


# DIAMEDICA INC.

# MANAGEMENT'S DISCUSSION & ANALYSIS

## FOR THE THREE MONTHS ENDED MARCH 31, 2016 and 2015

Dated: May 26, 2016

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Minneapolis, Minnesota, 55447
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All references in this management's discussion and analysis ("MD&A") to "the Company", "DiaMedica", "we", "us", or "our" refer to DiaMedica Inc. and the subsidiaries through which it conducts its business, unless otherwise indicated.

The following MD&A is prepared as of May 26, 2016 for DiaMedica for the three months ended March 31, 2016 and 2015 and should be read in conjunction with the unaudited condensed consolidated interim financial statements for the three months ended March 31, 2016 and 2015 and the audited consolidated financial statements and accompanying notes for the years ended December 31, 2015 and 2014, which have been prepared by management in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board ("IASB"). This MD&A also should be read in conjunction with the Company's Annual Information Form dated April 27, 2016. Additional information regarding the Company is available on SEDAR at http://www.sedar.com and on the Company's website at http://www.diamedica.com.

All amounts are in Canadian dollars, unless otherwise indicated.

## GOING CONCERN

The Company's condensed consolidated interim financial statements have been prepared using IFRS that are applicable to a going concern, which contemplates the realization of assets and settlement of liabilities and commitments in the normal course of business. There are material uncertainties that cast significant doubt about the appropriateness of the use of the going concern assumption because the Company has experienced operating losses and cash outflows from operations since incorporation, has an accumulated deficit of $47.6 million, a net asset deficiency of $1.3 million and a working capital deficiency of $0.8 million as of March 31, 2016. Further, the Company's cash resources are not sufficient for the next twelve months of planned operations; additional funding will be required in order to continue the Company's research and development and other operating activities as it has not reached successful commercialization of its products. The Company's ability to continue as a going concern is dependent on its ability to continue obtaining sufficient funds to conduct its research and development, and to successfully commercialize its products.

The Company's future operations are therefore dependent upon its ability to secure additional funding, generate product revenues, and negotiate license agreements with partners. There can be no assurance that the Company will be successful in commercializing its products, entering into strategic agreements with partners, or raising additional capital on favorable terms or at all. While the Company has taken measures to preserve cash, the Company will not have enough cash on hand to sustain operations until the end of fiscal 2016 unless further funds have been raised. Further, there can be no assurance that the Company will be successful in raising additional capital on favorable terms or at all. The availability of financing will be affected by the results of scientific and clinical research, the ability to attain regulatory approvals, the state of the capital markets generally with particular reference to life sciences' companies and other relevant commercial considerations. If the Company cannot secure additional financing on favorable terms or at all, the Company will have to consider additional strategic alternatives. Such additional strategies may include delays of product development expenditures, exploring the monetization of certain intangible assets, as well as seeking to out-license and/or divest assets through a merger, sale or liquidation of the Company.

The ability of the Company to continue as a going concern and to realize the carrying value of its assets and settle its liabilities and commitments when due is dependent on many factors, including, but not limited to the successful completion of the actions taken or planned which are intended to mitigate the material uncertainties related to adverse conditions and events that cast significant doubt about the validity of the going concern assumption used in preparing these consolidated financial statements. There can be no assurance that the Company will be able to obtain sufficient financing to meet future operational needs or that other strategies will be sufficient to permit the Company to continue as a going concern.

The Company's unaudited condensed consolidated interim financial statements for the three months ended March 31, 2016 and 2015 do not reflect adjustments in the carrying values of the Company's assets and liabilities, expenses, and the balance sheet classification used, that would be necessary if the going concern assumption was not appropriate. Such adjustments could be material.

# CAUTIONARY STATEMENT ABOUT FORWARD-LOOKING STATEMENTS

This MD&A contains forward-looking statements within the meaning of applicable securities laws. All statements contained herein, other than statements of historical facts, are forward-looking statements. The words “believe”, “anticipate”, “estimate”, “plan”, “expect”, “intend”, “may”, “project”, “will”, “would”, and similar expressions and the negative of such expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements contained in this MD&A include, but are not limited to, statements with respect to our:

- expected future loss and accumulated deficit levels;
- projected financial position and estimated cash burn rate;
- intention to commercialize our products for the treatment of stroke and potential additional indications;
- intention to develop any of our drugs either on our own or in partnership with others;
- intention to carry out trials on our products for the treatment of stroke and potential additional indications, and intention to publish the results thereof;
- intention to obtain regulatory approval for our products;
- expectations with respect to the cost of the testing and commercialization of our products;
- sales and marketing strategy;
- expectations regarding any future financings;
- anticipated sources of revenue;
- anticipated cost savings;
- ability to obtain the substantial capital required to fund research and operations;
- intentions regarding the protection of our intellectual property;
- business strategy; and
- intention with respect to dividends.

All forward-looking statements reflect our beliefs and assumptions based on information available at the time the assumption was made. These forward-looking statements are not based on historical facts but rather on management’s expectations regarding future activities, results of operations, performance, future capital, and other expenditures (including the amount, nature, and sources of funding thereof), competitive advantages, business prospects, and opportunities. By its nature, forward-looking information involves numerous assumptions, inherent risks, and uncertainties, both general and specific, known and unknown, that contribute to the possibility that the predictions, forecasts, projections, or other forward-looking statements will not occur. Factors which could cause future outcomes to differ materially from those set forth in the forward-looking statements include, but are not limited to:

- our ability to successfully initiate or complete clinical studies on a timely basis;
- our ability to reproduce the results of previously conducted clinical studies;
- our ability to obtain, on satisfactory terms or at all, the capital required for product development, operations and marketing;
- our ability to attract patients to our clinical trials;
- general economic, business and market conditions;
- product development delays and other uncertainties related to new product development;
- our ability to attract and retain business partners and key personnel;
- our inability to either commercialize our products or to commercialize our products profitably;
- operating losses and the extent of any future losses;
- our ability to operate as a going concern;
- our inability to establish or manage manufacturing, development or marketing collaborations;
- delay of, or failure to obtain, necessary regulatory approvals and, ultimately, product launches;
- dependence on third parties for successful commercialization of our products;
- inability to obtain quantities of development product in sufficient quantity or at standards acceptable to complete studies;
- the risk of termination or conversion to non-exclusive licenses or our inability to enforce our rights under our licenses;

- our ability to obtain patent protection and protect our intellectual property rights;
- commercialization limitations imposed by intellectual property rights owned or controlled by third parties;
- uncertainty related to intellectual property liability rights and liability claims asserted against us;
- uncertainty of recovery of advances to subsidiaries;
- impact of competitive products and pricing;
- future levels of government funding;
- our ability to meet all of the requirements and conditions for registering our Common Shares with the U.S. Securities and Exchange Commission; and
- other factors discussed under "Risk Factors".

Events or circumstances could cause our actual results to differ materially from those estimated or projected and expressed in, or implied by, these forward-looking statements. You also should consider carefully the matters discussed under "Risk Factors" in this MD&A. Additional risk factors are described in our current AIF. We undertake no obligation to update publicly or otherwise revise any forward-looking statements or the foregoing list of factors, whether as a result of new information or future events or otherwise, except as required by securities legislation.

# BUSINESS

## Overview

DiaMedica is a clinical stage biopharmaceutical company primarily focused on the development of novel recombinant proteins and monoclonal antibodies. Our lead product is DM199, a recombinant human KLK1 (rhKLK1 or tissue kallikrein-1) protein engineered to duplicate the actions of the naturally occurring human KLK1 protein produced in the pancreas, kidneys, and salivary glands of humans as a response to oxidative stress challenges. We believe DM199 has the potential to treat a large number of diseases with unmet needs where the KLK1 system is integral to the body's response to insult, including, but not limited to, acute vascular diseases of the brain, kidneys, and heart. The current primary focus for the development of DM199 is on acute ischemic stroke ("AIS") and diabetic kidney disease.

Recombinant tissue plasminogen activator ("tPA") is the only drug approved for the treatment of AIS in the U.S. and Europe. The use of tPA is severely limited by a narrow time window for administration of only 3 to 4.5 hours post-stroke. Thus the number of stroke patients that actually receive tPA therapy is only a small fraction of patients who suffer from an AIS. There is a very large unmet clinical need for a treatment option beyond the narrow tPA treatment window.

Kailikang® is a human urine-extracted KLK1 protein marketed by Techpool Bio-Pharma Inc. ("Techpool"), which has been approved for the treatment of AIS in China with a treatment window of up to 48 hours post-stroke. More than 40 published clinical studies conducted by diverse groups have demonstrated a beneficial effect of Kailikang® treatment in AIS, including a comprehensive meta-analysis covering 24 clinical studies involving 2,433 patients which concludes that "[human urinary KLK1] appears to ameliorate neurological deficits for patients with acute ischemic stroke and to improve long-term outcomes, though a few treated patients suffered from transient hypotension," (Journal of Evidence-Based Medicine. 2012 Feb;5(1):31-9).

The only Food and Drug Administration ("FDA") approved therapeutic-based treatment is tissue plasminogen activator ("tPA"), a protein involved in the breakdown of blood clots (thrombolysis) to re-establish normal blood flow (recanalization). However, tPA is only effective if administered within 3 to 4.5 hours post-stroke (Del Zoppo et al., (2009). Stroke J. Cereb. Circ. 40, 2945–2948), as outside this therapeutic window tPA is not only ineffective, but its use leads to a greater risk of hemorrhage (bleeding in the brain). As such, it is estimated that in the U.S. only 2-5% of AIS patients are treated with tPA (Miller et al., *The Neurohospitalist*. 2011 Jul; 1(3): 138-147). As a consequence of this limited time window, only a small percentage of stroke victims are treated with the currently available therapy; most simply receive supportive or "palliative" care.

