



**MANAGEMENT'S DISCUSSION & ANALYSIS**  
**FOR THE THREE MONTHS ENDED**  
**MARCH 31, 2017 and 2016**

Dated: May 15, 2017



**DiaMedica**  
THERAPEUTICS

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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 Therapeutics Inc. (formerly DiaMedica Inc.) and the subsidiaries through which it conducts its business, unless otherwise indicated.

The following MD&A is prepared as of May 15, 2017 for DiaMedica for the three months ended March 31, 2017 and 2016 and should be read in conjunction with the unaudited condensed consolidated interim financial statements and accompanying notes for the three months ended March 31, 2017 and 2016, 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, 2017. 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>.

In the fourth quarter of 2016, the Company changed its presentation currency from Canadian dollars ("CAD\$") to USD\$. All amounts are in United States dollars ("USD\$"), unless otherwise indicated.

## **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 are intended to identify forward-looking statements. The forward-looking statements contained in this MD&A include, but are not limited to, statements with respect to our:

- ability to obtain future funding on favorable terms, or at all, from any of the following: potential equity investment, government funding, existing and future corporate alliances, or licensing transactions with third parties; and the receipt of timing of any payments by us or to us in respect to such arrangements;
- projections for the DM199 development plan and progress of each of our products and technologies, particularly with respect to timely completion of studies, clinical trials, study outcomes, product manufacturing, and regulatory approval;
- expectation about our products' safety, tolerability, route of administration, or efficacy in diabetic kidney disease, acute ischemic stroke, or any other disease state;
- plans to market, distribute, and sell our products and the level of acceptance by the marketplace; and
- descriptions of our products' mechanisms of action, potential side-effect profile, and plans for discovering and developing new products.

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 are included but not limited to:

- the risks related to clinical trials, including our ability to attract patients to our clinical trials; potential delays and cost overruns; the failure to demonstrate efficacy and safety;
- our ability to reproduce the results of previously conducted clinical studies and/or comparisons to other forms of KLK1, including Kailikang®;
- our ability to displace other forms of KLK1, including Kailikang®;
- the risk of negative results of clinical trials or adverse safety events by us or others related to our product candidates;
- our inability to either commercialize our products or to commercialize our products profitably;
- our inability to establish or manage manufacturing, development or marketing collaborations;

- the delays or negative outcomes from the regulatory approval process;
- the risks of reliance on third parties for the planning, conduct, and monitoring of clinical trials, and for the manufacture of the drug product;
- our ability to obtain quantities of development product in sufficient quantity or at standards acceptable to complete studies;
- our ability to collect the R&D tax incentive or other opportunities identified by the Company;
- the uncertainty related to intellectual property liability rights and liability claims asserted against us and our ability to adequately protect proprietary information and technology from competitors;
- the potential for product liability claims; and
- the financial risks related to the fluctuation of foreign currency rates and expenses denominated in foreign currencies.

all as further and more fully described under the heading “Risk Factors” in this MD&A and in our Annual Information Form.

Although the forward-looking statements contained in this MD&A are based upon what our management believes to be reasonable assumptions, we cannot assure readers that actual results will be consistent with these forward-looking statements.

Any forward-looking statements represent our estimates only as of the date of this MD&A and should not be relied upon as representing our estimates as of any subsequent date. We undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events, except as required by securities legislation.

## **BUSINESS**

DiaMedica Therapeutics is a clinical stage biopharmaceutical company primarily focused on the development of novel recombinant proteins. Our lead product is DM199, a recombinant human KLK1 (“rhKLK1” or “tissue kallikrein-1”) protein. We believe DM199 has the potential to treat several 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 nephropathy (“DN”), also known as diabetic kidney disease (“DKD”).

### **Commercialization Partnerships and Other Strategic Initiatives**

The Company will 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 explore potential agreement(s) with such pharmaceutical and biotechnology companies to conduct Phase III trials, file the appropriate NDA (new drug application) and ultimately market and sell the drug products we develop. We believe this will reduce the capital requirements to perform the large multi-center 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 has received several licensing term sheets from Asian pharmaceutical companies for potential regional licensing rights and the Company is continuing discussions for potential licensing and/or joint venture opportunities. Since April 1<sup>st</sup>, the Company has continued on going discussions with potential partners.

### **Corporate Update**

On December 20, 2016, the Company reported positive results of its bridging study. The study compared multiple doses of intravenous and subcutaneous (injection under skin) dosing of DM199 to identify a dose and delivery route that most closely compares to or improves the pharmacokinetic (movement of drugs within the body) and pharmacodynamics (what the body does to a drug) profile of the approved urinary tissue kallikrein (“uKLK1”), trade name Kailikang® (“reference drug”). Kailikang®, via daily intravenous delivery, has been approved and is believed to be widely used in the Republic of China for the treatment of AIS. The study identified a dose of DM199 via intravenous

administration that produced pharmacokinetic and pharmacodynamic activity comparable to those produced by the reference drug.

The study results demonstrated the dose dependent levels of DM199, one of which was shown to be comparable to what is seen with the reference drug. The Phase I controlled trial was an open-label single ascending study, where healthy volunteers received one of four single doses of DM199 (n=12), administered as a 30-minute intravenous infusion. Plasma DM199 concentration, biomarker concentrations, and other safety and pharmacokinetic parameters were measured in the trial.

On March 13, 2017, the Company also reported that the study identified an intravenous dose of DM199 having a similar profile to urinary KLK1 but with an improved subcutaneous dose of DM199 producing sustained plasma levels superior to the reference drug. The reference drug is administered intravenously and has a very short half-life.

The DM199 subcutaneous delivery provides sustained levels of the KLK1 protein, offering a potentially superior profile to the reference drug, which has a very short exposure window. The dosing of DM199 will be significantly more convenient and potentially provide improved efficacy to the short half-life of the reference drug. DM199 has the same amino acid sequence and identical biochemical activity as the reference drug, and has demonstrated similar physiological effects.

The Company intends to initiate a Phase II trial for AIS in the third quarter of 2017. The Company is also preparing to initiate clinical trial(s) for other indications.

On April 17, 2017, the Company completed a \$2 million non-brokered private placement with a U.S.-based family office. The Company issued 10,526,315 million units at \$0.19 per unit with each unit consisting 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 \$0.23 at any time prior to expiry. The Company intends to use the offering proceeds toward advancing its research and development program, including the DM199 clinical trial, and for general corporate purposes.

On March 20, 2017, the Company announced that the European Patent Office has issued European Patent No. 2854841, entitled "Human Tissue Kallikrein 1 Glycosylation Isoforms", containing claims that cover the composition of matter of DiaMedica's product candidate, DM199, and pharmaceutical compositions comprising DM199. The patent protects key composition of matter of DM199's proprietary recombinant kallikrein protein. The expanded patent protection adds European protection to DiaMedica's intellectual property portfolio related to DM199 that includes U.S. Patent No. 9364521 which provides expanded composition of matter protection for DM199.

On May 1, 2017, the Company announced that the U.S. Patent and Trademark Office has issued U.S. Patent No. 9,616,015, entitled "Formulation of Human Tissue Kallikrein-1 for Parenteral Delivery and Related Methods", for DM199. The patent protects the methods of parenterally administering DM199 to patients in need where absorption into the circulation via methods such as IV or subcutaneous administration improves systemic pharmacokinetics ("PK"), bioavailability, safety, and/or convenience related to IV or other forms of administration. The Company believes these methods of delivery could more completely address the needs of patients by offering better options for acute and chronic therapy.

Based on recent clinical trial results and related matter, DiaMedica also recently filed for new worldwide patent coverage, including in the U.S., Europe, China, and Japan for dosing, route of administration, formulation, and for numerous indications.

## **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 tissue kallikrein-1 protein engineered to replicate 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, vascular diseases of the brain, kidneys, and heart. The current primary focus for the development of DM199 is on AIS and DN.

