketplace.

Because of the high degree of expertise necessary to produce chemical products, and applicable legal and regulatory requirements such as current GMP requirements, it is a time-consuming process to arrange for an alternative manufacturer. We may not be able to identify and qualify any such manufacturers on a timely basis, which may cause significant delay in our development process. Even if we are able to identify and qualify an alternative manufacturer, we may not be able to obtain favourable terms on any manufacturing agreement we enter into with them. We have relied and will continue to rely on contract manufacturers for the foreseeable future to produce quantities of products and substances necessary for research and development, pre-clinical trials, human clinical trials and product commercialization. It will be important to us that such products can be manufactured at a cost and in quantities necessary to make them commercially viable. At this point in time, we have not attempted to identify, and do not know whether there will be, any third party manufacturers which will be able to meet our needs with respect to timing, quantity and quality for commercial production. In addition, if we are unable to contract for a sufficient supply of required products and substances on acceptable terms, or if we should encounter delays or difficulties in our relationships with manufacturers, our research and development, pre-clinical and clinical testing would be delayed, thereby delaying the submission of products for regulatory approval or the market introduction and subsequent sales of such products. Any such delay may have a material adverse effect on our business, financial condition and results of operations.

**Inability to manage our future growth could impair our business, financial condition, and results of operations.**

Our future growth, if any, may cause a significant strain on our management and our operational, financial and other resources. Our ability to manage our growth effectively will require us to implement and improve our operational, financial, manufacturing and management information systems and to expand, train, manage and motivate our employees. These demands may require the hiring of additional management personnel, the development of additional expertise by management and the acquisition of additional capital assets. Any increase in resources devoted to research, product development and sales, marketing and distribution efforts without a corresponding increase in our operational, financial and management information systems could have a material adverse effect on our business, financial condition and results of operations.

**Acquisitions of companies or technologies may result in disruptions to our business.**

As part of our business strategy, we may acquire additional assets or businesses 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;
- 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;
- 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.

**If certain milestones under the Lilly in-licensing agreement are achieved, we will be required to make cash milestone payments.**

Under the terms of the Lilly in-licensing agreement, we and our future collaborative partner, if any, are required to make payments of up to \$40 million upon the occurrence of certain milestone events. However, our future collaborative partner may or may not have sufficient financial resources to make such milestone payments. We may still need to seek additional funding through public or private equity or debt financing, or we may be required to divert capital that would otherwise have been used for research or development projects, which could adversely affect our business, financial condition, prospects or results of operations.

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

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. Companies including, but not limited to, Boston Scientific, GlaxoSmithKline, Johnson & Johnson, Medtronic, Pfizer, Sanofi-Aventis, Astra Zeneca and Novartis all have products in development or in the market that could potentially compete with our venakalant product candidates.

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, or may achieve earlier patent protection or product commercialization than us, or that such competitors will commercialize products that will render our product candidates obsolete, possibly before we are able to commercialize them. Currently, these companies and institutions also compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our projects. Once we develop a marketable product, in addition to the foregoing, we will 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.

**We are subject to the risks associated with the use of hazardous materials in research and development conducted by us.**

Our research and development activities involve the use of hazardous materials and chemicals. We are subject to federal, provincial, state, local and foreign laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. The risk of accidental contamination or injury from these materials cannot be completely eliminated, despite our efforts to comply with applicable safety standards. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources. We have secured a blanket property insurance policy to cover costs related to accidental damage to our properties and interruption of our business. If we are required to institute additional safety procedures because we are found not to be in compliance or if more stringent or additional regulations are adopted, we may be required to incur significant costs to comply with environmental laws and regulations, which might have a material adverse effect on our business, financial condition, and results of operations.

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

In recent years, 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 United States, Canada 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 potential products. Significant changes in the healthcare system in the United States, Canada, 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 ability to raise capital. Moreover, our ability to commercialize products may be adversely affected to the extent that these proposals have a material adverse effect on our business, financial condition and results of operations.