DM199 is being positioned to treat AIS patients with therapy beginning up to 48 hours after the first sign of symptoms, thereby filling a large unmet need of patients who cannot receive tPA and replacing Kailikang® in China, potentially making therapy available to hundreds of thousands of patients who currently have no options. DiaMedica believes

that its proprietary DM199 protein allows for a higher purity and lower cost of goods product in comparison to Kailikang® while also addressing any potential supply constraints which makes Kailikang® potentially difficult and expensive to produce with the limited source of human urine. We believe these factors make DM199 a better-positioned product for regulatory approval worldwide as a recombinant protein is able to meet the rigorous manufacturing standards required for approval in comparison to a urine-derived protein.

DiaMedica is currently preparing to conduct a bridging study to determine pharmacokinetic and pharmadynamic profile of intravenous uKLK1 compared to intravenous and subcutaneous DM199 to establish dosing and delivery for Phase II/III studies based on approved Kailikang® dose. The Company intends to initiate a Phase II trial for AIS after completion of the bridging study. The Company is also considering initiating clinical trials for other indications including diabetic kidney disease.

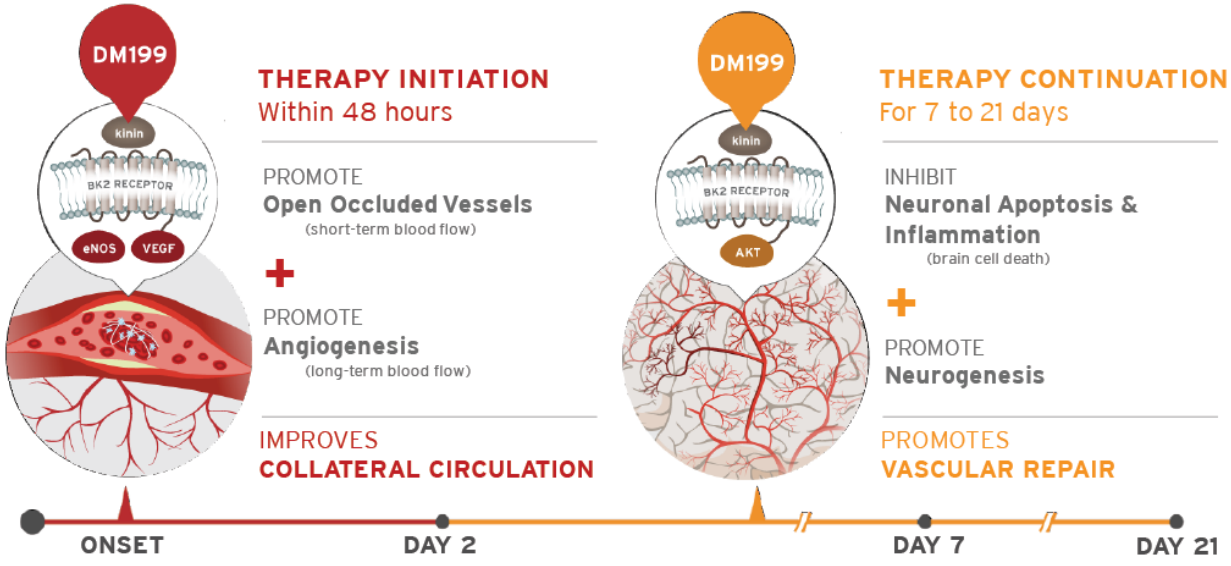
## DM199 Development Path

### *DM199 Mechanism*

The most well-characterized activity of naturally occurring KLK1 is its enzymatic cleavage of kininogen to produce bradykinin ("BK") like peptides, collectively known as kinins, which activate either directly or indirectly subtypes of both bradykinin receptors ("BK-B1", "BK-B2"). Activation of BK receptors by kinins set in motion a large number of complex metabolic pathways in response to ischemia within the body, the response which can include improved blood flow (through vasodilation), an anti-inflammatory response, cell repair through angiogenesis or vasculogenesis, and decrease of apoptosis. There is a large body of scientific studies that show tissue kallikrein-mediated release increases blood flow in a variety of tissues including kidney and heart (Stone et al., 2009. Arterioscler. Thromb. Vasc. Biol. 29, 657-664) and that this is likely the primary mode by which kallikrein treatment addresses brain pathologies caused by acute ischemic stroke.

Kinins have a short half-life *in vivo* as they are rapidly degraded by ubiquitous enzymes and serpins, most notable are Alpha-1 anti-trypsin, Kallistatin, and Protein C inhibitor. KLK1 activity also is tightly regulated by these inhibitor proteins found throughout the body. Because of these multilayered regulatory systems, it is plausible that levels of bradykinin drop below optimum levels in pathological conditions such as AIS. Treatments that provide additional supplies of active KLK1 (such as DM199) can serve to increase or maintain sufficient bradykinin levels and thereby promote BK-B2 receptor activation. DiaMedica believes DM199 has the potential to treat a broad spectrum of clinical scenarios where re-establishing blood flow and reducing inflammation in patients is vital to preserving organ function (e.g. brain, kidney, and heart).

**DM199 Acute Ischemic Stroke: Proposed Mechanism**



## DM199 Targeted Indications

### *Acute Ischemic Stroke*

According to the World Health Organization ("WHO"), each year approximately 15 million people worldwide suffer a stroke of which 5.5 million will die and 5.0 million will be permanently disabled (WHO Atlas of Heart Disease and Stroke Sec. 15 p 50). Worldwide, stroke is the leading cause of adult disability and the second leading cause of death in developed countries.

Each year in the US, approximately 795,000 people continue to experience a new or recurrent stroke (ischemic or hemorrhagic). Approximately 610,000 of these are first events and 185,000 are recurrent stroke events. In 2013, stroke caused approximately 1 of every 20 deaths in the United States. On average, someone in the United States has a stroke every 40 seconds, and someone dies from a stroke every 4 minutes. The cost including health care services, medications, and lost productivity is estimated to be approximately $34 billion USD (Mozaffarian. 2015. American Heart Association Circ. 2015; e29-322).

Risk factors for stroke include advanced age, hypertension (high blood pressure), previous stroke or transient ischemic attack ("TIA"), diabetes, high cholesterol, cigarette smoking, and atrial fibrillation.

A stroke is the rapidly developing loss of brain function due to disturbance in the blood supply to the brain. As a result, the affected area of the brain becomes inactive and eventually dies. Strokes can be classified into two major categories: acute ischemic stroke and hemorrhagic stroke. Acute ischemic strokes are those that are caused by interruption of the blood supply by a blood clot (ischemia), while hemorrhagic strokes result from rupture of a blood vessel or an abnormal vascular structure. About 87% of strokes are acute ischemic strokes, with the remainder classified as hemorrhagic.

At the site of blood flow blockage, there exist two major ischemic zones - the core ischemic zone with only 10-25% blood flow, and the surrounding ischemic penumbra having partially reduced blood flow (Ramos-Cabrer, et al., 2011, Stroke J. Cereb. Circ. 42, S7–S11). The core zone suffers from a severe lack of glucose and oxygen, which rapidly depletes energy stores and triggers the loss of ion gradients, ultimately leading to neuronal cell apoptosis (excitotoxicity), all within minutes. The ischemic penumbra zone however may remain viable for several hours via collateral arteries that branch from the main occluded artery in the core zone. Unfortunately, penumbra zone neuronal cell death also eventually occurs due to inflammation and apoptosis, as collateral blood supply is inadequate to maintain cellular function indefinitely. Approximately 20% of persons who progress to cerebral infarction and approximately 10% of those who suffer a cerebral hemorrhage have a history of evolution of deficit over several hours to several days (and rarely, longer). As such, next generation stroke therapies are being developed to protect the viable cells of the penumbra with anti-apoptotic, pro-angiogenesis, or immunomodulation functions during the hours to a week after a stroke (Ramos-Cabrer, et al., (2011). Stroke J. Cereb. Circ. 42, S7–S11; Sinden, J. and Muir (2012). Int. J. Stroke Off. J. Int. Stroke Soc. 7, 426–434).

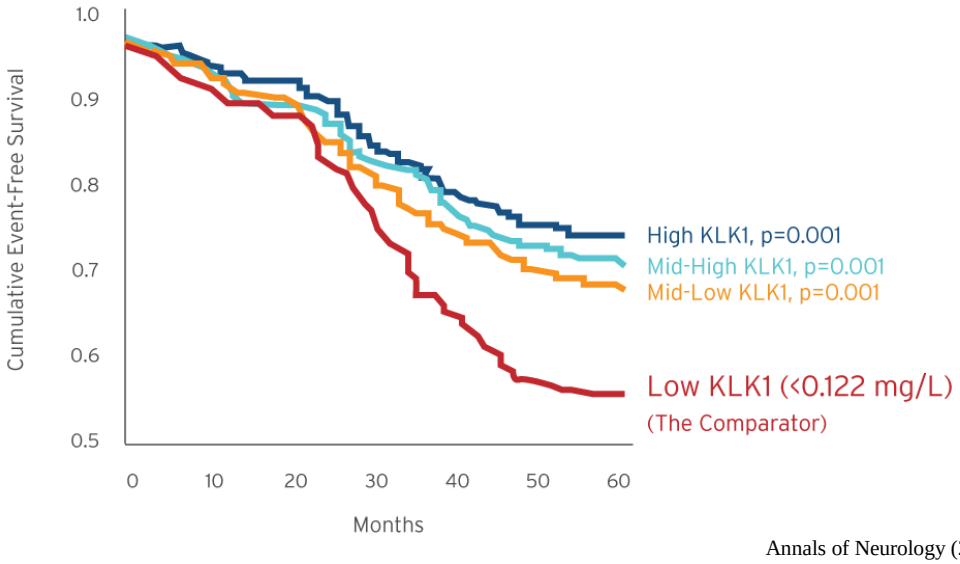
As time goes on, a lack of blood flow in the ischemic zone (infarct) leads to fluid build up (edema) and swelling which creates intracranial pressure. This pressure on the brain leads to tissue compression resulting in additional ischemia. Additional events in acute ischemic stroke include vascular damage to the blood vessel lining or endothelium, loss of structural integrity of brain tissue and blood vessels, and activation of the immune system and inflammation. A stroke can lead to permanent damage with memory loss, speech problems, reading and comprehension difficulties, physical disabilities, and emotional behavioral problems being commonly observed outcomes.