Recombinant tissue plasminogen activator (“tPA”) is the only drug approved for the treatment of AIS in the United States of America (the “United States” or 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<sup>®</sup> is a human urine-extracted KLK1 protein marketed by Techpool Bio-Pharma Inc. (“Techpool”), which we believe 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<sup>®</sup> 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 AIS 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).

In the United States and Europe, the only Food and Drug Administration (“FDA”) approved drug treatment is tissue plasminogen 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).

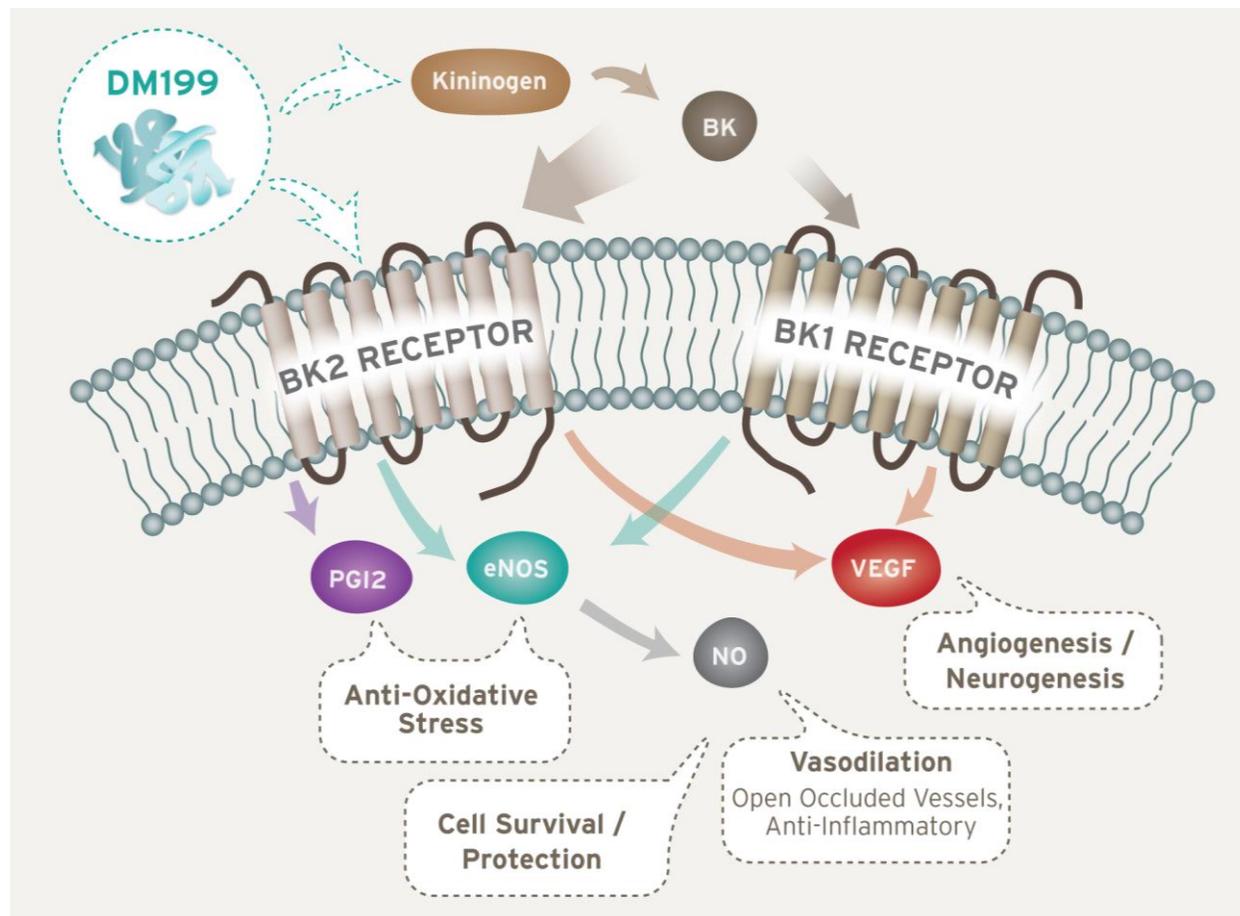
DM199 is being positioned to treat AIS patients with therapy beyond the current window of 3-4.5 hours for tPA to up to 48 hours after the first sign of symptoms, thereby filling a large unmet need of patients who cannot receive tPA and replacing Kailikang<sup>®</sup> in China, potentially making therapy 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<sup>®</sup> while also addressing any potential supply constraints which makes Kailikang<sup>®</sup> 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.

### ***DM199 Mechanism***

DM199 is a purified recombinant form of KLK1 that likely has multiple physiological effects to help treat both AIS and DN. 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. Kinins bind to the bradykinin receptors (BK1R and BK2R) in the kallikrein-kinin system (“KKS”), which set in motion a large number of complex metabolic pathways in response to ischemia including improved blood flow (through vasodilation), anti-inflammatory response, cell repair through angiogenesis or vasculogenesis, and decreased apoptosis. DM199 has been shown to breakdown bradykinins thus creating more kinins in animal models of renal injury (Charest-Morin et al., 2015. *Pharmacol. Res. Perspect*, 3(2): e00119). Additionally, there is a large body of scientific evidence demonstrating KLK1-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). This is likely the primary mode by which kallikrein treatment addresses various diseases including DN and AIS.

Kinins have a short half-life *in vivo* as they are rapidly degraded by ubiquitous enzymes and serpins, most notable are alpha-1 antitrypsin, kallistatin, and protein C inhibitor. KLK1 activity also is tightly regulated by these inhibitor proteins found throughout the body. Through these multilayered regulatory systems, it is plausible that levels of bradykinin drop below optimum levels in pathological conditions such as AIS and DN. Treatments that provide additional supplies of active KLK1 (such as DM199) can serve to increase or maintain sufficient bradykinin levels and thereby promote BK receptor activation. Previous research demonstrated activation of BK1R and BK2R by kinins to protect the kidneys from high blood pressure and high blood glucose. Specific downstream mechanisms include elevation of intracellular calcium, release of nitric oxide (NO), and activation of prostaglandin 2 (PGI2) and

endothelial nitric oxide synthase (eNOS), involved in antioxidative stress, cell survival and vasodilation (Kakoki & Smithies. 2009. *Kidney Int*, 75, 1019-1030; Kayashima et al. 2012. *Curr. Opin. Nephrol. Hypertens*, 21, 92-96). Further downstream physiological effects include blood pressure regulation, vasodilation, and angiogenesis (specifically through the activation of VEGF).



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 Targeted Indications

#### Acute Ischemic Stroke

A stroke is the rapidly developing loss of brain tissue/function due to disturbance in the blood supply. As a result, the affected area of the brain becomes inactive and eventually dies. Strokes can be classified into two major categories: AIS and hemorrhagic stroke. AIS are those that are caused by interruption of the blood supply by a blood clot (ischemia), while a hemorrhagic stroke results from rupture of a blood vessel or an abnormal vascular structure. About 87% of strokes are acute ischemic strokes (Center for Disease Control and Prevention; Stroke Fact Sheet, 2013), with the remainder classified as hemorrhagic. Worldwide, stroke is the leading cause of adult disability and the second leading cause of death in developed countries. 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. 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). Each year in

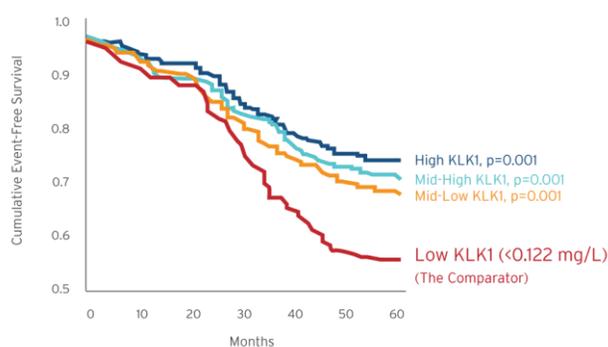


(2009). *Stroke* J. Cereb. Circ. 40, 2945–2948). Outside this therapeutic window tPA is not only ineffective but leads to a greater risk of hemorrhage (bleeding in the brain). It is estimated that in the U.S. only 2-5% of AIS patients are treated with tPA (Miller et al., *The Neurohospitalist*. 2011 Jul; 1(3): 138-147), while the rest of patients receive supportive or palliative care. The long-term costs of stroke are substantial, with many patients requiring extended hospitalization, extended physical therapy, or rehabilitation, and many require long-term institutional or family care.