The ongoing debt crisis in Europe has caused certain countries in the European Union to announce austerity measures aimed at reducing costs in areas such as health care and has increased pressure on certain countries in the European Union, and on third party payors in those countries, to force companies to decrease the prices at which their healthcare products are sold in those countries. The debt crisis has also given rise to concerns that some countries in the European Union may not be able to pay for healthcare products at all. It is uncertain how long these effects will last, or whether this economic condition will worsen or improve. The economic condition of certain countries in the European Union may reduce our ability to obtain appropriate pricing and adequate reimbursement for products that we or our collaborative partners would commercialize in such countries following regulatory approval, which would lower potential revenues from such products and could have a material adverse effect on our business, financial condition and results of operations.

In addition, companies such as ours have been subjected to additional scrutiny by the U.S. federal government in recent years. The Office of Inspector General of the United States Department of Health and Human Services, or OIG, has increased the number of inspections of companies such as ours. Further, the number of investigations caused by employees or others, commonly referred to as *qui tam* actions, have increased markedly in recent years. Even if we have committed no wrongdoing, responding to such OIG investigations or other government investigations could adversely impact our operations and could have a material adverse effect on our business, financial condition and results of operations.

**U.S. federal legislation could adversely impact our ability to economically price our potential products.**

In the United States and other countries, 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. In many of the markets where we or our collaborative partner would commercialize a product following regulatory approval, the prices of pharmaceutical products are subject to direct price controls by law and to drug reimbursement programs with varying price control mechanisms. In the United States, there has been an increased focus on drug pricing in recent years. Although there are currently no direct government price controls over private sector purchases in the United States, federal legislation requires pharmaceutical manufacturers to pay prescribed rebates on certain drugs to enable them to be eligible for reimbursement under certain public health care programs such as Medicaid. Various states have adopted further mechanisms under Medicaid that seek to control drug prices, including by disfavoring certain higher priced drugs and by seeking supplemental rebates from manufacturers. Managed care has also become a potent force in the market place that increases downward pressure on the prices of pharmaceutical products.

U.S. federal legislation enacted in December 2003 has altered the way in which physician-administered drugs covered by Medicare are reimbursed. Under this new reimbursement methodology, physicians are reimbursed based on a product's average sales price. This reimbursement methodology has generally led to lower reimbursement levels. This U.S. federal legislation has also added an outpatient prescription drug benefit to

Medicare, effective January 2006. The benefits are provided primarily through private entities, which will attempt to negotiate price concessions from pharmaceutical manufacturers. These negotiations may increase pressures to lower prices. While this law specifically prohibits the U.S. government from interfering in price negotiations between manufacturers and Medicare drug plan sponsors, some members of the U.S. Congress are pursuing legislation that would permit the U.S. government to use its enormous purchasing power to demand discounts from pharmaceutical companies, thereby creating de facto price controls on prescription drugs. In addition, this U.S. law requires the U.S. Congress to consider cost containment measures in the event that Medicare cost increases exceed a certain level. These cost containment measures could include some sorts of limitations on prescription drug prices. The viability of our products and our results of operations could be materially harmed by the different features of the Medicare prescription drug coverage legislation, by the potential effect of such legislation on amounts that private insurers will pay for our products and by related healthcare reforms that may be enacted or adopted in the future.

If we succeed in bringing one or more products to market, there can be no assurance that these products will be considered cost effective and that reimbursement to the consumer will be available or will be sufficient to allow us to sell our products on a competitive basis. Given the potential market constraints on pricing, the availability of competitive products in these markets may further limit our flexibility in pricing and in obtaining adequate reimbursement for our potential products. If adequate coverage and reimbursement levels are not provided by government and third party payors for uses of our products, the market acceptance of our products would be adversely affected.

**The use of pharmaceutical products may expose us to product liability claims.**

The products we are developing, and will attempt to develop, will undergo extensive clinical testing and will require approval from the applicable regulatory authorities prior to sale in the United States, Canada, the European Union and other countries or regions. However, despite all reasonable efforts to ensure safety, it is possible that we or our partners will sell products which are defective, to which patients react in an unexpected manner, or which are alleged to have harmful side effects. The sale of such products may expose us to potential liability. Additionally, we may be exposed to product liability claims in the development of the products through 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. 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, any liability that we may have as a result of the manufacture of any products could have a material adverse effect on our financial condition, business and results of operations, to the extent insurance coverage for such liability is not available. At present, we have secured limited product liability coverage in an amount equal to what we believe are industry norms for our current stage of development, which may or may not cover all potential liability claims if any arose. Obtaining insurance of all kinds has recently become increasingly more costly and difficult and, as a result, such insurance may not be available at all, may not be available on commercially acceptable terms or, if obtained, may be insufficient to satisfy asserted claims.

