

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT  
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 5, 2020

DIAMEDICA THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

British Columbia  
(State or other jurisdiction  
of incorporation)

Two Carlson Parkway, Suite 260  
Minneapolis, Minnesota  
(Address of principal executive offices)

001-36291  
(Commission  
File Number)

(763) 312-6755

(Registrant's telephone number, including area code)

Not Applicable  
(IRS Employer  
Identification No.)

55447  
(Zip Code)

Not Applicable

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)  
 Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)  
 Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))  
 Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Voting common shares, no par value per share	DMAC	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

## **Item 2.02 Results of Operations and Financial Condition.**

On August 5, 2020, DiaMedica Therapeutics Inc. (the Company) filed with the United States Securities and Exchange Commission (the SEC) a preliminary prospectus supplement (the Preliminary Prospectus Supplement) in connection with a proposed public offering of the Company's voting common shares, no par value per share (the Public Offering). The Preliminary Prospectus Supplement contains certain preliminary unaudited financial information of the Company and its subsidiaries as of and for the three and six months ended June 30, 2020. The preliminary unaudited financial information is furnished in Exhibit 99.1 to this Current Report on Form 8-K, which is incorporated by reference into this Item 2.02 of this report.

The information contained in Item 2.02 of this report and Exhibit 99.1 to this report shall not be deemed to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (Exchange Act), and shall not be incorporated by reference into any filings made by the Company under the Securities Act of 1933, as amended (Securities Act), or the Exchange Act, except as may be expressly set forth by specific reference in such filing.

### **Item 8.01 Other Events.**

As noted above, on August 5, 2020, in connection with the Public Offering, the Company filed the Preliminary Prospectus Supplement to its shelf registration statement on Form S-3 (File No. 333-235775), which became effective on January 9, 2020, pursuant to Rule 424(b) under the Securities Act. In addition to certain preliminary unaudited financial information of the Company and its subsidiaries as of and for the three and six months ended June 30, 2020 referred to in Item 2.02 above, the Company included updated summary business information and certain updated risk factor disclosure in the Preliminary Prospectus Supplement. The updated summary business information and certain updated risk factor disclosure are filed as Exhibits 99.2 and 99.3, respectively, to this report and are incorporated herein by reference.

In addition, the Company disclosed in the Preliminary Prospectus Supplement that it intends to use a portion of the net proceeds of the Public Offering, if completed, to add a new third cohort III to its REDUX trial to be comprised of participants with Type II diabetes mellitus with chronic kidney disease (CKD), hypertension and albuminuria, in addition to the two current cohorts. The Phase II trial named REDUX, Latin for restore, is a multi-center, open-label investigation of approximately 60 participants with CKD, who are being enrolled in two cohorts (30 per cohort). The study is being conducted in the United States at up to 10 sites and is focused on participants with two specific causes of CKD. Cohort I of the study is focused on non-diabetic, hypertensive African Americans with Stage II or III CKD. African Americans are at greater risk for CKD than Caucasians, and those who have the APOL1 gene mutation are at an even higher risk. The study is designed to capture the APOL1 gene mutation as an exploratory biomarker in this cohort. Cohort II of the study is focused on participants with IgA Nephropathy (IgAN). The proposed cohort III of the study is also intended to enroll 30 participants, raising the total REDUX trial target enrollment to 90 participants. The study is evaluating two dose levels of the DM199 product candidate within each cohort. Study participants will receive DM199 by subcutaneous injection twice weekly for 95 days. The primary study endpoints include safety, tolerability, blood pressure, albuminuria and kidney function, which will be evaluated by changes from baseline in estimated glomerular flow rate and albuminuria, as measured by the urinary albumin to creatinine ratio.