We believe that stroke represents an area of tremendous unmet medical need, and KLK1 treatment (such as DM199) could provide tremendous opportunity for more effective therapy. Recently, in a pre-clinical neurological study, a single-dose of DM199 increased cerebral blood flow by 37% ( $P < 0.005$ ), especially when neurons were depolarizing (data on file at DiaMedica). Furthermore, higher endogenous KLK1 plasma levels are associated with better outcomes following 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 (*Annals of Neurology* (2011) 70:265-73).

### KLK1 Levels - Event Free Survival Functions

Clinical studies demonstrate lower incidence of recurrent stroke and longer “event free” periods over five years in patients who suffered an initial stroke but had high levels of endogenous KLK1 (Zhang et al. 2011. *Ann. Neurol*, 70, 265-273). DiaMedica believes DM199 has the potential to preserve “at risk” brain tissue by increasing cerebral blood flow, 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*.



*Annals of Neurology* (2011) 70:265-73

DM199 is being positioned to treat AIS patients with therapy beyond the current window of 3-4.5 hours for tPA to up to 48 hours after first sign of symptoms, thereby filling a large unmet need of patients who cannot receive tPA. This could potentially make therapy available to the millions of patients worldwide who currently have limited options regarding stroke therapy.

### Urinary Tissue Kallikriin-1 approved for stroke treatment in China

A urine-extracted version of KLK1 (uKLK1) is currently used to treat AIS in the People’s Republic of China. The Chinese product is isolated from human urine and is marketed under the name Kailikang® (Urinary Kallidinogenase for Injection) by Techpool. Kailikang® is prescribed to stroke patients intravenously up to 48 hours post-stroke.

More than 40 published clinical studies show a beneficial effect of Kailikang® treatment in AIS, including a meta-analysis covering 24 clinical studies involving 2,433 patients. The review used well-established methods for meta-analysis and 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,” (Zhang C., et al. 2012; *J Evid Based Med.* ;5(1):31-9).

In a double-blinded, placebo-controlled trial of 446 patients treated with uKLK1 or placebo administered up to 48 hours after a stroke showed significantly better scores on the European Stroke Scale and Activities of Daily Living at three weeks post treatment and after three months using the Barthel Index (Ding D et al., 2007. *Chin J Neurol* 40(5); 306-310).

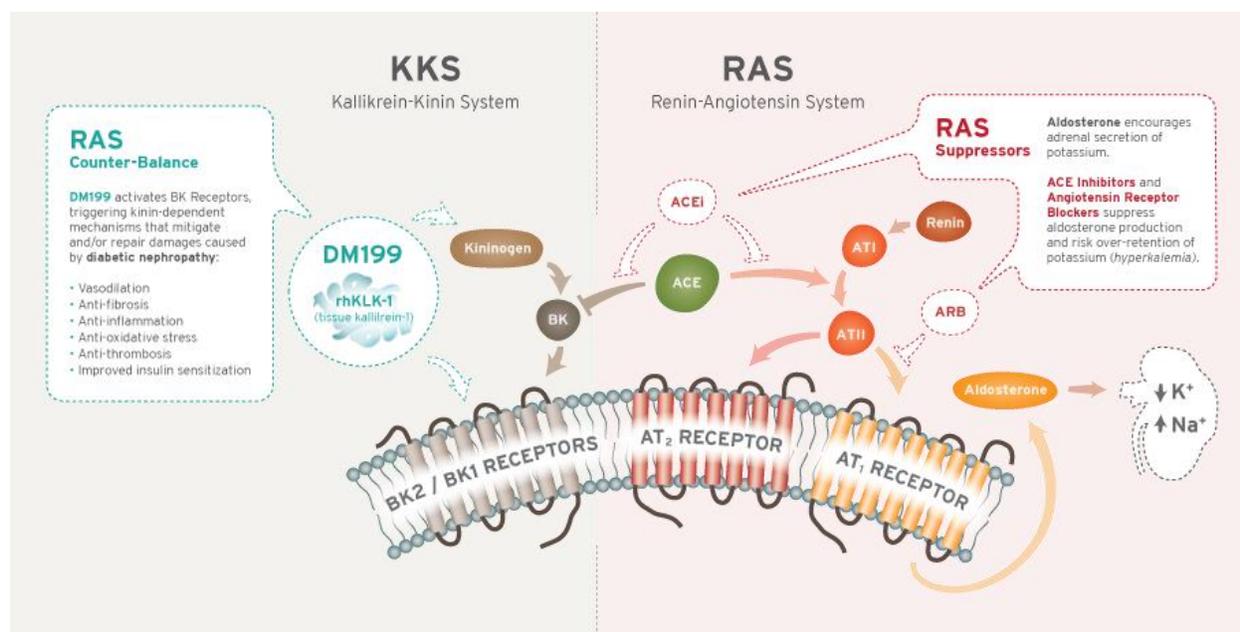
DiaMedica believes DM199 is an ideal candidate for improved therapy for the nearly 15 million people annually who experience an AIS.

### Diabetic Kidney Disease

DN or DKD is a form of chronic kidney disease and is a common complication of both Type 1 and Type 2 Diabetes. Additionally, people with hypertension and/or familial history for DN are at increased risk. DN is characterized by the gradual loss of kidney function and is the leading cause of end-stage renal disease (“ESRD”) which requires hemodialysis and/or renal transplant. Diabetes has become the primary cause of kidney disease in the United States and the associated incidence of diabetic nephropathy is on the rise. The following summarizes the size of the DN market:

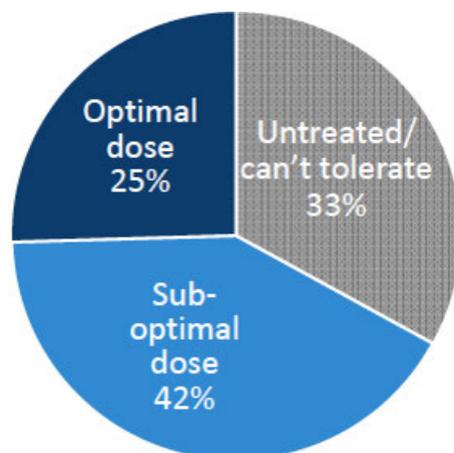
- 5-10 million people in the U.S. are diagnosed with DN (National Chronic Kidney Disease Fact Sheet 2014, CDC DDT)
- 120 million people in China are diagnosed with DN (*Journal of Diabetes Research* Vol 2015, Decision Resources, 28 Jan 2014)
- 40 percent of all diabetics will develop DN (Reutens, AT.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

### DM199 Proposed Mechanism: Kidney Disease



Clinically, DN is characterized by a progressive decline in glomerular filtration rate (“GFR”) leading to an increase in urine albumin/albuminuria, hypertension and increase risk of cardiovascular morbidity/mortality. The known underlying causes of DN often begin with an increase in blood glucose, which leads to the thickening of the glomerular membrane, known as fibrosis. As the GFR becomes impaired, abnormal amounts of protein and urine are released into the tubules through damaged capillary pores. Additionally, increased blood glucose leads to increased blood pressure, reactive oxygen species, advanced glycated end product formation, and inflammation. As this continues, structural components of the kidney (the nephron) begin to collapse, resulting in cell ischemia and cell death. As the renal damage continues, a progressive thickening of the basement membrane is seen along with continued pathological changes in the cell and inflammation. Early stages of DN are characterized as microalbuminuria (small amounts of protein leak into the urine). Late stages are characterized as macroalbuminuria (large amount of protein in the urine). The rate of decline depends on the type of diabetes, genetic predisposition, glycemic controls, and blood pressure. At the final stages of DN, the kidneys fail completely and dialysis or a kidney transplant is needed.