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

As a technology-driven company, intellectual input from key management and scientists is critical to achieve our scientific and 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 scientific or 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.

We have employment contracts with all of our key executives, which include incentive provisions for the granting of stock options that vest over time, designed to encourage such individuals to stay with us. However, a declining share price, whether as a result of disappointing progress in our 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 were to lose our foreign private issuer status under U.S. federal securities laws, we would likely incur additional expenses associated with compliance with the U.S. securities laws applicable to U.S. domestic issuers.**

As a foreign private issuer, we are exempt from certain of the provisions of the U.S. federal securities laws. For example, the U.S. 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 U.S. 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 following a loss of our foreign private issuer status. 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.

**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. In addition, we have elected to report our financial results in U.S. GAAP commencing in 2010, which may also have an adverse impact on our future financial position or results of operations. Compliance with changing regulations of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations, and standards relating to corporate governance and public disclosure are creating uncertainty for companies such as ours, and insurance costs are increasing as a result of this uncertainty.

**We have entered into an exclusive in-licensing agreement through our Swiss subsidiary and are engaged in international operations. These international operations subject us to political, regulatory, legal, tax and economic risks and uncertainties.**

We entered into the exclusive in-licensing agreement with Lilly for GED-aPC through Cardiome Development AG, our wholly-owned subsidiary, which was continued into Switzerland from British Columbia in November 2007.

Our international operations subject us to varying degrees of political, regulatory, legal, tax and economic risks and uncertainties, particularly in countries with different legal systems. These risks and uncertainties vary from country to country and include, but are not limited to, the uncertainties of, or changes in, foreign laws, governmental regulations and policies, potentially adverse tax consequences, currency conversion and control risks, restrictions on foreign exchange and repatriation, restrictions on foreign investment and changing political

conditions. Depending on how these laws, regulations and policies were to be applied or changed, we could suffer adverse financial consequences.

**We may face exposure to adverse movements in foreign currency exchange rates while completing international clinical trials and when our products are commercialized, if at all.**

We intend to generate revenue and expenses internationally that are likely to be primarily denominated in U.S. and other foreign currencies. Our intended international business will be subject to risks typical of an international business including, but not limited to, differing tax structures, a myriad of regulations and restrictions, and general foreign exchange rate volatility. 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, results of operations, financial condition and cash flows will not be materially adversely affected by exchange rate fluctuations.

### **DIVIDENDS AND DISTRIBUTIONS**

We have not declared or paid any dividends or distributions on our common shares or other securities since our incorporation. We currently anticipate that we will retain any earnings to finance expansion and development of our business. Any future determination to pay dividends or distributions will be at the discretion of our board of directors and will depend upon our results of operations, financial condition, current and anticipated cash needs, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deem relevant.

### **CAPITAL STRUCTURE**

Our authorized share capital consists of an unlimited number of common shares and an unlimited number of preferred shares, issuable in series. As at March 26, 2012, 61,129,091 common shares were issued and outstanding and no preferred shares were issued and outstanding. In addition, as of March 26, 2012, there were 4,762,941 common shares issuable upon the exercise of outstanding stock options at a weighted average exercise price of Cdn.\$7.11 per common share. All of the common shares are of the same class and, once issued, rank equally as to entitlement to dividends, voting powers (one vote per share) and participation in assets upon dissolution or winding-up. No common shares have been issued subject to call or assessment. The 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 bylaws and in the *Canada Business Corporations Act*.

Preferred shares may be issued 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. On July 24, 2008, we amended our articles to create the Series A Preferred Shares. As at March 26, 2012, there are no Series A Preferred Shares issued and outstanding.

The Series A Preferred Shares are convertible into common shares of Cardiome at the option of either the holder or us, depending on the circumstances, and automatically, immediately prior to the completion of a change of control (as such term is defined in the share rights and restrictions attached to our Series A Preferred Shares). The initial conversion ratio, which is subject to adjustment, is one common share for each Series A Preferred Share so converted.