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As part of the updated business summary information, the Company disclosed in the Preliminary Prospectus Supplement that, as of August 5, 2020, the Company had enrolled 18 subjects, including 7 African American subjects into cohort I and 11 subjects with IgAN into cohort II of the REDUX study. Due to actions implemented to combat the novel strain of the coronavirus, or COVID-19, pandemic, the Company has experienced and continues to experience slower than expected enrollment in the REDUX clinical trial related to the reduction or suspension of activities at its clinical study sites as they address staff and patient safety concerns. The Company anticipates that the COVID-19 pandemic will likely continue to adversely affect the Company's ability to recruit or enroll subjects and it cannot provide any assurance as to when all sites will be able to resume enrollment or any guidance at this time as to when it will complete enrollment in the study. While results observed to date in the REDUX study indicate a safety profile consistent with past studies, there is insufficient data at this time for the Company to evaluate or comment upon efficacy.

This report, including the exhibits hereto, shall not constitute an offer to sell or the solicitation of an offer to buy any securities of the Company, which is being made only by means of a written prospectus meeting the requirements of Section 10 of the Securities Act, nor shall there be any sale of the Company's securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of such jurisdiction.

**Item 9.01 Financial Statements and Exhibits.**

(d) *Exhibits.*

<b>Exhibit No.</b>	<b>Description</b>
99.1	<a href="#">Updated Financial Information (furnished herewith)</a>
99.2	<a href="#">Updated Business Disclosure (filed herewith)</a>
99.3	<a href="#">Updated Risk Factor Disclosure (filed herewith)</a>

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**DIAMEDICA THERAPEUTICS INC.**

By: /s/ Scott Kellen  
Scott Kellen  
Chief Financial Officer and Secretary

Dated: August 5, 2020

## Updated Financial Information

Our consolidated financial statements as of and for the three and six months ended June 30, 2020 are not expected to be available until after this offering is completed. Our preliminary research and development expense for the three and six months ended June 30, 2020 and cash, cash equivalents and marketable securities balance as of June 30, 2020 are set forth below. This financial information has been prepared by and is the responsibility of our management. Our independent registered public accounting firm has not audited, reviewed or performed any procedures with respect to this preliminary financial data or the accounting treatment thereof and does not express an opinion or any other form of assurance with respect thereto. We expect to announce our full financial results for the three and six months ended June 30, 2020 subsequent to the completion of this offering. While we are currently unaware of any items that would require us to make adjustments to the financial information set forth below, it is possible that we or our independent registered public accounting firm may identify such items as we finalize our unaudited financial statements, and any resulting changes could be material. Accordingly, undue reliance should not be placed on these preliminary estimates. These preliminary estimates are not necessarily indicative of any future period and should be read together with “Risk Factors,” “Cautionary Note Regarding Forward-Looking Statements,” and our consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

(in thousands)	<b>Three Months Ended June 30, 2020</b>	<b>Six Months Ended June 30, 2020</b>
Research and development expense	\$ 1,629	\$ 3,010
	<b>June 30, 2020</b>	
Cash and cash equivalents	\$ 4,955	
Marketable securities		6,844
Total cash and cash equivalents and marketable securities	\$ 11,799	

## Updated Summary Business Information

### Our Company

We are a clinical stage biopharmaceutical company primarily focused on the development of novel recombinant, or synthetic, proteins. Our goal is to use our patented and licensed technologies to establish our company as a leader in the development and commercialization of therapeutic treatments from novel recombinant proteins. Our current focus is on chronic kidney disease (CKD) and acute ischemic stroke (AIS). We plan to advance DM199, our lead drug candidate, through required clinical trials to create shareholder value by establishing its clinical and commercial potential as a therapy for CKD and AIS.

DM199 is a recombinant form of human tissue kallikrein-1 (KLK1). KLK1 is a serine protease (protein), produced primarily in the kidneys, pancreas and salivary glands, which plays a critical role in the regulation of local blood flow and vasodilation (the widening of blood vessels which decreases blood pressure) in the body, as well as an important role in inflammation and oxidative stress (an imbalance between potentially damaging reactive oxygen species, or free radicals, and antioxidants in the body). We believe DM199 has the potential to treat a variety of diseases where healthy functioning requires sufficient activity of KLK1 and its system, the kallikrein-kinin system (KKS).