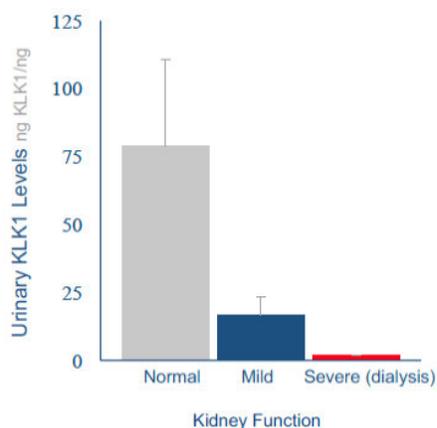
Current treatment strategies for DN include the strict control of high blood pressure and high blood sugar. Blood pressure medications including angiotensin converting enzyme inhibitors (“ACEi”) and angiotensin receptor blockers (“ARBs”) are commonly prescribed to control hypertension and slow the progression of DN. We currently are aware of only one ACEi drug, captopril, that is formally approved by the FDA to treat diabetic nephropathy. However, approximately 20% of patients eventually progress to ESRD and require hemodialysis, peritoneal dialysis, or renal transplant. Furthermore, the treatment with ACEi and ARBs has been linked to hyperkalemia (elevated blood potassium levels), which increases the risk for abnormal heart rhythms and sudden death. In fact, two clinical trials investigating the use of ACEi and ARB combination therapy in kidney disease were stopped prematurely because participants developed hyperkalemia. The added complication of hyperkalemia results in 42% of patients receiving suboptimal dosing and 33% of patients untreated because they can’t tolerate the treatment. There are an estimated 2.5 million patients in the U.S. with comorbid DN and hyperkalemia (USRDS 2011, Truven data, and CDC).



RAS inhibitor treatment in CKD patients

Estimates based on data adapted from Treatment Algorithm Quantitative study, June 2013

*KLK1 Levels – In Kidney Disease Patients, by Stage of Diseases*



Immunopharmacology 44 1999. 183–192

Further supporting the hypothesis that an intact KKS is critical for normal kidney function are a series of observations that the amount KLK1 released into the urine appears to be inversely correlated with the severity of disease in patients with chronic kidney disease, such as DN. Urinary KLK1 excretion was decreased in patients with both mild (not requiring dialysis) and severe (kidney failure/hemodialysis) renal disease compared to controls (Naicker et al. *Immunopharmacology* 44 1999. 183–192). The severity of the disease was negatively correlated with KLK1 excretion. Decreases in urinary KLK1 activity was seen especially when the reduction was associated with decreased glomerular filtration rate. Additionally, ACEi efficacy requires intact KLK1 levels (Goto et al., 1995. *Circulation Research*, 77: 611-621; Alhenc-Gelas et al., 2011. *Current Pharm Design*, 17: 2654-2662). In a disease state where levels are already low, the effectiveness of ACEi could be compromised. We believe DM199 is advantageous over ACEi because it restores already depleted KLK1 levels.

There is a significant need for alternative treatment strategies of DN. DiaMedica believes DM199 could compliment the use of ACEi or ARBs to improve kidney functions without increasing the risk for hyperkalemia. We believe DM199 balances the renin-angiotensin system (“RAS”) that ACEi and ARBs work through by generating kinins to activate the bradykinin receptors in the KKS. Activation of the BK receptors repair the renal system following DN by improving vasodilation, anti-fibrosis, anti-inflammation, anti-oxidative stress, anti-thrombosis, and insulin sensitization. A significant differentiation between DM199 and ACEi and ARB treatment is that with DM199 hyperkalemia might be avoidable with a bradykinin receptor-specific agonist (Kidney International).

*Porcine Tissue Kallikrein-1 approved for DN treatment in China*

Porcine KLK1 is derived from the pancreas and is currently used to treat DN in the People’s Republic of China. Over 20 clinical papers have been published demonstrating the positive effects of the KLK1 protein alone or combined with an ARB or an ACEi. These studies have ranged from a few weeks to six months in length and demonstrate a time dependent improvement in kidney disease based on urinary albumin excretion rate (UAER) and other clinical endpoints of kidney disease.

In a study of 200 participants with diabetes, participants were treated with KLK1 or a blood thinner for 60 days. The amount of protein in the urine decreased significantly from baseline in the KLK1 group compared to the blood thinner group. When participants were divided into mild and severe DN, participants with mild DN showed a more robust treatment effect with KLK1 than the severe group, suggesting KLK1 treatment is most effective at early stages of DN (Zhao&Rong, 2005; *Chinese Lib. Classif*). In a similar study, KLK1 treated participants showed significant improvements in markers of renal function (Han & Shi, 2013, *J. N. China Pharmacy 10(2)*) and renal hemodynamics (Zhang et al., 2016. *Shandong Med J*, 56(6)).

In a study treating 68 participants with early DN with either an ARB or an ARB+KLK1, after one month of treatment, participants receiving the combination therapy had significantly lower levels of serum cystatin, an endogenous marker of kidney function and tightly correlates with GFR (Du et al., 2012, *J. Xinxiang Med Col 29(8)*).

In a six-month, Phase II randomized, placebo-controlled clinical trial of 90 participants treated daily with an ARB or an ARB + KLK1, the combination group showed statistically significant improvement in UAER and in urine  $\beta$ 2-microglobulin measured after 6 months of treatment. Of note, the combination treatment group's UAER levels were brought from 134.8  $\mu$ g/mg to 21.1  $\mu$ g/mg, which is lower than the clinical diagnosis for DN (urine albumin >30  $\mu$ g/mg per 24hrs (Wang et al., 2011, *Chin J Diabetes 19 (8)*).

In a 30-day Phase II clinical study of 68 patients treated with 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 DN.

### **KLK1 – Companion Diagnostic Test**

A growing body of evidence indicates KLK1 insufficiency is associated with multiple disease states including hypertension, DN and AIS (discussed in detail above). Measurements of endogenous KLK1 activity in both urine and plasma are inversely correlated with disease severity (Chao et al., 2006. *Biol. Chem*, 387: 637-641; (Naicker et al. 1999. *Immunopharmacology*, 44: 183–192; Zhang C., et al. 2012; *J Evid Based Med.* ;5(1):31-9). Importantly, the decrease in urinary protein occurs in a disease state (e.g. DN), where a primary hallmark is increased secretion of many other proteins. In this way, KLK1 is a potentially unique and powerful diagnostic tool for such diseases. DiaMedica is currently developing a companion diagnostic, DMDx, to measure KLK1 levels.

### **DM199 Clinical Studies**

The Company has conducted five clinical trials with DM199 including single ascending doses, multiple ascending doses, and a pilot study in Type 2 diabetic patients. DM199 was safe, well tolerated and demonstrated clear activity in patients by measured changes in blood pressure over two clinical studies. Results in healthy participants show that DM199 exhibits a favorable pharmacokinetic (PK), measuring blood levels, 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 much greater than anticipated efficacious treatment. This is consistent with the DM199 mechanism of action as seen in pre-clinical primate studies. Similarly, the 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 11 or 28-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 two 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. Blood glucose levels were also measured despite the short trial length and small trial size. Longer term studies are required to properly evaluate the effect on blood glucose, red blood cell turnover takes 3 months. A reduction in fasting blood glucose was observed in the lower DM199 dose vs. baseline ( $p < 0.05$ ). Blood pressure was also monitored during the 28-day study with a statistically

significant reduction from baseline blood pressure observed in patients receiving DM199. This was not observed in the placebo group.

In the fall of 2016, DiaMedica initiated a Phase Ib study with DM199 designed to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics in healthy volunteers. Specifically, this study compares multiple doses of intravenous and subcutaneous dosing of DM199 to identify a dose and delivery route that most closely compared to or improves upon the pharmacokinetic and pharmacodynamics profile of the approved urinary KLK1. To date, the study has demonstrated DM199 subcutaneous delivery method provides sustained levels of the KLK1 protein. This may provide significantly more convenient drug delivery and improved efficacy compared to the short half-life of urinary KLK1.