All or any part of the outstanding Series A Preferred Shares may be redeemed at any time at a redemption price equal to \$11.00 per share plus any declared and unpaid dividends thereon.

The holders of the Series A Preferred Shares are entitled to dividends if, as and when declared and payable to the holders of common shares. The holders of outstanding Series A Preferred Shares, if any, are entitled, in the event of the liquidation, winding-up or dissolution of Cardiome, prior to any payment to the holders of common shares or shares ranking subordinate to the Series A Preferred Shares, to a repayment of capital plus any declared and unpaid dividends. The holders of the Series A Preferred Shares have the right to attend all meetings of the shareholders of Cardiome (except meetings at which only holders of another class or series of shares are entitled to vote) and to vote at such meetings, together with the holders of common shares as if they were a single class of shares at a rate of one vote per common share that each holder of Series A Preferred Shares would be entitled to upon conversion of all of such holder's Series A Preferred Shares upon any matter submitted to the shareholders of Cardiome, except those matters required by law to be submitted to a class vote of the holders of Series A Preferred Shares, in which case the Series A Preferred Shares carry one vote per share.

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 Stock Market, or NASDAQ, require a quorum for shareholder meetings to be not less than 33 1/3% 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 Toronto Stock Exchange, or the TSX, in Canada (trading symbol: COM) and in the United States on NASDAQ (trading symbol: CRME).

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

Month	High	Low	Close	Volume
Jan-11	7.00	6.04	6.30	1,118,331
Feb-11	6.83	5.30	5.62	1,036,867
Mar-11	5.56	4.10	4.12	669,655
Apr-11	5.41	3.92	5.15	1,406,094
May-11	5.70	4.61	5.09	866,947
Jun-11	5.01	3.75	4.24	610,041
Jul-11	5.50	3.91	4.75	779,246
Aug-11	4.75	3.32	3.73	703,263
Sep-11	3.88	3.35	3.58	322,773
Oct-11	3.65	3.12	3.30	220,620
Nov-11	3.45	1.90	1.98	756,927
Dec-11	2.72	1.94	2.68	789,808

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

Month	High	Low	Close	Volume
Jan-11	7.10	6.05	6.24	4,752,600
Feb-11	6.92	5.35	5.77	4,120,200
Mar-11	5.77	4.21	4.28	4,295,400
Apr-11	5.70	4.07	5.36	7,455,800
May-11	5.86	4.80	5.20	5,514,100
Jun-11	5.19	3.85	4.45	4,157,800
Jul-11	5.84	4.06	5.01	7,172,400
Aug-11	5.16	3.36	3.84	5,642,500
Sep-11	3.93	3.21	3.29	4,095,600

<b>Month</b>	<b>High</b>	<b>Low</b>	<b>Close</b>	<b>Volume</b>
Oct-11	3.59	2.86	3.35	4,194,400
Nov-11	3.43	1.90	2.04	4,201,900
Dec-11	2.67	1.86	2.63	5,287,500

### **PRIOR SALES**

On July 25, 2008, we issued 2,272,727 Series A Preferred Shares to CR Intrinsic at a price of \$11.00 per share for gross proceeds of approximately \$25 million. On October 6, 2009, 2,272,727 Series A Preferred Shares were converted into common shares on a one-to-one basis at the option of CR Intrinsic. No Series A Preferred Shares remain outstanding subsequent to the conversion.

### **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 <sup>(5)</sup> 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 2010 to present – Chairman, Cardiome Pharma Corp.; August 2009 to Aug 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.; April 1998 to February 2006 – President, Cardiome Pharma Corp.
Jackie M. Clegg <sup>(3)(4)</sup> Washington, DC, United States Director	September 2, 2004	September 2001 to present – Founder and Managing Partner, Clegg International Consultants, L.L.C.; July 2007 to present - Member of board of directors of Chicago Mercantile Exchange; September 2003 to July 2007 - Member of board of directors of Chicago Board of Trade; July 2006 to present – Member of the board of directors of Brookdale Senior Living; June 2009 to present – Member of the board of directors for the Public Welfare Foundation.