CKD and AIS patients suffer from impaired blood flow to the kidneys and brain, respectively. These patients also tend to exhibit lower than normal levels of endogenous (produced by the body) KLK1. We believe treatment with DM199 could replenish levels of KLK1, thereby allowing the natural function of KKS to release bradykinin in the body where and when needed, generating beneficial nitric oxide and prostacyclin, setting in motion metabolic pathways that can improve blood flow (through vasoregulation), dampen inflammation and protect tissues and end-organs from ischemic damage, supporting structural integrity and normal functioning.

Today, forms of KLK1 derived from human urine and porcine pancreas are sold in Japan, China and Korea to treat AIS, CKD, retinopathy, hypertension and related vascular diseases. We believe millions of patients have been treated with these KLK1 therapies and the data from more than 100 published papers and studies support their clinical benefit. However, there are numerous regulatory, commercial and clinical drawbacks associated with KLK1 derived from human urine and porcine pancreas which can be overcome by developing a synthetic version of KLK1 such as DM199. We believe higher regulatory standards are the primary reason why KLK1 derived from human urine and porcine pancreas are not currently available and used in the United States or Europe. We are not aware of any synthetic version of KLK1 with regulatory approval for human use in any country, nor are we aware of any synthetic version in development other than our drug candidate, DM199.

As described in more detail below, positive top-line results from ReMEDy, a 92-subject study in acute ischemic stroke, including the achievement of primary safety and tolerability endpoints and no DM199-related serious adverse events, were announced in May 2020. In addition, there was also a demonstrated therapeutic effect in participants that received tissue plasminogen activator (tPA) prior to enrollment but not in participants receiving mechanical thrombectomy prior to enrollment according to top-line Phase II results.

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We have conducted numerous internal and third-party analyses to evaluate the structural and functional performance of DM199 as compared to KLK1 derived from human urine. The results of these studies have demonstrated that DM199 is structurally and functionally equivalent to KLK1 derived from human urine in that (i) the amino acid structure of DM199 is identical to the human urine form, (ii) the enzymatic and pharmacokinetic profiles are substantially similar to human urinary derived KLK1 and (iii) the physiological effects of DM199 on blood pressure mirror that of human urinary derived KLK1. We believe that the results of this work suggest that the therapeutic action of DM199 will be the same or better than that of the forms of KLK1 marketed in Asia. In addition, we have completed enrollment in seven clinical trials with DM199 treating over 200 subjects, and the results have shown that DM199 has been safe and well-tolerated. However, DM199 has not been, and we cannot provide any assurance that it ultimately will be, determined to be safe or effective for purposes of granting marketing approval by the U.S. Food and Drug Administration (FDA) or any comparable agency.

Our recombinant form of DM199 is protected by issued composition of matter and delivery patents in the United States and Europe (expiration 2033); a pending worldwide patent (expiration 2038) that covers a range of DM199 dose levels and dosing regimens useful for treating a wide range of diseases associated with microvascular dysfunction; an exclusive license with our manufacturing partner for use of their cell line and proprietary expression system for manufacturing synthetic KLK1; and numerous trade-secrets. In addition, we believe DM199 cannot be reverse engineered to develop a copycat version of our therapy. This adds additional protection to our intellectual property, especially as we evaluate DM199 licensing.

### Our Programs

The primary focus for our DM199 program development is currently on CKD and AIS. The current status of our product candidates in clinical development is as follows:

PROGRAM	THERAPEUTIC INDICATIONS	DEVELOPMENT STAGE			
		PRE-CLINICAL	PHASE I	PHASE II	PHASE III
DM199 KIDNEY DISEASE	IgA Nephropathy (IgAN)	<i>REDUX Study</i>			
	African Americans with CKD (APOL1) <sup>1</sup>	<i>REDUX Study</i>			
	Diabetic Kidney Disease (DKD) <sup>2</sup>	<i>REDUX Study</i>			
DM199 STROKE	Acute Ischemic Stroke	<i>REMEDY Study - completed</i>			

1. Due to the heightened risk of African Americans with the APOL1 genetic mutation to progress to end-stage renal disease, participants in this cohort will be tested for the presence of the APOL1 genetic mutation.
2. Initiation of this cohort and development for this indication is contingent upon successful completion of this offering.