Due to this devastating chain of events, the clinical priority is to remove the blood clot blockage as soon as possible after onset and re-establish normal blood flow. Currently, the only FDA approved therapeutic-based treatment is tissue plasminogen activator ("tPA"), a protein involved in the breakdown of blood clots (thrombolysis) to re-establish normal blood flow (recanalization). However, tPA is only effective if administered within 3-4.5 hours of an acute ischemic stroke (Del Zoppo et al., (2009). Stroke J. Cereb. Circ. 40, 2945–2948), as outside this therapeutic window tPA is not only ineffective but its use leads to a greater risk of hemorrhage (bleeding in the brain). As such, it is estimated that in the U.S. only 2-5% of AIS patients are treated with tPA (Miller et al., *The Neurohospitalist*. 2011 Jul; 1(3): 138-147). As a consequence of this limited time window, only a small percentage of stroke victims are treated with the currently available therapy; most simply receive supportive or "palliative" care. The long-term costs

of stroke are substantial, with many patients requiring extended hospitalization, extended physical therapy, or rehabilitation (for those patients that are capable of entering such programs), and many require long-term institutional or family care.

Stroke represents an area of tremendous unmet medical need. Lower tissue KLK1 levels in the blood have also been independently associated with first-ever stroke and lower long term survival and are an independent predictor of recurrence after an initial stroke. In a 2,478 patient case-controlled clinical study of KLK1 levels in stroke patients, higher KLK1 activity is predictive of fewer stroke recurrences and longer event-free survival time. Event free survival functions were measured using Kaplan-Meier survival curves (Annals of Neurology (2011) 70:265-73).

**KLK1 Levels - Event Free Survival Functions – Kaplan-Meier Survival Curves**




Annals of Neurology (2011) 70:265-73

Published preclinical and clinical research with a naturally occurring KLK1 protein has demonstrated reduced blood pressure, cell death, and inflammation and increased angiogenesis (creation of new blood vessels) and neurogenesis. DiaMedica believes DM199 has the potential to preserve "at risk" brain tissue by establishing better collateral circulation, decreasing inflammation, reducing apoptosis, and helping generate collateral circulation by initiating angiogenesis and vasculogenesis. Results from an animal study of DM199 first generation product, DM99, demonstrated proliferation of neuroprotections *in vitro* and *in vivo*.

DM199 is being positioned to treat ischemic stroke patients with therapy beginning up to 48 hours after first sign of symptoms, thereby filling a large unmet need of patients who cannot receive tPA, and potentially making therapy available to hundreds of thousands of patients who currently have no options.

*Urinary Tissue Kallikrien-1 approved for stroke treatment in China*

A urine-extracted version of KLK1 ("uKLK1") is currently used to treat AIS in the Peoples Republic of China. The Chinese product is marketed under the name Kailikang® (Urinary Kallidinogenase for Injection) by Techpool Bio-Pharma Inc. (Techpool), and is isolated from human urine. Kailikang® is prescribed to stroke patients up to 48 hours post-stroke and is given by intravenous administration.

More than 40 published clinical studies that show a beneficial effect of Kailikang® treatment in AIS, including a meta-analysis covering 24 clinical studies involving 2,433 patients (Journal of Evidence-Based Medicine (2012) 5: 31-39). The review used well-established methods for meta-analysis. The authors conclude that "[human urinary KLK1]

appears to ameliorate neurological deficits for patients with acute ischemic stroke and to improve long-term outcomes, though a few treated patients suffered from transient hypotension," (J Evid Based Med. 2012 Feb;5(1):31-9).

In a double-blinded, placebo-controlled trial of 446 patients treated with uKLK1 or placebo up to 48 hours after a stroke, significant differences were found in the European Stroke Scale and Activities of Daily Living at three weeks of treatment and at three months using the Barthel Index with uKLK1 treated vs placebo (Chin J Neurol, May 2007, Vol 40, No 5).

### *Diabetic Kidney Disease*

Diabetic kidney disease ("DKD"), also known as diabetic nephropathy, is a complication that occurs with some people with diabetes. DKD is a form of chronic kidney disease, characterized by the gradual loss of kidney function. It is most common among people with Type 2 diabetes and hypertension and affects 26 million American adults. Diabetes has become the primary cause of kidney disease in the United States and the associated incidence of diabetic nephropathy is also on the rise. The following summarizes the size of the DKD market:

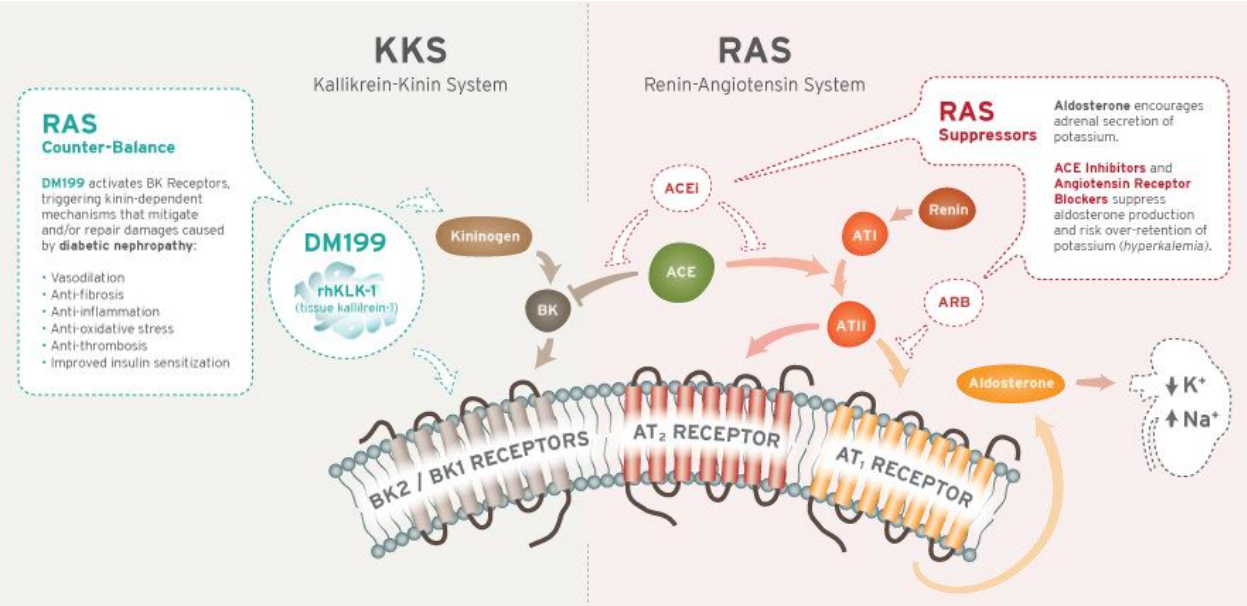
- 5-10 million people in the U.S. with DKD (National Chronic Kidney Disease Fact Sheet 2014, CDC DDT)
- 120 million people in China with DKD (*Journal of Diabetes Research* Vol 2015, Decision Resources, 28 Jan 2014)
- 40 percent of all diabetics will develop DKD (Reutens, AT. *Med Clin N Am* 2013: 97(1-18))
- $11.7 billion chronic kidney disease potential market (*Decision Resources*, 28 Jan 2014)

Clinically, DKD is characterized by a progressive increase in urine albumin/albuminuria and a decline in glomerular filtration rate ("GFR"), hypertension, and a high risk of cardiovascular morbidity and mortality.

Management of DKD includes treatment of the underlying Type 2 diabetes and/or hypertension. Blood pressure medications such as angiotensin converting enzyme ("ACE") inhibitors and angiotensin receptor blockers ("ARBs") are commonly prescribed to control hypertension and slow the progression of DKD. Nevertheless, most patients continue to have a decline in kidney function. About 20 percent of patients eventually progress to end-stage renal disease ("ESRD") and require hemodialysis, peritoneal dialysis, or renal transplant. DKD is a serious medical condition and needs treatments with new mechanisms of action that target pathways other than the renin-angiotensin-aldosterone system ("RAAS") in order to slow or reverse the progression of the disease.