<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)(4)</sup> Georgia, United States Director	October 14, 2004	Head of Advanced Technology Development Center – Biosciences and Start-Up Company Catalyst, Georgia Institute of Technology, Enterprise Innovation Institute (November 2009 – present); October 2008 to November 2009 – Head of Operations and Commercial Development for Altea Therapeutics Corporation; June 2006 to July 2008 – President and Chief Executive Officer of Tikvah Therapeutics Inc.; January 2006 to May 2006 – Global Senior Vice President, Regulatory, Safety, and Quality, and External Affairs, Solvay Pharmaceuticals, Inc.; May 2000 to December 2005 – President and CEO, Solvay Pharmaceuticals, Inc.
Peter W. Roberts <sup>(3)(4)</sup> British Columbia, Canada Director	September 18, 2005	November 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 audit committee of WebTech Wireless Inc.; March 2004 – Retired as Chief Financial Officer and Corporate Secretary of Sierra Wireless, Inc..
Richard M. Glickman <sup>(2)(5)(6)</sup> British Columbia, Canada Director	December 11, 2006	January 2002 to July 2007 – Co-founder, Chairman and Chief Executive Officer, Aspreva Pharmaceuticals Corporation
William L. Hunter <sup>(2)(5)</sup> British Columbia, Canada Director	June 11, 2007	1997 to October 2011 – President and Chief Executive Officer and Founder of Angiotech Pharmaceuticals, Inc.
Douglas G. Janzen British Columbia, Canada President and Chief Executive Officer <sup>(1)</sup> , Director	January 6, 2003	August 2009 to present – President and Chief Executive Officer, Cardiome Pharma Corp.; March 2006 to August 2009 – President and Chief Business Officer, Cardiome Pharma Corp.; January 2003 to March 2006 – Chief Financial Officer, Cardiome Pharma Corp.; March 2012 to present – Member of the board of directors of ICo Therapeutics Inc.

<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>
Curtis Sikorsky British Columbia, Canada Chief Financial Officer	June 9, 2006	June 2006 to present - Chief Financial Officer, Cardiome Pharma Corp.; April 2005 - June 2006 – Vice President, Finance, Nxtphase T&D Corporation; November 2002 to April 2005 – Vice President, 360networks Canada Ltd.
Donald A. McAfee Washington, United States Executive Scientist	October 1, 2004	February 2007 to present – Chief Scientific Officer, Cardiome Pharma Corp.; October 2004 to February 2007 – Vice President, New Product Development, Cardiome Pharma Corp.
Karim Lalji British Columbia, Canada Senior Vice President, Commercial Affairs	September 14, 2006	February 2007 to present – Senior Vice President, Commercial Affairs, Cardiome Pharma Corp.; September 2006 to February 2007 – Senior Vice President, Commercial Affairs, Cardiome Pharma Corp. (part-time); December 2006 to February 2007 - Vice President of Business Strategy and New Product Commercialization, Sepracor Inc.; July 2003 to December 2006 – Vice President, New Product Commercialization and Business Analytics, Sepracor Inc.
Sheila M. Grant British Columbia, Canada Vice President, Product Development – vernakalant	August 1, 2003	April 2005 to present – Vice President of Product Development – vernakalant, Cardiome Pharma Corp.; August 2003 to April 2005 – Vice President, Commercial Affairs, Cardiome Pharma Corp.

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- (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. Janzen was appointed our President and Chief Executive Officer. Prior to being appointed Chief Executive Officer, Mr. Janzen was our President and Chief Business Officer, and prior to that, our Chief Financial Officer.
  - (2) Member of the Compensation Committee.
  - (3) Member of the Corporate Governance Committee.
  - (4) Member of the Audit Committee.
  - (5) Member of the Nominating Committee.
  - (6) Lead Independent Director.

As at March 26, 2012, our directors and executive officers owned, or exercised control of or direction over, directly or indirectly, less than 1% 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., and CEO for Synapse Technologies Inc. Mr. Rieder is currently the Chief Executive Officer of ESSA Pharma Inc. and is non-executive chairman of the board of directors of Akela Pharma Inc.