Based on previous clinical trials, pre-clinical studies, the approved dosing of Kailikang<sup>®</sup>, and external analysis, DiaMedica has identified dosing of DM199 via subcutaneous and IV delivery for future clinical trials on DN and/or AIS. In multiple clinical trials, DM199 was shown to be safe and well tolerated in healthy volunteers and diabetic patients. The dose limiting tolerability was orthostatic hypotension at high dosing levels. In a recently completed bridging study comparing the PK profiles of DM199 to Kailikang<sup>®</sup>, we believe that we have identified the potentially optimal dosing levels for acute ischemic stroke and diabetic kidney disease. A dose of DM199 administered via IV infusion mimicked the anticipated drug profile of IV-administered urinary KLK1 (Kailikang<sup>®</sup>). This study also identified a dose of DM199 via subcutaneous injection having a superior PK profile that maintains KLK1 levels throughout day. The Company believes this profile could improve the efficacy of DM199.

## RESULTS OF OPERATIONS

### For the three months ended March 31, 2017 and 2016

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, 2017 was \$1,308,903 compared to a loss of \$399,348 for the three months ended March 31, 2016. The increase in net loss for the three months ended March 31, 2017 over the comparable periods of the prior year was due mainly to the DM199 bridging study.

### Research and Development

Components of research and development expenses for the three months ended March 31, 2017 and 2016 were as follows:

	2017	2016
	\$	\$
Research and development programs, excluding the below	936,691	95,473
Salaries, fees, and short-term benefits	192,483	100,441
Share-based compensation	28,454	30,691
Depreciation of property and equipment	(638)	(383)
	<b>1,156,990</b>	<b>226,222</b>

For the three months ended March 31, 2017, research and development costs increased due to the DM199 bridging study. Salaries, fees, and short-term benefits increased over the comparable period mainly from an increase in staff.

### General and Administrative

Components of general and administrative expenses for the three months ended March 31, 2017 and 2016 were as follows:

	2017	2016
	\$	\$
General and administrative, excluding the below	57,877	55,644
Salaries, fees, and short-term benefits	60,598	24,397
Share-based compensation	17,089	44,641
	<b>135,564</b>	<b>124,682</b>

For the three months ended March 31, 2017, general and administrative costs increased mainly from to an increase in staff. Share-based compensation decreased due mainly to the forfeiture of stock options.

### Finance costs (income) and other income

Finance costs for the three months ended March 31, 2017 of \$8,180 was lower than the finance income of \$12,975 recorded in same period of 2016 mainly from net foreign exchange gains, partially offset by interest expense.

### 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, 2017, the Company had cash totaling \$938,520 compared to \$1,736,361 as at December 31, 2016. On April 17, 2017, the Company completed a \$2 million private placement with a U.S.-based family office.

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 and has an accumulated deficit of \$48 million as at March 31, 2017. 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. These circumstances cast significant doubt as to the ability of the Company to continue as a going concern and hence the appropriateness ultimately of the use of accounting principles applicable to a going concern.

The Company's future operations are therefore dependent upon its ability to generate product revenues, negotiate license agreements with partners, and secure additional funds. 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 that these or other strategies will be sufficient to permit the Company to continue as a going concern.

The Company is actively pursuing additional financing to further develop the Company's scientific initiatives and completed several financings in 2016, including a \$4 million strategic investment by Hermed Capital Healthcare Fund, a private equity fund initiated through a partnership between Fosun Pharmaceutical and SK Group. On April 17, 2017, the Company completed a \$2 million private placement with a U.S.-based family office.

Additionally, DiaMedica Australia is applying for an R&D Tax Incentive, a research and development tax offset program established by the Australian Tax Office for eligible research and development activities which could provide refundable investment tax credits of 45% of eligible research and development activities which at December 31, 2016 aggregate to approximately AUD\$250,000. There are no guarantees that the Company will receive these credits. The Company has not recognized investment tax credits at March 31, 2017 in its financial statements related to this incentive program in accordance with the Company's accounting policies.

These and other opportunities identified and available to the Company will enable the Company to further its research and development program, including DM199's clinical studies.

*Common shares issued – for the three months ended March 31, 2017 and to the date of this MD&A*

On April 17, 2017, the Company completed a non-brokered private placement of 10,526,315 units at a price of \$0.19 per unit for aggregate proceeds of approximately \$2,000,000. Each unit consists of one common share and one half common share purchase warrant. Each whole warrant entitles the holder to purchase one common share at a price of \$0.23 at any time prior to expiry on April 17, 2019. The warrant expiry date can be accelerated at the option of the Company, in the event that the volume-weighted average trading price of the Company's common shares exceeds \$0.30 per common share for any 10 consecutive trading days.

During the three months ended March 31, 2017 and to the date of this MD&A, 60,000 common shares were issued on the exercise of options for gross proceeds of \$6,749.

*Common shares issued – for the year ended December 31, 2016*

On September 8, 2016, the Company completed the second tranche of a non-brokered private placement of 15,000,000 common shares at a price of \$0.20 per share for aggregate gross proceeds of \$3,000,000 (\$2,614,282 net of issue costs).

On August 22, 2016, the Company completed the first tranche of a non-brokered private placement of 5,000,000 common shares at a price of \$0.20 per share for aggregate gross proceeds of \$1,000,000 (\$990,769 net of issue costs).

On April 22, 2016, the Company issued 50,000 common shares for settlement of a debt to a vendor at an issue price of CAD\$0.20 per common share.

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 CAD\$0.16 per unit for aggregate gross proceeds of approximately \$445,544 and \$409,160 net of issue costs (CAD\$610,000 and CAD\$560,188 respectively). 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 CAD\$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 CAD\$0.25 prior to expiry on February 18, 2018.

On February 25, 2016, the Company completed the second tranche of a non-brokered private placement of 875,000 units at a price of CAD\$0.16 per unit for aggregate gross proceeds of approximately \$101,710 and \$85,590 net of issue costs (CAD\$140,000 and CAD\$117,810 respectively). 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 CAD\$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 CAD\$0.25 prior to expiry on February 25, 2018.

During the year ended December 31, 2016, 25,880 common shares were issued on the redemption of deferred share units and 3,482,150 common shares were issued on the exercise of warrants for gross proceeds of \$617,212 and 10,891,087 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, 2017 and 2016, and to the date of this MD&A is presented below:

Balance, December 31, 2015	82,275,430
Shares issued under private placement	24,687,500
Shares issued on warrant exercise	3,482,150
Shares issued for settlement of debt	50,000
Shares issued on redemption of deferred share units	25,880
Balance as at December 31, 2016	110,520,960
Shares issued on warrant exercise	60,000
Balance as at March 31, 2017	110,580,960
Shares issued under private placement	10,526,315
Balance as at the date of the MD&A	121,107,275

### 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, 2017:

	Number of Options	2017 Weighted average exercise price in CAD\$
Balance, December 31, 2016	8,557,000	\$0.38
Granted	413,334	\$0.23
Exercised	(60,000)	\$0.15
Expired/cancelled	(1,125,000)	\$0.81
Forfeited	(324,000)	\$0.15
Balance, end of period	7,461,334	\$0.32
Options exercisable, end of period	3,360,084	\$0.45

From January 1, 2017 to the date of this MD&A, 60,000 common shares were issued on the exercise of options for gross proceeds of \$6,749, 1,125,000 options expired unexercised, and 324,000 options were forfeited.