DM199 activates the bradykinin receptors and via the kallikrein-kinin system counter-balances the renin-angiotensin system, triggering kinin-dependent mechanisms that mitigate and/or repair damages caused by diabetic nephropathy and potentially improving vasodilation, anti-fibrosis, anti-inflammation, anti-oxidatinve stress, anti-thrombosis, and insulin sensitization. DiaMedica believes that DM199 could improve kidney function without increasing the risks of increased hyperkelemia as seen with ACEi and ARB's. Hyperkalemia is the result of elevated blood potassium (K+) levels which increases the risk of abnormal heart rhythms and sudden death. The risk of hyperkalemia results in potentially suboptimal dosing and discontinuation of ACEi and ARB treatment for DKD patients. There is an estmated 2.5 million patients in the U.S. that have DKD and hyperkalemia (USRDS 2011, Truven data, and CDC).

### DM199 Proposed Mechanism: Kidney Disease




Over 10 clinical papers have been published demonstrating the positive effects of the KLK1 protein combined with valsartan, an ARB. These studies have ranged from one to six months in length and demonstrated a time dependent improvement in kidney disease based on urinary albumin excretion rate and other clinical endpoints of kidney disease.

A potential differentiation between DM199 and ACEi and ARB's treatments is that with DM199, hyperkalemia might be avoidable with a bradykinin receptor-specific agonists (Kidney International, 4 February 2009).

In a six-month, Phase II randomized, placebo-controlled clinical trial of 90 patients treated daily with valsartan, an ARB, and ARB + KLK1, statistically significant differences were found at six months in the urinary albumin excretion rate ("UAER") (Chin J Diabetes, August 2011, Vol 19, No 8), which measures kidney health. In addition to improvement in UAER, the urine B2-microglobulin was also significantly improved.

In a 30-day Phase II clinical study of 68 patients treated with valsartan, an ARB, and ARB + KLK1, the UAER demonstrated statistical improvement with ARB + KLK1 compared to ARB alone (Jour. Xinxiang Med College, 2012, Vol 29, No 8).

DiaMedica is preparing to potentially conduct a clinical trial in patients with moderate diabetic kidney disease.

### DM199 Clinical Studies

The Company has conducted four clinical trials with DM199 including single ascending doses, multiple ascending doses, and a pilot study in Type 2 diabetic patients. DM199 was safe and well tolerated and demonstrated clear activity in patients as measured changes in blood pressure over multiple clinical studies. Results in healthy volunteers also show that DM199 exhibits a favorable PK profile with extended half-life (time required to reduce concentration of drug in body by one-half), supporting potential once weekly dosing. The dose limiting tolerability was orthostatic hypotension at dose levels greater than anticipated efficacious dosing levels and is consistent with the DM199 mechanism of action and as seen in pre-clinical primate studies. A primary adverse event of urinary KLK1 at high doses has been hypotension.




DiaMedica has also successfully completed a Phase I study in Type 2 diabetic ("T2D") patients. The randomized, double-blinded, placebo-controlled study enrolled ten T2D patients. The patients were dosed with either DM199 at three single ascending dose levels or placebo over an 8-day period. DM199 was well-tolerated at all three dose levels by the diabetic patients with no dose limiting side effects. In this study, there was a statistically significant decrease in systolic blood pressure at both the 3 and 15 ug/kg doses.

In a pilot trial conducted in 36 Type 2 diabetes patients, patients were given DM199 once every 3 days over a 28-day period. Patients were sequestered for 28 days during the study. The primary endpoints of adverse events, vital signs (including blood pressure, pulse, and body temp), electrocardiogram, clinical laboratory tests, local tolerability at injection site, anti-drug antibody, and pharmacokinetics were all met. Fasting blood glucose levels in the placebo group surprisingly decreased (not increased) during study, thereby confounding study results. The study was designed for placebo patients to have an increase in glucose levels and glucose levels in DM199 treatment group to stabilize or ideally decrease and thereby demonstrate a difference compared to placebo.

Blood pressure was also monitored during the 28-day study with statistically significant difference compared to placebo during the 28-day study at 15 µg/Kg dose.

Based on a review of the dosing in the four clinical trials, approved dosing of Kailikang® and the Company's external analysis, DiaMedica plans to focus future clinical trials on acute ischemic stroke and kidney disease at dosing levels significantly lower than the low dose used, larger study design, target more severe patients, and provide more frequent dosing.

### Commercialization Partnerships and Other Strategic Initiatives

Where appropriate, we intend to seek corporate partnerships or other strategic initiatives with established pharmaceutical and biotechnology companies to continue the development of our technologies through later stage clinical trials. We plan to enter into agreements with such pharmaceutical and biotechnology companies to conduct Phase III trials, file the appropriate NDA, and ultimately market and sell the drug products we develop. We believe this will eliminate the need for us to raise the significant capital required to perform the large multi-centre pivotal trials required for regulatory approval of our drug candidates and to build the resources necessary to market prescription pharmaceuticals, thereby mitigating the risks inherent in late-stage clinical drug development.

The Company is under confidentiality agreements with numerous Asian pharmaceutical firms and have ongoing discussions and correspondence, including having received multiple term sheets with proposed terms regarding partnering in connection with licensing the rights to DM199 for use in China. However, such discussions and other correspondence have not yet resulted in any binding agreements and there is no assurance that they ever will. Additionally, there is no assurance that the Company will secure the type of partnership or strategic initiative discussed above.

# RESULTS OF OPERATIONS

### For the three months ended March 31, 2016 and 2015

Since inception, the Company has incurred losses while advancing the research and development of its therapeutic products. Net loss for the three months ended March 31, 2016 was $456,014 compared to a loss of $562,104 for the three months ended March 31, 2015. The decrease in net loss for the three months ended March 31, 2016 over the comparable period of the prior year was due mainly to lower staffing costs.

### Research and Development

Components of research and development expenses for the three months ended March 31, 2016 and 2015 were as follows:

| | **2016** | 2015 |
|---|---|---|
| | **$** | $ |
| Research and development programs, excluding the below | **131,256** | 111,693 |
| Salaries, fees, and short-term benefits | **138,086** | 246,757 |
| Share-based compensation | **42,194** | 25,018 |
| Depreciation of property and equipment | **(526)** | 3,171 |
| | **311,010** | 386,639 |

Research and development salaries, fees, and short-term benefits for the three months ended March 31, 2016 decreased over the comparable period due mainly to a reduction in staff. Share-based compensation increased due mainly to the issuance of stock options in 2015.

### General and Administrative

Components of general and administrative expenses for the three months ended March 31, 2016 and 2015 were as follows:

| | **2016** | 2015 |
|---|---|---|
| | **$** | $ |
| General and administrative, excluding the below | **76,499** | 83,104 |
| Salaries, fees, and short-term benefits | **33,542** | 14,443 |
| Share-based compensation | **61,372** | 29,678 |
| | **171,413** | 127,225 |

General and administrative expenses decreased over the comparable period due mainly to cost containment plans implemented during the fourth quarter of 2014. Salaries, fees, and short-term benefits decreased period due mainly to a reduction in staff. Share-based compensation decreased due mainly to the expiration of options held by former employees.

### Finance costs (income)

Finance costs for the three months ended March 31, 2016 of $17,838 was lower than the same period of 2015 amount of $42,105 due to net foreign exchange gains.

## LIQUIDITY AND CAPITAL RESOURCES

Since inception, the Company has financed its operations from public and private sales of equity, the exercise of warrants and stock options, interest income on funds available for investment and government grants and tax credits. As at March 31, 2016, the Company had cash totaling $432,805 compared to $229,930 at December 31, 2015.

The Company's future operations are dependent upon its ability to secure additional funding, generate product revenues, and negotiate license agreements with partners. There can be no assurance that the Company will be successful in commercializing its products, entering into strategic agreements with partners, or raising additional capital on favorable terms or at all. While the Company is taking measures to preserve cash while it continues to search for additional sources of funding, including negotiating deferred payment terms with vendors and reducing expenses, the Company will not have enough cash on hand to sustain operations to the end of fiscal 2016 unless further funds have been raised. The availability of financing will be affected by the results of scientific and clinical research, the ability to attain regulatory approvals, the state of the capital markets generally with particular reference to life sciences' companies, and other relevant commercial considerations. If the Company cannot secure additional financing on favourable terms or at all, the Company will have to consider additional strategic alternatives beyond the cost saving measures described above. Such additional strategies may include delays of product development expenditures and exploring the monetization of certain intangible assets, as well as seeking to out-license and/or divest assets through a merger, sale, or liquidation of the Company.

During the first quarter of 2015, the Company negotiated deferred payment terms with a vendor for the payment of services which occurred prior to January 1, 2015. In accordance with the agreement, the Company will pay the vendor €381,860 over a period of 2 years until the amount is paid in full. This liability carries an interest rate of 0.5% per month compounded annually.

Additionally, €379,922 which is non-interest bearing is due and payable to the vendor on or about February 2017. These payment terms may be accelerated under the terms of the agreement if the Company was to raise specified amounts of equity through a financing during the term of the agreement. The deferred payments are unsecured.

As at March 31, 2016 and December 31, 2015, the current portion of the obligation above included in accounts payable and accrued liabilities is $364,060 (€245,274) and $363,148 (€241,631), respectively.

### *Common shares issued – for the three months ended March 31, 2016*

On February 18, 2016, the Company completed the first tranche of a non-brokered private placement of 3,812,500 units at a price of $0.16 per unit for aggregate gross proceeds of approximately $610,000 ($560,188 net of cash issue costs). Each unit consisted of one common share and one half of one common share purchase warrant. Each whole warrant entitles the holder to purchase one common share at a price of $0.25 at any time prior to expiry on February 18, 2018. In connection with the financing, the Company issued 148,300 compensation warrants and paid a finder's fee of 4% of the aggregate gross proceeds. Each compensation warrant entitles the holder to acquire one common share at an exercise price of $0.25 prior to expiry on February 18, 2018.