**Doug G. Janzen, President and Chief Executive Officer & Director.** Mr. Janzen is Cardiome's President and Chief Executive Officer, and serves on Cardiome's Board of Directors. Mr. Janzen joined Cardiome in 2003 as Chief Financial Officer, and served as President and Chief Business Officer from March 2006 to August 2009. He has been instrumental in developing and implementing Cardiome's operational strategy and in the advancement of Cardiome's corporate development and the strengthening of its financial position. Mr. Janzen currently serves as a director for a number of public and private technology companies and as a director for various industry trade associations. Prior to joining Cardiome, Mr. Janzen served as Managing Director, Health Sciences and Partner at Sprott Securities, Inc., a Toronto-based investment bank.

**Curtis Sikorsky, CA, Chief Financial Officer.** Mr. Sikorsky is Cardiome's Chief Financial Officer, with responsibility for overseeing our financial operations. He joined Cardiome in June 2006, bringing over ten years of public and private company experience as well as three years of direct audit and tax experience. Prior to joining Cardiome, he was Vice President of Finance at NxtPhase T&D Corporation, a private Vancouver-based energy technology company. He has also held senior financial roles including Vice President and Corporate Controller with 360networks inc. and Corporate Controller with WIC Western International Communications. Mr. Sikorsky began his career with KPMG performing audit, tax and accounting work for major clients. He is a Chartered Accountant and holds a Bachelor of Commerce Degree from the University of Saskatchewan.

**Donald A. McAfee, Ph.D. Executive Scientist.** Dr. McAfee is Cardiome's Executive Scientist. He joined Cardiome in October 2004 as Vice President of New Product Development. He has been a scientist and manager in academia and industry for more than 40 years. As Founder, Chief Executive Officer, and Chief Technical Officer of Aderis Pharmaceuticals, Inc. (formerly Discovery Therapeutics, Inc.), Dr. McAfee led the introduction of a number of clinical candidates including a therapeutic patch for Parkinson's disease now marketed, and adenosine receptor based cardiovascular therapeutics and diagnostics still in development.

**Jackie M. Clegg, Director.** Ms. Clegg currently serves as a Managing Partner of Clegg International Consultants, LLC. Ms. Clegg is a member of the board of directors of the Chicago Mercantile Exchange, Brookdale Senior Living and is the Audit Committee Chair of The Public Welfare Foundation, a not for profit organization. Previously, Ms. Clegg served on the board of directors of Javelin Pharmaceuticals, Inc., Blockbuster Inc., the Chicago Board of Trade, and IPCRe. She has served as the chair of special committees for divestiture, mergers and acquisitions and has served as the chair of various audit committees. Previously, Ms. Clegg served in the U.S. Government as Vice Chair, First Vice President and Chief Operating Officer of the Export-Import Bank of the United States, or Ex-Im Bank. Prior to joining Ex-Im Bank, she served as a staff member on the U.S. Senate Committee on Banking International Finance Subcommittee and as an associate staff member to the U.S. Senate Committee on Appropriations.

**Harold H. Shlevin, Ph.D., Director.** Dr. Shlevin is Head of the Advanced Technology Development Center – Biosciences and Start-Up Company catalyst in the Enterprise Innovation Institute of the Georgia Institute of Technology. In this general faculty role, Dr. Shlevin assists faculty in identifying technology worthy of commercialization, catalyzes formation of new start-up bioscience companies, and mentors 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 and an Advisor to Clearside Biomedical, Inc., an

ophthalmic pharmaceutical and medical device company. 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 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. 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. His past industry experience includes leadership roles at G.D. Searle and Co., Revlon Health Care Group, Ciba-Geigy Corporation, Bausch and Lomb Pharmaceuticals, and he was a founder of Ciba Vision Ophthalmics. 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 Probtect Corporation, a rational drug design and molecular genetics firm, where he established and introduced the first licensed DNA-based forensic and paternity testing services in Canada. He has served on numerous biotechnology boards including roles as Chairman of Life Sciences B.C. (formerly the British Columbia Biotechnology Alliance), Director of the Canadian Genetic Disease Network and a member of the federal government's National Biotechnology Advisory Committee. Dr. Glickman currently serves as a member of the British Columbia Innovation Council and a Director for the Vancouver Aquarium. Dr. Glickman received the Ernst & Young Entrepreneur of the Year 2004 Award for the Pacific Region Life Sciences Group and has received both Canada's and British Columbia's Top 40 under 40 Award for Entrepreneurs and has been the recipient of 2006 BC Biotech Leadership Award.