### Warrants

The following tables reflect the activity of the warrants since December 31, 2015 and to the date of this MD&A:

Balance, December 31, 2015	14,373,237
Warrants issued under private placement	2,562,050
Warrants exercised	(3,482,150)
Warrants expired	(10,891,087)
Balance as at December 31, 2016 and March 31, 2017	2,562,050
Warrants issued under private placement	5,263,158
Balance as at the date of the MD&A	7,825,208

The following table reflects the warrants outstanding as of the date of the MD&A:

Expiry Date	Number of Warrants	Exercise Price	Exercise Total
February 18, 2018	2,054,550	CAD\$0.25	CAD\$513,638
February 25, 2018	507,500	CAD\$0.25	CAD\$126,875
April 17, 2019	5,263,158	USD\$0.23	USD\$1,210,526
	7,825,208		

### Shareholder rights plan

The Company adopted a shareholder rights plan agreement (the "Plan"). 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 is set to expire at 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 (20%) 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 (50%) 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 sixty (60) days. If at the end of sixty (60) days at least 50 percent (50%) 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 ten (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 Deferred Share Unit Plan (the "DSU Plan") promotes greater alignment of long-term interests between non-executive directors and executive officers of the Company and its shareholders through the issuance of deferred share units ("DSUs"). Since the value of a DSU increases or decreases with the market price of the common shares, DSUs reflect a philosophy of aligning the interests of directors and executive officers by tying compensation to share price performance. For the three months ended March 31, 2017, no units were issued (2016 – no units issued) for payment

of directors' fees. The Company has reserved for issuance up to 2,000,000 common shares under the DSU Plan and 423,676 DSUs were outstanding as at March 31, 2017 (2016 – 74,556).

### **Commitments**

As at March 31, 2017 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 \$47,776 over the next 12 months and \$23,633 from 13-24 months. The Company's largest commitment is with the leasing company for DiaMedica's U.S. office. As at March 31, 2017, the Company has future commitments totaling \$48,781 to this company.

The Company enters into research and 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 development 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, 2017 and 2016 was as follows:

	2017	2016
		As restated note 2(c)
	\$	\$
Salaries, fees, and short-term benefits	174,961	87,790
Share-based compensation	38,696	48,892
	213,657	136,682

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, 2017, the key management personnel control 3.0% (2016 – 4.1%) 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 unaudited condensed consolidated interim financial statements as at March 31, 2017 and 2016 relate to accrued bonuses, vacation payable, and accounts payable. There have been no guarantees provided or received for any related party 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 National Instrument 52-109 – *Certification of Disclosure in Issuers' Annual and Interim Filings*, 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 and valuation of share-based compensation and warrants as follows:

### ***Functional currency***

The functional currency of the Company is the CAD\$. The functional currency determination was conducted through an analysis of the consideration factors identified in IAS 21, *The Effects of Changes in Foreign Exchange Rates*. During the fourth quarter of 2016, the Company has adopted the USD\$ as the presentation currency for the consolidated entity to better reflect the total business activities of its entities and improves investors' ability to compare our total financial results with other publicly traded businesses in our industry (most of which are based in the United States and report in USD\$).

### ***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, 2016 and have been applied consistently to all periods presented in the annual audited consolidated financial statements.

During the fourth quarter of 2016, the Company has adopted the USD\$ as the presentation currency for the consolidated entity to better reflect the total business activities of its entities and improves investors' ability to compare the Company's total financial results with other publicly traded businesses in the Company's industry (most of which

are based in the United States and report in USD\$). Information regarding the change in presentation currency can be found in note 3(b) of the annual audited consolidated financial statements as at December 31, 2016 and 2015.

### *New standards and interpretations adopted*

#### *IAS 7, Disclosure Initiative ("IAS 7")*

Amendments to IAS 7 require disclosures that enable users of financial statements to evaluate changes in liabilities arising from financing activities, including both changes arising from cash flow and non-cash changes. The amendments apply prospectively for annual periods beginning on or after January 1, 2017. The adoption of these amendments were not material to these condensed consolidated interim financial statements.

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

#### *IFRS 2, Share Based Payments ("IFRS 2")*

The amendments to IFRS 2 provide clarification on how to account for certain types of share-based payment transactions. The amendments provide requirements on the accounting for: the effects of vesting and non-vesting conditions on the measurement of cash-settled share-based payments; share-based payment transactions with a net settlement feature for withholding tax obligations; and a modification to the terms and conditions of a share-based payment that changes the classification of the transaction from cash-settled to equity-settled. The amendments apply for annual periods beginning on or after January 1, 2018. As a practical simplification, the amendments can be applied prospectively. Retrospective, or early, application is permitted if information is available without the use of hindsight. The extent of the impact of adoption of the amendments on the unaudited condensed consolidated interim financial statements has not yet been determined.

#### *IFRS 9, Financial Instruments ("IFRS 9")*

IFRS 9 which replaces IAS 39, *Financial Instruments: Recognition and Measurement* establishes principles for the financial reporting of financial assets and financial liabilities that will present relevant and useful information to users of financial statements for their assessment of the amounts, timing and uncertainty of an entity's future cash flows. Under IFRS 9, financial assets are classified and measured based on the business model in which they are held and the characteristics of their cash flows. In addition, under IFRS 9 for financial liabilities measured at fair value, changes in fair value attributable to changes in credit risk will be recognized in other comprehensive income, with the remainder of the changes recognized in profit or loss. However, if this requirement creates or enlarges an accounting mismatch in profit or loss, the entire change in fair value will be recognized in profit or loss. This new standard is effective for annual periods beginning on or after January 1, 2018. Early adoption is permitted. The extent of the impact of adoption of the amendments on the unaudited condensed consolidated interim financial statements has not yet been determined.

#### *IFRS 15, Revenue from Contracts with Customers ("IFRS 15")*

IFRS 15 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 extent of the impact of adoption of the standard on the unaudited condensed consolidated interim financial statements has not yet been determined.

IFRS 16, *Leases* (“IFRS 16”)

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 on the unaudited condensed consolidated interim financial statements has not yet been determined.

## 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.

	Q1-2017	Q4-2016	Q3-2016	Q2-2016	Q1-2016	Q4-2015	Q3-2015	Q2-2015
Revenue	<i>nil</i>	<i>nil</i>	<i>nil</i>	<i>nil</i>	<i>nil</i>	<i>nil</i>	<i>nil</i>	<i>nil</i>
Net loss for the period	\$1,308,903	\$441,862	\$936,289	\$513,298	\$331,695	\$553,474	\$250,333	\$337,180
Loss per share	\$0.01	\$0.03	\$0.01	\$0.01	\$0.01	\$0.02	\$0.00	\$0.01
Cash	\$938,520	\$1,736,361	\$2,970,678	\$363,229	\$333,671	\$166,134	\$140,874	\$455,372

Research and development and general and administrative for 2015 decreased due mainly to cost containment plans implemented during fourth quarter 2014. Research and development increased in the fourth quarter of 2015, and in subsequent periods as the Company proceeded to implement plans to refocus efforts in AIS and DN. In Q3 2016 and Q1 2017, the net loss for the period increased as a result of the DM199 clinical trial program.

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 Our Financial Position and Need for Additional Capital**

*We expect to incur future losses and may never become profitable.*

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, 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, 2017 of over \$48 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.

*We will require additional funds to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of our product candidates or develop new product candidates.*

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.

*We currently have no product revenue and will not be able to maintain our operations and research and development without additional funding.*

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.

*We are exposed to the financial risk related to the fluctuation of foreign exchange rates and the degrees of volatility of those rates.*

We may be adversely affected by foreign currency fluctuations. To date, we have been primarily funded through issuances of equity and proceeds from the exercise of warrants and stock options, which are all denominated both in Canadian and U.S. dollars. Also, a portion of our expenditures are in US dollars, euros, and Australian dollars, 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 our Business and our Industry

*Our prospects depend on the success of our product candidates which are at early stages of development, and we may not generate revenue for several years, if at all, from those products.*

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.