The $0.16 unit issue price was allocated to common shares in the amount of $0.12 per common share and the unit warrants were allocated a price of $0.04 per half-warrant. The costs of the issue were allocated on a pro rata basis to the common shares and unit warrants. Accordingly, $403,335 was allocated to common shares and $156,853 to the unit warrants, net of issue costs. Assumptions used to determine the value of the unit warrants and compensation warrants were: dividend yield 0%; risk-free interest rate 0.4%; expected volatility 192%; and average expected life of 24 months.

On February 25, 2016, the Company completed the second tranche of a non-brokered private placement of 875,000 units at a price of $0.16 per unit for aggregate gross proceeds of approximately $140,000 ($117,810 net of issue costs). Each unit consisted of one common share and one half of one common share purchase warrant. Each whole warrant entitles the holder to purchase one common share at a price of $0.25 at any time prior to expiry of February 25, 2018. In connection with the financing, the Company issued 70,000 compensation warrants and paid a finder's fee of 8% of the aggregate gross proceeds. Each compensation warrant entitles the holder to acquire one common share at an exercise price of $0.25 prior to expiry on February 25, 2018.

The $0.16 unit issue price was allocated to common shares in the amount of $0.11 per common share and the unit warrants were allocated a price of $0.05 per half-warrant. The costs of the issue were allocated on a pro rata basis to the common shares and unit warrants. Accordingly, $83,645 was allocated to common shares and $34,165 to the unit warrants, net of issue costs. Assumptions used to determine the value of the unit warrants and compensation warrants were: dividend yield 0%; risk-free interest rate 0.5%; expected volatility 192%; and average expected life of 24 months.

During the three months ended March 31, 2016, 347,350 common shares were issued on the exercise of warrants for gross proceeds of $34,735 and 2,546,487 warrants expired unexercised.

### *Common Shares*

The continuity of the number of issued and outstanding common shares of the Company for the three months ended March 31, 2016, and to the date of this MD&A is presented below:

| | |
|---|---|
| Balance, December 31, 2015 | 82,275,430 |
| Shares issued under private placement | 4,687,500 |
| Shares issued under warrant exercise | 347,350 |
| Balance as at March 31, 2016 | 87,310,280 |
| Shares issued for settlement of debt | 50,000 |
| Shares issued under warrant exercise | 385,000 |
| Balance as at the date of the MD&A | 87,745,280 |

### *Stock Options*

The Company has a stock option plan which is administered by the Board of Directors of the Company with stock options granted to directors, management, employees and consultants as a form of compensation. The shareholders approved the adoption of a stock option plan on September 22, 2011 as amended and restated on October 23, 2015 reserving for issuance up to 10% of the Company's issued and outstanding common shares. The aggregate number of shares reserved includes all compensation and incentive plans, including the stock option plan and the DSU Plan. Options granted vest at various rates and have terms of up to 10 years.

The following table reflects the activity under the Company's stock option plan for the three months ended March 31, 2016:

| | | **2016** |
|---|---|---|
| | **Number of Options** | **Weighted average exercise price** |
| Balance, December 31, 2015 | **6,412,000** | **$0.49** |
| Granted | **500,000** | **$0.16** |
| Expired/cancelled | **(170,000)** | **$1.31** |
| Balance, end of period | **6,742,000** | **$0.45** |
| Options exercisable, end of period | **3,090,167** | **$0.77** |

### *Warrants*

The following tables reflect the activity of the warrants for the three months ended March 31, 2016:

| Issue Date | Expiry Date | Warrants Issued # | Exercise Price $ | Exercised Warrants # | Expired Warrants # | Warrants Outstanding # |
|---|---|---|---|---|---|---|
| March 13, 2015 | March 13, 2016 | 227,350 | $0.10 | 227,350 | | - |
| March 22, 2013 | March 22, 2016 | 2,555,587 | $1.10 | 9,100 | 2,546,487 | - |
| May 27, 2014 | May 27, 2016 | 1,549,600 | $1.00 | | | 1,549,600 |
| June 19, 2015 | June 19, 2016 | 4,875,000 | $0.20 | | | 4,875,000 |
| June 19, 2015 | June 19, 2016 | 420,000 | $0.10 | 120,000 | | 300,000 |
| November 25, 2015 | November 25, 2016 | 4,500,000 | $0.20 | | | 4,500,000 |
| November 25, 2015 | November 25, 2016 | 254,800 | $0.10 | | | 254,800 |
| February 18, 2016 | February 18, 2018 | 1,906,250 | $0.25 | | | 1,906,250 |
| February 18, 2016 | February 18, 2018 | 148,300 | $0.25 | | | 148,300 |
| February 25, 2016 | February 25, 2018 | 437,500 | $0.25 | | | 437,500 |
| February 25, 2016 | February 25, 2018 | 70,000 | $0.25 | | | 70,000 |
| **Balance** | | **16,944,387** | | **356,450** | **2,546,487** | **14,041,450** |

During the three months ended March 31, 2016, 347,350 common shares were issued on the exercise of warrants for gross proceeds of $34,735 and 2,546,487 warrants expired unexercised.

### Shareholder rights plan

The shareholders of the Company approved the adoption of a shareholder rights plan agreement (the “Plan”) on September 22, 2011. The Plan is designed to provide adequate time for the Board of Directors and the shareholders to assess an unsolicited takeover bid for DiaMedica, to provide the Board of Directors with sufficient time to explore and develop alternatives for maximizing shareholder value if a takeover bid is made, and to provide shareholders with an equal opportunity to participate in a takeover bid and receive full and fair value for their Common Shares. The Plan had been set to expire at the close of the Company's annual meeting of shareholders in 2014. At the Company’s Annual General and Special Meeting of Shareholders on July 24, 2014, shareholders approved a resolution to renew the Plan and extend the expiration date to the close of the Company’s annual meeting of shareholders in 2017.

The rights issued under the Plan will initially attach to and trade with the Common Shares and no separate certificates will be issued unless an event triggering these rights occurs. The rights will become exercisable only when a person, including any party related to it, acquires, or attempts to acquire 20 percent or more of the outstanding Common Shares without complying with the "Permitted Bid" provisions of the Plan or without approval of the Board of Directors. Should such an acquisition occur or be announced, each right would, upon exercise, entitle a rights holder, other than the acquiring person and related persons, to purchase Common Shares at a 50 percent discount to the market price at the time.

Under the Plan, a Permitted Bid is a bid made to all holders of the Common Shares and which is open for acceptance for not less than 60 days. If at the end of 60 days at least 50 percent of the outstanding Common Shares, other than those owned by the offeror and certain related parties have been tendered, the offeror may take up and pay for the Common Shares but must extend the bid for a further 10 days to allow other shareholders to tender. The issuance of Common Shares upon the exercise of the rights is subject to receipt of certain regulatory approvals.

### Deferred Share Units Plan

The shareholders of the Company approved the adoption of a deferred share units plan on September 22, 2011 as amended and restated on October 23, 2012 (the “DSU Plan”) reserving for issuance up to 2,000,000 common shares under the DSU Plan. The purpose of the DSU Plan is to provide an alternative form of compensation for directors’

fees and annual and special bonuses payable to senior officers and directors of the Corporation. For the three months ended March 31, 2016, no units were issued (2015 – no units issued). The DSU Plan is equity-settled and the fair value of units granted, which vest upon issuance, is included in share-based compensation expense.

### Commitments

As at March 31, 2016 and in the normal course of business, the Company had obligations to make future payments, representing research and development contracts and other commitments that are known and committed in the amount of $222,257 over the next 12 months. The Company has renewed its commitment with the leasing company of its U.S. office for a term through February 2019 with payments aggregating $31,665 over the next 12 months, $32,619 from 13-24 months, and $30,654 from 25-36 months. As at March 31, 2016, the Company has future commitments totaling $94,938 to this company.

The Company enters into research, development, and license agreements in the ordinary course of business where the Company receives research services and rights to proprietary technologies. Milestone and royalty payments that may become due under various agreements are dependent on, among other factors, clinical trials, regulatory approvals and ultimately the successful development of a new drug, the outcome and timing of which is uncertain.

The Company periodically enters into research and license agreements with third parties that include indemnification provisions customary in the industry. These guarantees generally require the Company to compensate the other party for certain damages and costs incurred as a result of claims arising from research and development activities undertaken by or on behalf of the Company. In some cases, the maximum potential amount of future payments that could be required under these indemnification provisions could be unlimited. These indemnification provisions generally survive termination of the underlying agreement. The nature of the indemnification obligations prevents the Company from making a reasonable estimate of the maximum potential amount it could be required to pay. Historically, the Company has not made any indemnification payments under such agreements and no amount has been accrued in the accompanying consolidated financial statements with respect to these indemnification obligations.

## RELATED PARTY TRANSACTIONS

The key management personnel of the Company are the Directors, the President and Chief Executive Officer, Chief Financial Officer and the Vice Presidents.

Compensation for key management personnel of the Company for the three months ended March 31, 2016 and 2015 was as follows:

| | **2016** | 2015 |
|---|---|---|
| | **$** | $ |
| Salaries, fees, and short-term benefits | **120,694** | 137,448 |
| Share-based compensation | **67,217** | 40,870 |
| | **187,911** | 178,318 |

Executive officers and directors participate in the stock option plan and certain officers participate in the Company's health plan. Directors receive annual and meeting fees for their services. As at March 31, 2016, the key management personnel control 4.1% (2015 – 4%) of the voting shares of the Company.