### ***Chronic Kidney Disease***

CKD is a widespread health problem that generates significant economic burden throughout the world. According to the National Kidney Foundation, approximately 30 million Americans and 120 million Chinese suffer from this debilitating and potentially life-threatening condition. CKD is characterized by a progressive decline in overall kidney function, increasing the risk of premature death, cardiovascular events and hospitalization. End-stage renal disease (ESRD) is the final stage of CKD and requires ongoing dialysis or a kidney transplant to survive. However, many patients suffer serious health consequences or die from CKD prior to developing ESRD. Currently, there is no cure for CKD and treatment involves management of the symptoms of the disease. Blood pressure medications, such as angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB), are often prescribed to control hypertension, and hopefully, slow the progression of CKD. Nevertheless, according to the National Kidney Foundation, many of these patients continue to show declining kidney function. We believe DM199 offers a potentially novel approach for the treatment of CKD because KLK1 protein plays a vital role in normal kidney function. Since patients with moderate to severe CKD often excrete abnormally low levels of KLK1 in their urine, we believe that DM199 may prevent or reduce further kidney damage by increasing levels of KLK1 and restoring the protective KKS to regulate the production and release of nitric oxide and prostacyclin.

### ***Acute Ischemic Stroke***

According to the World Health Organization, each year approximately 15 million people worldwide suffer a stroke, of which 5.0 million will die and 5.0 million will be permanently disabled. According to the U.S. Center for Disease Control and Prevention approximately 87% of all strokes are ischemic in nature, a blockage of blood flow in/to the brain. We believe that stroke represents an area of significant unmet medical need and a KLK1 treatment (such as DM199) could provide a significant patient benefit, in particular given its proposed therapeutic window of up to 24 hours after the first sign of symptoms. Currently, the only FDA-approved pharmacological intervention for AIS is tissue plasminogen activator (tPA), which must be given within 4.5 hours of symptom onset. Treating patients with tPA during this time window can be challenging because it is difficult to determine precisely when symptoms began and a patient must undergo complex brain imaging before treatment to rule out a hemorrhagic stroke, a ruptured blood vessel causing bleeding within the brain. Mechanical thrombectomy, a procedure in which the clot is removed using catheter-based tools, is also available to certain patients. Despite the availability of these treatments, we believe they are relevant to approximately 10% of ischemic stroke patients due to the location of the clot, the elapsed time after the stroke occurred or other safety considerations. Thus, we believe DM199 may offer significant advantages over the current treatment options in that it fills a serious, unmet need for patients who cannot receive tPA or mechanical thrombectomy. Additionally, DM199 may also offer a complimentary follow-on treatment for patients who initially receive tPA or mechanical thrombectomy treatments by enabling sustained blood flow improvements to the brain during the critical weeks and months after a stroke. Based on the number of strokes each year (approximately 1.7 million in the U.S., Europe and Japan and 15 million worldwide) and considering the \$8,500 estimated cost per patient for the current standard of care, tPA, we believe the annual market opportunity for DM199 could be significant.