*We rely and will continue to rely on third parties to plan, conduct, and monitor our preclinical and clinical trials, and their failure to perform as required could cause substantial harm to our business.*

We rely and will continue to rely on third parties to conduct a significant portion of our preclinical and clinical development activities. Preclinical activities include *in vivo* studies providing access to specific disease models, pharmacology and toxicology studies, and assay development. Clinical development activities include trial design, regulatory submissions, clinical patient recruitment, clinical trial monitoring, clinical data management and analysis, safety monitoring, and project management. If there is any dispute or disruption in our relationship with third parties, or if they are unable to provide quality services in a timely manner and at a feasible cost, our active development programs may face delays. Further, if any of these third parties fails to perform as we expect or if their work fails to meet regulatory requirements, our testing could be delayed, cancelled, or rendered ineffective.

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

We rely on contract manufacturing organizations (“CMOs”) to manufacture our product candidates for our preclinical studies and clinical trials. We rely on CMOs for manufacturing, filling, packaging, storing, and shipping of drug product in compliance with current Good Manufacturing Practice (“cGMP”) regulations applicable to our products. The FDA ensures the quality of drug products by carefully monitoring drug manufacturers’ compliance with cGMP regulations. The cGMP regulations for drugs contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product.

There can be no assurances that CMOs will be able to meet our timetable and requirements. If we are unable to arrange for alternative third-party manufacturing sources on commercially reasonable terms or in a timely manner, we may be delayed in the development of our product candidates. Further, contract manufacturers must operate in compliance with cGMP and failure to do so could result in, among other things, the disruption of product supplies. Our dependence upon third parties for the manufacture of our products may adversely affect our profit margins and our ability to develop and deliver products on a timely and competitive basis.

*If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we would incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.*

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct preclinical studies in animals and extensive clinical trials in humans to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive and difficult to design and implement, can take many years to complete, and has uncertain outcomes. The outcome of preclinical studies and early clinical trials may not predict the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials. We do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any of our product candidates in any jurisdiction. A product candidate may fail for safety or efficacy reasons at any stage of the testing process. A major risk we face is the possibility that none of our product candidates under development will successfully gain market approval from the FDA or other regulatory authorities, resulting in us being unable to derive any commercial revenue from them after investing significant amounts of capital in multiple stages of preclinical and clinical testing.

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

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

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

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

*We may not be able to file INDs to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed in a timely manner, or at all.*

Prior to commencing clinical trials in the United States for any of our product candidates, we may be required to have an allowed IND for each product candidate and to file additional INDs prior to initiating any additional clinical trials for DM199. We believe that the data from previous preclinical studies will support the filing of additional INDs, to enable us to undertake additional clinical studies as we have planned. However, submission of an IND may not result in the FDA allowing further clinical trials to begin and, once begun, issues may arise that will require us to suspend or terminate such clinical trials. Additionally, even if relevant regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, these regulatory authorities may change their requirements in the future. Failure to submit or have effective INDs and commence clinical programs will significantly limit our opportunity to generate revenue.

*If we have difficulty enrolling patients in clinical trials, the completion of the trials may be delayed or cancelled.*

As our product candidates advance from preclinical testing to clinical testing, and then through progressively larger and more complex clinical trials, we will need to enroll an increasing number of patients that meet our eligibility criteria. There is significant competition for recruiting stroke patients in clinical trials, and we may be unable to enroll the patients we need to complete clinical trials on a timely basis or at all. The factors that affect our ability to enroll patients are largely uncontrollable and include, but are not limited to, the following:

- size and nature of the patient population;
- eligibility and exclusion criteria for the trial;
- design of the study protocol;
- competition with other companies for clinical sites or patients;
- the perceived risks and benefits of the product candidate under study;
- the patient referral practices of physicians; and
- the number, availability, location, and accessibility of clinical trial sites.

*Regulatory approval processes are lengthy, expensive, and inherently unpredictable. Our inability to obtain regulatory approval for our product candidates would substantially harm our business.*

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.

***We may not achieve our publicly announced milestones according to schedule, or at all.***

From time to time, we may announce the timing of certain events we expect to occur, such as the anticipated timing of results from our clinical trials. These statements are forward-looking and are based on the best estimates of management at the time relating to the occurrence of such events. However, the actual timing of such events may differ from what has been publicly disclosed. The timing of events such as initiation or completion of a clinical trial, filing of an application to obtain regulatory approval, or announcement of additional clinical trials for a product candidate may ultimately vary from what is publicly disclosed. These variations in timing may occur as a result of different events, including the nature of the results obtained during a clinical trial or during a research phase, problems with a CMO or a CRO or any other event having the effect of delaying the publicly announced timeline. We undertake no obligation to update or revise any forward-looking information, whether as a result of new information, future events or otherwise, except as otherwise required by law. Any variation in the timing of previously announced milestones could have a material adverse effect on our business plan, financial condition or operating results, and the trading price of common shares.

***We face competition from other biotechnology and pharmaceutical companies and our financial condition and operations will suffer if we fail to effectively compete.***

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.

***We heavily rely on the capabilities and experience of our key executives and scientists and the loss of any of them could affect our ability to develop our products.***

We depend on our management personnel. We also depend on our scientific and clinical collaborators and advisors, all of whom have outside commitments that may limit their availability to us. In addition, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled scientific, managerial, medical, clinical, and regulatory personnel, particularly as we expand our activities and seek regulatory approvals for clinical trials. We enter into agreements with our scientific and clinical collaborators and advisors, key opinion leaders, and academic partners in the ordinary course of our business. We also enter into agreements with physicians and institutions who will recruit patients into our clinical trials on our behalf in the ordinary course of our business. Notwithstanding these arrangements, we face significant competition for these types of personnel from other companies, research and academic institutions, government entities and other organizations. We cannot predict our

success in hiring or retaining the personnel we require for continued growth. The loss of the services of any of our executive officers or other key personnel could potentially harm our business, operating results, or financial condition

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state health-care fraud and abuse laws and regulations, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a substantial impact on our business and results of operations, including the imposition of substantial fines or other sanctions.

***We may expand our business through the acquisition of companies or businesses or by entering into collaborations or by in-licensing product candidates, each of which could disrupt our business and harm our financial condition.***

We have in the past and may in the future seek to expand our pipeline and capabilities by acquiring one or more companies or businesses, entering into collaborations, or in-licensing one or more product candidates. Acquisitions, collaborations and in-licenses involve numerous risks, including, but not limited to:

- substantial cash expenditures;
- technology development risks;
- potentially dilutive issuances of equity securities;
- incurrence of debt and contingent liabilities, some of which may be difficult or impossible to identify at the time of acquisition;
- difficulties in assimilating the operations of the acquired companies;
- potential disputes regarding contingent consideration;
- diverting our management's attention away from other business concerns;
- entering markets in which we have limited or no direct experience; and
- potential loss of our key employees or key employees of the acquired companies or businesses.

We have experience in making acquisitions, entering collaborations, and in-licensing product candidates, however, we cannot provide assurance that any acquisition, collaboration, or in-license will result in short-term or long-term benefits to us. We may incorrectly judge the value or worth of an acquired company or business or in-licensed product candidate. In addition, our future success would depend in part on our ability to manage the rapid growth associated with some of these acquisitions, collaborations and in-licenses. We cannot provide assurance that we would be able to successfully combine our business with that of acquired businesses, manage a collaboration or integrate in-licensed product candidates. Furthermore, the development or expansion of our business may require a substantial capital investment by us.

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

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

development of our product candidates, and our business and financial results could be materially and adversely affected.

*We may not be able to reproduce the results of previously conducted clinical studies and/or comparisons to other forms of KLK1, including Kailikang<sup>®</sup>, thereby displacing other forms of KLK1, including Kailikang<sup>®</sup>.*

The Company intends to conduct clinical trials to determine the pharmacokinetic and pharmacodynamic profile of Kailikang<sup>®</sup> compared to DM199. While there have been numerous studies demonstrating the efficacy of Kailikang<sup>®</sup>, 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 or displace other forms of KLK1 in the market.