Amounts due to related parties, including amounts due to key management personnel are unsecured and interest free, and settlement occurs in cash. Additionally, amounts due to related parties in note 6 of the consolidated financial statements for the three months ended March 31, 2016 and 2015 relate to accrued bonuses, vacation payable, and accounts payable. There have been no guarantees provided or received for any related party receivables or payables.

## OFF-BALANCE SHEET ARRANGEMENTS

The Company does not have any off-balance sheet arrangements.

## INTERNAL CONTROLS OVER FINANCIAL REPORTING

As a result of the Company's limited administrative staffing levels, internal controls which rely on segregation of duties in many cases are not possible. Due to resource constraints and the present stage of the Company's development, the Company does not have sufficient size and scale to warrant the hiring of additional staff to address this potential weakness at this time. To help mitigate the impact of this, the Company is highly reliant on the performance of compensating procedures and senior management's review and approval.

As a venture issuer, the Company is not required to certify the design and evaluation of the Company's disclosure controls and procedures ("DC&P") and internal controls over financial reporting ("ICFR"), and as such has not completed such an evaluation.

Investors should be aware that inherent limitations on the ability of certifying officers of a venture issuer to design and implement on a cost effective basis DC&P and ICFR as defined in NI 52-109 may result in additional risks to the quality, reliability, transparency and timeliness of interim and annual filings and other reports provided under securities legislation.

## CRITICAL ACCOUNTING ESTIMATES

The preparation of financial statements in conformity with IFRS requires management to make judgments, estimates, and assumptions that affect the application of accounting policies and the reported amounts of assets and liabilities, revenue and expenses, and the related disclosures of contingent assets and liabilities. Actual results could differ materially from these estimates and assumptions. We review our estimates and underlying assumptions on an ongoing basis. Revisions are recognized in the period in which the estimates are revised and may impact future periods.

We have applied significant judgments, estimates, and assumptions to the determination of functional currency, valuation of share-based compensation and warrants, and to the measurement, period of use, and potential impairment of intangible assets as follows:

### *Functional currency*

Judgment is required in determining the appropriate functional currency of DiaMedica USA Inc. The Canadian functional currency was determined by assessing the currency that mainly influences costs and the currency in which DiaMedica finances its operations. A change in the functional currency could result in material differences in the amounts recorded in the statements of loss and comprehensive loss for foreign exchange gains or losses.

### *Valuation of share-based compensation and warrants*

Management measures the costs for share-based compensation and warrants using market-based option valuation techniques. Assumptions are made and estimates are used in applying the valuation techniques. These include estimating the future volatility of the share price, expected dividend yield, expected risk-free interest rate, future employee turnover rates, future exercise behaviors, and corporate performance. Such estimates and assumptions inherently are uncertain. Changes in these assumptions affect the fair value estimates of share-based payments and warrants.

## CHANGES IN ACCOUNTING POLICIES

The Company's principal accounting policies are outlined in the Company's annual audited consolidated financial statements for the year ended December 31, 2015 and have been applied consistently to all periods presented in the unaudited condensed consolidated interim financial statements.

### *New standards and interpretations not yet effective*

#### IFRS 16, *Leases*

This standard introduces a single lessee accounting model and requires a lessee to recognize assets and liabilities for all leases with a term of more than twelve months, unless the underlying asset is of low value. A lessee is required to recognize a right-of-use asset representing its right to use the underlying asset and a lease liability representing its obligation to make lease payments. This standard substantially carries forward the lessor accounting requirements of IAS 17, *Leases*, while requiring enhanced disclosures to be provided by lessors. Other areas of the lease accounting model have been impacted, including the definition of a lease. The new standard is effective for annual periods beginning on or after January 1, 2019, which is when the Company intends to adopt IFRS 16 in its financial statements. The extent of the impact of adoption of the standard has not yet been determined.

#### IFRS 9, *Financial Instruments: Classification and Measurement*

IFRS 9 (2010) reflects the first phase of the IASBs work on the replacement of IAS 39, *Financial Instruments: Recognition and Measurement* and deals with the classification and measurement of financial assets and financial liabilities. This standard establishes two primary measurement categories for financial assets, amortized cost and fair value, and eliminates the existing categories of held to maturity, available for sale, and loans and receivables. The new classification will depend on the entity's business model and the contractual cash flow characteristics of the financial asset. The standard is expected to be effective for annual periods beginning on or after January 1, 2018. The Company is currently evaluating the impact of the above standard on its financial statements.

#### IFRS 15, *Revenue from Contracts with Customers*

IFRS 15, *Revenue from Contracts with Customers*, issued by the IASB in May 2014, is applicable to all revenue contracts and provides a model for the recognition and measurement of gains or losses from sales of some non-financial assets. The core principle is that revenue is recognized to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The standard will also result in enhanced disclosures about revenue, provide guidance for transactions that were not previously addressed comprehensively [for example, service revenue and contract modifications] and improve guidance for multiple-element arrangements. IFRS 15 is effective for annual periods beginning on or after January 1, 2018 and is to be applied retrospectively, with earlier adoption permitted. Entities will transition following either a full or modified retrospective approach. The Company is currently evaluating the impact of the above standard on its financial statements.

## SELECTED QUARTERLY FINANCIAL INFORMATION

The selected financial information provided below is derived from the Company's consolidated financial statements for each of the last eight quarters.

| | Q1-2016 | Q4-2015 | Q3-2015 | Q2-2015 | Q1-2015 | Q4-2014 | Q3-2014 | Q2-2014 |
|---|---|---|---|---|---|---|---|---|
| Interest income | $408 | $71 | $310 | $162 | $1,871 | $497 | $2,303 | $4,140 |
| Net loss for the period | $456,014 | $707,780 | $315,419 | $416,520 | $562,104 | $1,053,721 | $983,977 | $1,307,737 |
| Loss per share | $0.01 | $0.03 | $0.00 | $0.01 | $0.01 | $0.02 | $0.02 | $0.02 |
| Cash | $432,805 | $229,930 | $187,996 | $568,759 | $339,627 | $236,567 | $542,984 | $1,332,701 |

Research and development and general and administrative for 2015 and the first quarter of 2016 decreased due mainly to cost containment plans implemented during fourth quarter 2014. Research and development increased in the fourth quarter as the Company proceeded to implement plans to refocus efforts in stroke and other vascular diseases.

It is important to note that historical patterns of expenditures cannot be taken as an indication of future expenditures. The amount and timing of expenditures, and therefore liquidity and capital resources, may vary substantially from period to period depending on the business and research activities being undertaken at any one time and the availability of funding from investors and prospective commercial partners.

### Trend Information

Historical patterns of expenditures cannot be taken as an indication of future expenditures. The amount and timing of expenditures and therefore liquidity and capital resources vary substantially from period to period depending on the timing of manufacturing, and the initiation and completion of preclinical and clinical studies being undertaken at any one time and the availability of funding from investors and prospective commercial partners.

Other than as discussed above, the Company is not aware of any material trends related to the Company's business of product development, patents and licensing.

## RISKS AND UNCERTAINTY

An investment in our common shares involves a high degree of risk and should be considered speculative. An investment in our common shares should only be undertaken by those persons who can afford the total loss of their investment. You should consider carefully the risks and uncertainties described below, as well as other information contained in this MD&A. The risks and uncertainties below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we believe to be immaterial may also adversely affect our business. If any of the following risks occur, our business, financial condition and results of operations could be seriously harmed and you could lose all or part of your investment. Further, if we fail to meet the expectations of the public market in any given period, the market price of our common shares could decline.

We operate in a highly competitive environment that involves significant risks and uncertainties, some of which are outside of our control. We are subject to risks inherent in the biotechnology industry, including:

### Risks Related to the Early Stage of our Products and our Company

#### *Lack of Product Revenues; History of Operating Losses; Substantial Doubt about the Ability to Continue as a Going Concern*

There is substantial doubt about the appropriateness of the use of the going concern assumption because we have experienced operating losses and cash outflows from operations since incorporation, we had a working capital deficiency as of March 31, 2016, our cash resources are not sufficient for the next twelve months of planned operations, and we have not reached successful commercialization of our products. As of the date of this MD&A, we have not recorded any revenues from the sale of products. We have an accumulated deficit, based on our consolidated financial statements, since our inception through March 31, 2016 of over $47.6 million. Operating losses are expected to increase in the near term as we continue our product development efforts and are expected to continue until such time as product sales, royalty payments, licensing fees and/or milestone payments are sufficient to generate revenues to fund our continuing operations. We are unable to predict the extent of any future losses or when we will become profitable, if ever. Even if we do achieve profitability, we may not be able to sustain or increase profitability on an ongoing basis.

#### *Stage of Development*

We have compounds in various stages of development. Prior to commercialization of any potential product, significant additional investments will be necessary to complete the development of any of our products. Preclinical and clinical trial work must be completed before some of our products could be ready for use within the market that we have identified. We may fail to develop any products, to obtain regulatory approvals, to enter clinical trials, or to commercialize any products. Competitors may develop alternative products and methodologies to treat and diagnose

the disease indications we are pursuing, thus reducing our competitive advantages. We do not know whether any of our product development efforts will prove to be effective, meet applicable regulatory standards, obtain the requisite regulatory approvals, be capable of being manufactured at a reasonable cost, or successfully marketed. The products or processes we are currently developing are not expected to be commercially viable for several years and we may encounter unforeseen difficulties or delays in commercializing our products. In addition, our products may cause undesirable side effects. Results of early preclinical research may not be indicative of the results that will be obtained in later stages of preclinical or clinical research. If regulatory authorities do not approve our products or if we fail to maintain regulatory compliance, we would have limited ability to commercialize our products, and our business and results of operations would be harmed. If we do succeed in developing products, we will face many potential obstacles such as the need to develop or obtain manufacturing, marketing, and distribution capabilities.