**William Hunter, M.D., Director.** Dr. Hunter was one of Angiotech Pharmaceuticals Inc.'s, or Angiotech, co-founders and served as President and Chief Executive Officer of Angiotech for over 14 years until October 2011. He led Angiotech through significant corporate milestones from its initial rounds of private and public financings, to product commercialization and profitability. Active in a variety of business and scientific organizations, in addition to Cardiome, Dr. Hunter serves on the board of directors for Zalicus Pharmaceuticals Inc. in Boston (NASDAQ: ZLCS) and West Point Grey Academy in Vancouver. Dr. Hunter has been honoured with many awards including the 2006 Principal Award for Innovation from the Manning Foundation, the 2005 BC Innovation Council's Cecil

Green Award for Science and Technology Entrepreneurship and the co-recipient of 2006 NSERC Synergy Awards for Innovation along with Dr. Helen Burt, recognizing the collaboration between the University of British Columbia and Angiotech. Dr. Hunter received his BSc from McGill University, and MSc and MD from the University of British Columbia.

**Karim Lalji, Senior Vice President, Commercial Affairs.** Karim Lalji is Cardiome's Senior Vice President, Commercial Affairs. 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. 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 Medical Center in Boston, Massachusetts, an academic teaching hospital for Harvard Medical School. Mr. Lalji holds a Bachelors 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, Vice President, Product Development – vernakalant.** Ms. Grant is Cardiome's Vice President of Product Development for vernakalant. She is responsible for the overall management of the vernakalant (iv) and vernakalant (oral) programs. She has overseen development of vernakalant from its initial toxicology studies as a clinical candidate in 1999, through to its current stage of development. 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 a B.Sc. (Hons) degree from Essex University, U.K. and 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:

- 360networks inc., or 360networks, and each of the following subsidiaries: 360fibre ltd., 360finance ltd., Carrier Centers (Canada) Ltd., 360 Urbanlink Ltd., 360networks (CDN fiber) ltd., 360networks services ltd., 360cayer ltée, 360engineering ltd., 360pacific (Canada) ltd. and 360networks sub inc. (collectively, the “360 Canadian Subsidiaries”). On June 28, 2001, 360networks and the 360 Canadian Subsidiaries filed for creditor protection under the *Companies’ Creditors Arrangement Act* (“CCAA”) in the Supreme Court of British Columbia. Subsequent to the 360 Canadian Subsidiaries seeking protection under the CCAA and with the approval of the Supreme Court of British Columbia, Mr. Sikorsky was appointed a director of each of the 360 Canadian Subsidiaries.
- 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 effect 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.

## 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, Jackie M. Clegg 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, 2011 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, 2011 and December 31, 2010. During 2011 and 2010, KPMG LLP was our only external auditor.

	December 31, 2011	December 31, 2010
Audit Fees <sup>(1)</sup>	Cdn.\$411,620	Cdn.\$567,975
Audit-Related Fees <sup>(2)</sup>	Nil	Nil
Tax Fees <sup>(3)</sup>	Cdn.\$22,000	Nil
All Other Fees	Cdn.\$5,000	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 Denver, Colorado.

## **MATERIAL CONTRACTS**

We have not, during our financial year ended December 31, 2011, entered into any material contracts and do not have any material contracts entered into prior to our financial year ended December 31, 2011 but still in effect, other than contracts in the ordinary course of business, except for the following:

- (1) Collaboration and license agreement entered into on April 8, 2009 with Merck described in the section titled “General Development of the Business”.
- (2) North American Vernakalant (iv) Agreement entered into on October 16, 2003 with Astellas, as assigned to Merck, described in the section titled “Narrative Description of the Business”.
- (3) Development and license agreement entered into on April 30, 2007 with Lilly 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 2011 and 2010 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 *U.S. Securities Act of 1933*, as amended, and the applicable rules and regulations thereunder.

## **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 6, 2011.

### **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, 2011.

**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: December 5, 2011