*We face the risk of product liability claims, which could exceed our insurance coverage and produce recalls, each of which could deplete our cash resources.*

We are exposed to the risk of product liability claims alleging that use of our product candidates caused an injury or harm. These claims can arise at any point in the development, testing, manufacture, marketing, or sale of our product candidates and may be made directly by patients involved in clinical trials of our product candidates, by consumers or healthcare providers, or by individuals, organizations, or companies selling our products. Product liability claims can be expensive to defend, even if the product or product candidate did not actually cause the alleged injury or harm.

Insurance covering product liability claims becomes increasingly expensive as a product candidate moves through the development pipeline to commercialization. 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. However, there can be no assurance that such insurance coverage is or will continue to be adequate or available to us at a cost acceptable to us or at all. We may choose or find it necessary under our collaborative agreements to increase our insurance coverage in the future. We may not be able to secure greater or broader product liability insurance coverage on acceptable terms or at reasonable costs when needed. Any liability for damages resulting from a product liability claim could exceed the amount of our coverage, require us to pay a substantial monetary award from our own cash resources and have a material adverse effect on our business, financial condition, and results of operations. Moreover, a product recall, if required, could generate substantial negative publicity about our products and business, inhibit or prevent commercialization of other products and product candidates, or negatively impact existing or future collaborations.

*If we are unable to maintain product liability insurance required by our third parties, the corresponding agreements would be subject to termination, which could have a material adverse impact on our operations.*

Some of our licensing and other agreements with third parties require or might require us to maintain product liability insurance. If we cannot maintain acceptable amounts of coverage on commercially reasonable terms in accordance with the terms set forth in these agreements, the corresponding agreements would be subject to termination, which could have a material adverse impact on our operations.

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.

### Risks Related to Intellectual Property

*If we are unable to adequately protect and enforce our intellectual property, our competitors may take advantage of our development efforts or acquired technology and compromise our prospects of marketing and selling our key products.*

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.

*We may require additional third-party licenses to effectively develop and manufacture our key products and are currently unable to predict the availability or cost of such licenses.*

A substantial number of patents have already been issued to other biotechnology and pharmaceutical companies. To the extent that valid third-party patent rights cover our products or services, we or our strategic collaborators would be required to seek licenses from the holders of these patents in order to manufacture, use, or sell these products and services, and payments under them would reduce our profits from these products and services. We are currently unable to predict the extent to which we may wish or be required to acquire rights under such patents, the availability and cost of acquiring such rights, and whether a license to such patents will be available on acceptable terms, or at all. There may be patents in the U.S. or in foreign countries or patents issued in the future that are unavailable to license on acceptable terms. Our inability to obtain such licenses may hinder or eliminate our ability to manufacture and market our products.

*Changes in patent law and its interpretation could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.*

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property rights, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time consuming, and inherently uncertain. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our and our licensors' or collaborators' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the U.S. Patent and Trademark Office (USPTO), the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensors' or collaborators' ability to obtain new patents or to enforce existing patents and patents we and our licensors or collaborators may obtain in the future.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents, all of which could have a material adverse effect on our business and financial condition.

*Litigation regarding patents, patent applications, and other proprietary rights may be expensive, time consuming and cause delays in the development and manufacturing of our key products.*

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.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them.***

Because we rely on third parties to develop our products, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically restrict the ability of our collaborators, advisors, employees, and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs which may require us to share trade secrets under the terms of research and development collaboration or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development, or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets may impair our competitive position and could have a material adverse effect on our business and financial condition.

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

***Our common share price has been volatile in recent years, and may continue to be volatile.***

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.

***We have never paid dividends and do not expect to do so in the foreseeable future.***

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.

***We may issue additional common shares resulting in share ownership 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.

***It may be difficult for non-Canadian investors to obtain and enforce judgments against us because of our Canadian incorporation and presence.***

We are a corporation existing under the laws of Canada. Several of our directors and officers, and several of the experts are residents of Canada, and all or a substantial portion of their assets, and a substantial portion of our assets, are located outside the United States. Consequently, it may be difficult for holders of our securities who reside in the United States to effect service within the United States upon those directors and officers, and the experts who are not residents of the United States. It may also be difficult for holders of our securities who reside in the United States to realize in the United States upon judgments of courts of the United States predicated upon our civil liability and the civil liability of our directors, officers, and experts under the United States federal securities laws. Investors should not assume that Canadian courts (i) would enforce judgments of United States courts obtained in actions against us or such directors, officers, or experts predicated upon the civil liability provisions of the United States federal securities laws or the securities or “blue sky” laws of any state or jurisdiction of the United States, or (ii) would enforce, in original actions, liabilities against us or such directors, officers, or experts predicated upon the United States federal securities laws or any securities or “blue sky” laws of any state or jurisdiction of the United States. In addition, the protections afforded by Canadian securities laws may not be available to investors in the United States.

***If there are substantial sales of our common shares, the market price of our common shares could decline.***

Sales of substantial numbers of our common shares could cause a decline in the market price of our common shares. Any sales by existing shareholders or holders who exercise their warrants or stock options may have an adverse effect on our ability to raise capital and may adversely affect the market price of our common shares.

***Any failure to maintain an effective system of internal controls may result in material misstatements of our consolidated financial statements or cause us to fail to meet our reporting obligations or fail to prevent fraud; and in that case, our shareholders could lose confidence in our financial reporting, which would harm our business and could negatively impact the price of our common shares.***

Effective internal controls are necessary for us to provide reliable financial reports and prevent fraud. If we fail to maintain an effective system of internal controls, we might not be able to report our financial results accurately or prevent fraud; and in that case, our shareholders could lose confidence in our financial reporting, which would harm our business and could negatively impact the price of our common shares. 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. Even if we conclude that our internal control over financial reporting provides reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with IFRS as issued by the IASB, because of its inherent limitations, internal control over financial reporting may not prevent or detect fraud or misstatements. Failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our results of operations or cause us to fail to meet our future reporting obligations.

If we fail to timely achieve and maintain the adequacy of our internal control over financial reporting, we may not be able to produce reliable financial reports or help prevent fraud. Our failure to achieve and maintain effective internal control over financial reporting could prevent us from complying with our reporting obligations on a timely basis, which could result in the loss of investor confidence in the reliability of our consolidated financial statements, harm our business and negatively impact the trading price of our common shares.

***We are likely a “passive foreign investment company,” which may have adverse U.S. federal income tax consequences for U.S. shareholders.***

U.S. investors should be aware that we believe we were classified as a passive foreign investment company, or PFIC, during the tax years ended December 31, 2016 and 2015, and based on current business plans and financial expectations, we expect that we will be a PFIC for the current tax year and may be a PFIC in future tax years. If we are a PFIC for any year during a U.S. shareholder’s holding period of our common shares, then such U.S. shareholder

generally will be required to treat any gain realized upon a disposition of our common shares, or any so-called “excess distribution” received on our common shares, as ordinary income, and to pay an interest charge on a portion of such gain or distributions, unless the shareholder makes a timely and effective “qualified electing fund” election, or QEF Election, or a “mark-to-market” election with respect to our shares. A U.S. shareholder who makes a QEF Election generally must report on a current basis its share of our net capital gain and ordinary earnings for any year in which we are a PFIC, whether or not we distribute any amounts to our shareholders. A U.S. shareholder who makes the mark-to-market election generally must include as ordinary income each year the excess of the fair market value of the common shares over the shareholder’s adjusted tax basis therein. However, U.S. shareholders should be aware that there can be no assurance that the Company will satisfy the record keeping requirements that apply to a qualified electing fund, or that the Company will supply U.S. shareholders with information that such U.S. shareholders require to report under the QEF Election rules, in the event the Company is a PFIC and a U.S. shareholder wishes to make a QEF Election. Thus, U.S. shareholders may not be able to make a QEF Election with respect to their common shares. Each U.S. shareholder should consult its own tax advisors regarding the PFIC rules and the U.S. federal income tax consequences of the acquisition, ownership and disposition of our common shares.

### **Additional Information**

Additional information relating to the Company, including its Annual Information Form can be found on SEDAR at [www.sedar.com](http://www.sedar.com).