### *Reproducibility of Prior Clinical Studies*

The Company intends to conduct clinical trials to determine the pharmacokinetic and pharmadynamic profile of Kailikang® compared to DM199. While there have been numerous studies demonstrating the efficacy of Kailikang®, we rely on the scientific and clinical knowledge and experience of other biotechnology and pharmaceutical companies and organizations in conducting those clinical studies. No assurance can be given that we will be able to reproduce results of previously conducted studies.

## Risks and Uncertainties of Current Economic Conditions

To date, we have primarily relied on equity financing to fund our working capital requirements and drug development activities. A substantial amount of additional capital is needed to develop our products to a point where they may be commercially sold. Our future operations are dependent upon our ability to generate product sales, negotiate collaboration or license agreements, obtain research grant funding, defer expenditures or other strategic alternatives, and/or secure additional funds. While we are striving to achieve these plans, there is no assurance these and other strategies will be achieved or that such sources of funds will be available or obtained on favorable terms or obtained at all. Our ability to continue as a going concern is dependent on our ability to continue obtaining sufficient funds to conduct our research and development, and to successfully commercialize our products. See Liquidity and Capital Resources section above.

### *Additional Financing Requirements and Access to Capital*

We require significant additional funds for further research and development, planned clinical trials, and the regulatory approval process. We may raise additional funds for the aforementioned purposes through public or private equity or debt financing which may be dilutive, or through collaborations with other biotechnology companies, or financing from other sources may be undertaken. It is possible that financing will not be available or, if available, may not be on favorable terms. The availability of financing will be affected by the results of scientific and clinical research; the ability to attain regulatory approvals; market acceptance of our products; the state of the capital markets generally with particular reference to pharmaceutical, biotechnology, and medical companies; the status of strategic alliance agreements; and other relevant commercial considerations. If adequate funding is not available, we may be required to implement more aggressive cost reduction strategies than those currently contemplated; delay, reduce, or eliminate one or more of our product development programs; relinquish significant rights to product candidates or obtain funds on less favorable terms than we would otherwise accept; and/or divest assets through a merger, sale, or liquidation of the Company.

## Risks Related to Regulatory Matters

Potential investors should be aware of the risks, problems, delays, expenses, and difficulties which we may encounter in light of the extensive regulatory environment within which our business is carried out. Numerous statutes and regulations govern the manufacture and sale of non-therapeutic and human therapeutic products in the United States, Canada, and other countries that are the intended markets for our products and product candidates. Such legislation and regulation governs the approval of manufacturing facilities, the testing procedures, and controlled research that must be carried out, and the preclinical and clinical data that must be collected prior to marketing approval. Our

research and development efforts, as well as any future clinical trials, and the manufacturing and marketing of any products we may develop, will be subject to and restricted by such extensive regulation.

The process of obtaining necessary regulatory approvals is lengthy, expensive, and uncertain. We or our collaborators may fail to obtain the necessary approvals to commence or continue clinical testing or to manufacture or market our potential products in reasonable time frames, if at all. In addition, governmental authorities in the United States or other countries may enact regulatory reforms or restrictions on the development of new therapies that could adversely affect the regulatory environment in which we operate or the development of any products we may develop.

Completing clinical testing and obtaining required approvals is expected to take several years and to require the expenditure of substantial resources. There can be no assurance that clinical trials will be completed successfully within any specified period of time, if at all. Furthermore, clinical trials may be delayed or suspended at any time by us or by the various regulatory authorities if it is determined at any time that the subjects or patients are being exposed to unacceptable risks.

Any failure or delay in obtaining regulatory approvals would adversely affect our ability to utilize our technology and would therefore adversely affect our operations. Furthermore, no assurance can be given that our product candidates will prove to be safe and effective in clinical trials or that they will receive the requisite regulatory approval. Moreover, any regulatory approval of a drug which is eventually obtained may be granted with specific limitations on the indicated uses for which that drug may be marketed. Furthermore, product approvals may be withdrawn if problems occur following initial marketing or if compliance with regulatory standards is not maintained.

In addition, we rely to some extent on the availability of certain agents that are currently marketed by other firms. Such agents may become unavailable as a result of failing to meet regulatory requirements.

### *Uncertainties Related to Clinical Trials and Product Development*

Before obtaining regulatory clearance for the commercial sale of any of our products under development, we must demonstrate through preclinical studies and clinical trials that the potential product is safe and efficacious for use in humans for each target indication. The results from preclinical studies and early clinical trials may not be predictive of results that will be obtained in large clinical trials, and there can be no assurance that our clinical trials will demonstrate sufficient safety and efficacy necessary to obtain the requisite regulatory approvals or will result in marketable products. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials on similar compounds. The failure to adequately demonstrate the safety and efficacy of a product under development could delay or prevent regulatory clearance of the potential product and would have a material adverse effect on our success. Any drug is likely to produce some toxicity or undesirable side effects in animals and in humans when administered at sufficiently high doses and/or for sufficiently long periods of time. There can be no assurance that unacceptable toxicity or side effects will not occur at any dose level at any time in the course of human clinical trials of our potential products. The appearance of any such unacceptable toxicity or side effects in clinical trials could cause us or regulatory authorities to interrupt, limit, delay, or abort the development of any of our product candidates and could ultimately prevent their clearance by the United States Food and Drug Administration (FDA) or other regulatory authorities, for any or all targeted indications. Even after being cleared by the FDA or other regulatory authorities, a product may later be shown to be unsafe or not to have its purported effect, thereby preventing its widespread use or requiring withdrawal from the market. There can be no assurance that any of our products or product candidates will be safe when administered to patients.

The rate of completion of our clinical trials will be dependent upon, among other factors, the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of parties to clinical sites, and the eligibility criteria for the study. Delays in planned patient enrollment may result in increased costs, delays or termination of clinical trials, which could have a material adverse effect on our success.

In addition, we rely on third parties to assist us in overseeing and monitoring the clinical trials, which may result in delays in completing clinical trials, or the trials not being completed at all, if such third parties fail to perform under

their agreements with us or fail to meet regulatory standards in the performance of their obligations under such agreements. There can be no assurance that we will be able to submit a new drug application as scheduled if clinical trials are completed or that any such applications will be reviewed and cleared by the FDA or other regulatory authority in a timely manner or at all.

### *Clinical Trials Outside of the United States*

Our recently completed Phase I/II clinical trials of DM199 in patients with T2D was conducted in the Netherlands under EMA regulatory authority. We may conduct future clinical trials outside of the United States. While any such study would be conducted in accordance with international regulatory standards including compliance with Good Clinical Practice ("GCP") regulations and International Committee on Harmonization ("ICH") guidelines, there is a risk that the FDA may not accept the results in support of filing an Investigational New Drug ("IND") application.

### *Uncertainties Related to Forecasts*

Our expectations regarding the success of our product candidates and our business are based on forecasts which may include the commencement and completion of clinical trials and anticipated regulatory approval which may not be realized. The actual timing of these events can vary dramatically due to factors such as delays or failures in our clinical trials, the uncertainties inherent in the regulatory approval process, and delays in achieving manufacturing capacity and marketing infrastructure sufficient to commercialize our biopharmaceutical products. There can be no assurance that clinical trials involving our products will be successfully completed; that we will make regulatory submissions or receive regulatory approvals as forecasted; or that we will be able to adhere to our current schedule. The failure to do so could have a material adverse effect on us.

## Risks Related to our Business and our Industry

### *Rapid Technological Change*

The industry in which we operate is characterized by rapid and substantial technological change. There can be no assurance that developments by others will not render our products or technologies non-competitive or that we will be able to keep pace with technological developments. Our competitors may have developed or may be developing technologies which could become the basis for competitive products. Some of these products may prove to be more effective and less costly than our products.

### *Partnerships for Development and Commercialization of Technology*

We may need, but be unable to obtain, partners to support our development efforts and to commercialize our technology. Equity and/or debt financings alone may not be sufficient to fund the cost of developing our products, and we may need to rely on our ability to reach partnering arrangements to provide financial support for our discovery and development efforts.

In addition, in order to successfully develop and commercialize our technology, we may need to enter into a wide variety of arrangements with corporate sponsors, pharmaceutical companies, universities, research groups and others. While we have had previous research contracts, we may enter into additional arrangements with other contract research organizations. We may fail to obtain any such agreements on terms acceptable to us or at all. Even if we enter into these arrangements, we may not be able to satisfy our obligations under them, or renew or replace them after their original terms expire. Furthermore, arrangements of this nature may require us to grant certain rights to third parties, including exclusive marketing rights to one or more products, may require us to issue securities to our collaborators, or may contain other terms that are burdensome to us. If any of our collaborators terminate their relationship with us or fail to perform their obligations in a timely manner, the development or commercialization of our technology and potential products may be adversely affected.

### *Competition*

Technological competition is intense in the industry in which we operate. Competition comes from pharmaceutical companies, biotechnology companies, and universities, as well as companies that participate in each of the non-pharmaceutical markets we may attempt to address with our products. Many of our competitors have substantially greater financial and technical resources; more extensive research and development capabilities; and greater marketing, distribution, production, and human resources than we do. Moreover, competitors may develop products more quickly than us and may obtain regulatory approval for such products more rapidly than we do. Products and processes which are more effective than those that we intend to develop may be developed by our competitors. Research and development by others may render our technology products or processes non-competitive or obsolete.