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## Our Clinical Trials

### *Chronic Kidney Disease*

In July 2019, we completed a Phase Ib clinical trial of DM199 in participants with moderate or severe CKD caused by Type I or Type II diabetes. We initiated dosing patients in this study in February 2019. The study was performed to assess the pharmacokinetics (PK) of three dose levels of DM199 (3, 5 and 8  $\mu\text{g}/\text{kg}$ ), administered in a single subcutaneous dose, as well as the evaluation of safety, tolerability and secondary pharmacodynamic (PD) endpoints. The study results demonstrated that at the 3 $\mu\text{g}/\text{kg}$  dose level, the PK profiles were similar between moderate and severe CKD patients, and consistent with healthy subjects (normal kidney function) tested previously. Additionally, DM199 was well tolerated with no dose-limiting tolerability observed. There were no deaths, no discontinuations due to a treatment-related adverse event (AE) and no treatment-related significant adverse events (SAEs). AEs were minor and consistent with standard treatment(s) in the CKD patient population. We announced favorable overall interim PD results from the first 28 subjects that included short-term improvements in Nitric Oxide (NO), average increase of 35.2%, Prostaglandin E2 (PGE2), average increase of 41.2%, estimated glomerular flow rate (eGFR), average increase of 4.08 mL/min/1.73 $\text{m}^2$ , and the urinary albumin to creatinine ratio (UACR) excluding subjects with normal UACR levels, average decrease of 18.7%. PD results appeared to be drug related in that the greatest improvements occurred approximately 24 hours after DM199 administration and subsequently declined.

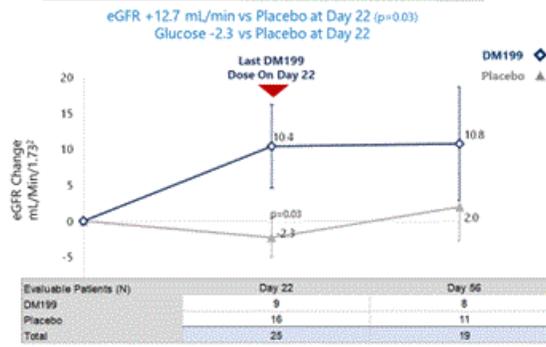
In December 2019, we began enrolling patients in a Phase II CKD trial named REDUX, Latin for restore, a multi-center, open-label investigation of approximately 60 participants with CKD, who are being enrolled in two cohorts (30 per cohort). The study is being conducted in the United States at up to 10 sites and will be focused on participants with two specific causes of CKD. Cohort I of the study is focused on non-diabetic, hypertensive African Americans with Stage II or III CKD. African Americans are at greater risk for CKD than Caucasians, and those who have the APOL1 gene mutation are at an even higher risk. The study is designed to capture the APOL1 gene mutation as an exploratory biomarker in this cohort. Cohort II of the study is focused on participants with IgA Nephropathy (IgAN). The study will evaluate two dose levels of DM199 within each cohort. Study participants will receive DM199 by subcutaneous injection twice weekly for 95 days. The primary study endpoints include safety, tolerability, blood pressure, albuminuria and kidney function, which will be evaluated by changes from baseline in eGFR and albuminuria, as measured by the UACR.

We intend to use a portion of the proceeds from this offering to begin enrollment in a third cohort in the REDUX trial comprised of participants with Type II diabetes mellitus with CKD, hypertension and albuminuria. In a post hoc analysis of endpoints in the ReMEDy trial, discussed below, a sub-set of participants with elevated blood glucose levels ( $>7$  mmol/l) and impaired kidney function (eGFR  $<90$ ) were observed to experience significant (mean +12.7 mL/min,  $p=0.03$ ) improvement in kidney function as measured by the estimated glomerular filtration rate compared to placebo and a trending reduction in blood glucose levels (mean 2.2 mmol/l) compared to placebo. Initiation of this third cohort and development for this indication is contingent upon successful completion of this offering.

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### DM199 FOR DKD FROM PHASE 2 REMEDY AIS STUDY

Post-Hoc Analysis in patients with eGFR < 90 mL/Min & Glucose > 7 mmol at Baseline



1. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193981#Chen> et al. Brain Behav. 2020;10:e01461.

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As of August 5, 2020, we have enrolled 18 subjects, including 7 African American subjects into cohort I and 11 subjects with IgAN into cohort II of the REDUX study. Due to actions implemented to combat the novel strain of the coronavirus (COVID-19) pandemic, we have experienced and continue to experience slower than expected enrollment in the REDUX clinical trial. We believe this is due to the reduction or suspension of activities at our clinical study sites as they address staff and patient safety concerns and patient concerns related to visiting clinical study sites in light of the pandemic. We anticipate that the COVID-19 pandemic will likely continue to adversely affect our ability to recruit or enroll subjects and we cannot provide any assurance as to when clinical sites will be able to resume enrollment at a normal rate or any guidance at this time as to when we will complete enrollment in the study. While results observed to date in the REDUX study indicate a safety profile consistent with past studies, there is insufficient data at this time to evaluate or comment upon efficacy.