### *Unproven Market*

Notwithstanding the estimated market potential for our products and product candidates, no assurance can be given that our projections and assumptions will prove to be correct owing to, in particular, competition from existing or new products and the yet to be established clinical viability of our identified drug candidates.

### *Management of Growth*

Engagement of a clinical trial and future pipeline development has placed, and is expected to continue to place, a significant strain on our managerial, operational, and technical resources. We expect operating expenses and staffing levels to increase in the future. To manage our growth, we must expand our operational and technical capabilities and our employee base while effectively administering multiple relationships with various third parties. There can be no assurance that we will be able to manage our expanding operations effectively. Any failure to implement cohesive management and operating systems, add resources on a cost-effective basis, or properly manage our expansion could have a material adverse effect on our business and results of operations.

### *Dependence on Key Personnel*

We depend on our management personnel. The loss of services of one or more of such persons could adversely affect our operations. It is necessary for us to continue to implement and improve our management systems and to continue to recruit and train new employees in order to manage our growth effectively. While we have been able to attract and retain skilled and experienced personnel in the past, no assurance can be given that we will be able to do so in the future.

### *Supply of Raw Materials*

We have selected manufacturers that we believe comply with Current Good Manufacturing Practices, (“cGMP”) and other applicable regulatory standards. Although the manufacturers are experienced, no assurance can be given that sufficient quantities for on-going studies and for future clinical trials will be produced, or produced on terms that are acceptable to us.

### *Systems Failures*

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failure. Any system failure, accident, or security breach that causes interruptions in our operations could result in a material disruption of our drug discovery programs. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability as a result, our drug discovery programs may be adversely affected, and the further development of our product candidates may be delayed. In addition, we may incur additional costs to remedy the damages caused by these disruptions or security breaches.

### *Effect of Insurers' Willingness to Pay for Products and Our Ability to Become Profitable*

Since health care insurers and other organizations may not pay for any products that we may develop or may impose limits on reimbursements, our ability to become profitable could be reduced. In both domestic and foreign markets, sales of potential products are likely to depend in part upon the availability and amounts of reimbursement from third party health care payor organizations, including government agencies; private health care insurers; and other health care payors, such as health maintenance organizations and self-insured employee plans. There is considerable pressure to reduce the cost of therapeutic products, and government and other third party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement for new therapeutic products and by refusing, in some cases, to provide any coverage for uses of approved products for disease indications for which marketing approval has not been granted. Significant uncertainty exists as to the reimbursement status of newly approved health care products or novel therapies. We can give no assurance that reimbursement will be provided by such payors at all or without substantial delay or, if such reimbursement is provided, that the approved reimbursement amounts will be sufficient to enable us to sell products we may develop on a profitable basis. Changes in reimbursement policies could also adversely affect the willingness of pharmaceutical companies to collaborate with us on the development of our product candidates. In certain markets, pricing or profitability of prescription pharmaceuticals is subject to government control.

### *Potential Product Liability*

A risk of product liability claims and related negative publicity is inherent in the development of human therapeutics and other products. Product liability insurance is expensive, its availability is limited, and it may not be offered on terms acceptable to us, if at all. The commercialization of our potential products could be inhibited or prevented by an inability to maintain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims. A product liability claim against us or the withdrawal of a product from the market could have a material adverse effect upon us and our financial condition. To protect against potential product liability risks, we have €450,000 per occurrence, €3.5 million clinical trial insurance and US$5.0 million product liability insurance coverage.

### *Foreign Currency Risk*

A portion of our expenditures are in US dollars and euros and, therefore, we are subject to foreign currency fluctuations which may, from time to time, impact our financial position and results of operations.

## Risks Related to Intellectual Property

### *Patents and Proprietary Rights*

We believe that patents and other proprietary rights are important to our business. Our policy is to file patent applications to protect technology, inventions, and improvements that may be important to the development of our business. We also rely upon trade secrets, know-how, continuing technological innovations, and licensing opportunities to develop and maintain our competitive position. We plan to enforce our issued patents and our rights to proprietary information and technology. We review third-party patents and patent applications, both to refine our own patent strategy and to identify useful licensing opportunities.

Our success depends, in part, on our ability to secure and protect our intellectual property rights and to operate without infringing on the proprietary rights of others or having third parties circumvent the rights owned or licensed by us. We have a number of patents, patent applications and rights to patents related to our compounds, products and technology, but we cannot be certain that they will be enforceable or provide adequate protection or that pending patent applications will result in issued patents.

To the extent that development, manufacturing, and testing of our products is performed by third party contractors, such work is performed pursuant to fee for service contracts. Under the contracts, all intellectual property, technology know-how, and trade secrets arising under such agreements are our exclusive property and must be kept confidential

by the contractors. It is not possible for us to be certain that we have obtained from the contractors all necessary rights to such technologies. Disputes may arise as to the scope of the contract or possible breach of contract. No assurance can be given that our contracts would be enforceable or would be upheld by a court.

The patent positions of pharmaceutical and biotechnology firms, ourselves included, are uncertain and involve complex questions of law and fact for which important legal issues remain unresolved. Therefore, it is not clear whether our pending patent applications will result in the issuance of patents or whether we will develop additional proprietary products which are patentable. Part of our strategy is based on our ability to secure a patent position to protect our technology. There is no assurance that we will be successful in this approach and failure to secure patent protection may have a material adverse effect upon us and our financial condition. Also, we may fail in our attempt to commercialize products using currently patented or licensed technology without having to license additional patents. Moreover, it is not clear whether the patents issued or to be issued will provide us with any competitive advantages or if any such patents will be the target of challenges by third parties, whether the patents of others will interfere with our ability to market our products, or whether third parties will circumvent our patents by means of alternate processes. Furthermore, it is possible for others to develop products which have the same effect as our products or technologies on an independent basis or to design around technologies patented by us. Patent applications relating to or affecting our business may have been filed by pharmaceutical or biotechnology companies or academic institutions. We have not detected any third-party patents that could interfere with our current projects. Such applications may conflict with our technologies or patent applications and such conflict could reduce the scope of patent protection which we could otherwise obtain or even lead to the rejection of our patent applications. There is no assurance that we can enter into licensing arrangements on reasonable commercial terms, or develop or obtain alternative technology in respect of patents issued to third parties that incidentally cover our products or production technologies. Any inability to secure licenses or alternative technology could result in delays in the introduction of some of our products or even lead to us being prevented from pursuing the development, manufacture, or sale of certain products. Moreover, we could potentially incur substantial legal costs in defending legal actions which allege patent infringement, or by initiating patent infringement suits against others. It is not possible for us to be certain that we are the creator of inventions covered by pending patent applications or that we were the first to invent or file patent applications for any such inventions. While we have used commercially reasonable efforts to obtain assignments of intellectual property from all individuals who may have created materials on our behalf (including with respect to inventions covered by our patent and pending patent applications), it is not possible for us to be certain that we have obtained all necessary rights to such materials. No assurance can be given that our patents, if issued, would be upheld by a court, or that a competitor's technology or product would be found to infringe on our patents. Moreover, much of our technology know-how that is not patentable may constitute trade secrets. Therefore, we require our employees, consultants, advisors, and collaborators to enter into confidentiality agreements either as stand-alone agreements or as part of their consulting contracts. However, no assurance can be given that such agreements will provide meaningful protection of our trade secrets, know-how, or other proprietary information in the event of any unauthorized use or disclosure of confidential information. Also, while we have used commercially reasonable efforts to obtain executed copies of such agreements from all employees, consultants, advisors, and collaborators, no assurance can be given that executed copies of all such agreements have been obtained.

### *Costs Stemming from Defense Against Third-Party Intellectual Property Infringement Claims*

Third parties may claim that we are using their proprietary information without authorization. Third parties may also have or obtain patents and may claim that technologies licensed to or used by us infringe their patents. If we are required to defend patent infringement actions brought by third parties, or if we sue to protect our own patent rights or otherwise to protect our proprietary information and to prevent its disclosure, we may be required to pay substantial litigation costs and managerial attention may be diverted from business operations even if the outcome is in our favor. In addition, any legal action that seeks damages or an injunction to stop us from carrying on our commercial activities relating to the affected technologies could subject us to monetary liability and require us or any third-party licensors to obtain a license to continue to use the affected technologies. We cannot predict whether we would prevail in any of these types of actions or that any required license would be available on commercially acceptable terms or at all. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources.

### Risks Related to the Company's Common Shares

#### *Share Price Volatility*

A number of factors could influence the volatility in the trading price of our common shares, including changes in the economy or in the financial markets, industry related developments, and the impact of material events and changes in our operations. Our quarterly losses may vary because of expenses we incur related to future research including the timing of costs for manufacturing and initiating and completing preclinical and clinical trials. Each of these factors could lead to increased volatility in the market price of our common shares. In addition, the market prices of the securities of our competitors may also lead to fluctuations in the trading price of our common shares.

#### *Dividends*

We have not declared or paid any cash dividends on our common shares to date. The payment of dividends in the future will be dependent on our earnings and financial condition and on such other factors as our board of directors considers appropriate. Unless and until we pay dividends, shareholders may not receive a return on their shares. There is no present intention by our board of directors to pay dividends on our common shares.

#### *Dilution*

Future dilution may occur due to additional future equity financing events by the Company. If outstanding options, warrants, or deferred share units of the Company are exercised into common shares, you will experience additional dilution.

## Additional Information

Additional information relating to the Company, including its Annual Information Form can be found on SEDAR at www.sedar.com.