#### Acute Ischemic Stroke

In May 2020, we announced top-line data from our Phase II ReMEDY trial assessing the safety, tolerability and markers of therapeutic efficacy of DM199 in patients suffering from AIS. We initiated treatment in this study in February 2018 and completed enrollment in October 2019 with 92 participants. The study drug (DM199 or placebo) was administered as an intravenous (IV) infusion within 24 hours of stroke symptom onset, followed by subcutaneous injections later that day and once every 3 days for 21 days. The study was designed to measure safety and tolerability along with multiple tests designed to investigate DM199's therapeutic potential including plasma-based biomarkers and standard functional stroke measures assessed at 90 days post-stroke. Standard functional stroke measurements include the Modified Rankin Scale, National Institutes of Health Stroke Scale, the Barthel Index and C-reactive protein, a measure of inflammation. The study met primary safety and tolerability endpoints and there were no DM199-related serious adverse events. In addition, there was also a demonstrated therapeutic effect in participants that received tPA prior to enrollment but not in participants receiving mechanical thrombectomy prior to enrollment.

Prior to enrollment, 44 of the 91 evaluable patients (48%) received a mechanical thrombectomy, a catheter-based treatment indicated for those who have a large vessel occlusion and can be treated within 6 to 24 hours of the onset of stroke symptoms. While approximately 20% of AIS patients are believed to be eligible for a mechanical thrombectomy, currently only about 5% to 10% receive the treatment due to elapsed time post-stroke or unavailability of the therapy at the hospital where they present. DM199 is intended to treat the approximately 90% of AIS patients who do not receive either mechanical thrombectomy or tPA. Treatment for these patients is limited to palliative therapies. Due to the large volume of participants receiving mechanical thrombectomy prior to enrollment in ReMEDy, and a disproportionate distribution of these participants between the active treatment and placebo groups, DM199 did not produce a therapeutic effect in the overall study analysis.

When participants treated with mechanical thrombectomy are excluded from the study data set, representing the group of participants most closely aligned with the target treatment population for DM199, a positive therapeutic effect was demonstrated. As shown in the table below, when evaluating the participants treated with DM199 (n=25) vs. palliative therapies and/or tPA (n=21), the results showed that 36% of participants receiving DM199 progressed to a full or nearly full recovery at 90 days (NIHSS: 0-1), compared to 14% of participants in the placebo group. This represents a 22% absolute increase in the proportion of participants achieving a full or nearly full recovery. Additionally, subject deaths decreased from 24% in the placebo group to 12% in the active therapy group, a 50% relative reduction.

<b>DM199 vs. Palliative Therapies and/or tPA</b>				
<b>NIHSS Outcomes at 90 Days</b>				
	<b>0-1</b>	<b>2-8</b>	<b>≥ 9</b>	<b>Death</b>
<b>Placebo (n=21)</b>	14%	57%	5%	24%
<b>DM199 (n=24)</b>	36%	36%	16%	12%

In addition, in the evaluable participants (n=91), a significant reduction in the number of participants with severe recurrent stroke was noted in the active treatment group: 1 (2%) patient treated with DM199 vs. 7 (16%) on placebo (p=0.028), with 4 of the 7 resulting in participant death.

Further, in reviewing evaluable participants (n=91), improvements in the following biomarkers were observed in participants treated with DM199, which we believe are consistent with the DM199 mechanism of action:

- Increased NO (+105%) and PGE2 (+54%) were observed at day 22 vs baseline (p<0.05). Placebo group was not statistically significant vs baseline (p>0.05). These changes noted in the active treatment group did not reach statistical significance compared to placebo.
  - Reduction in C-reactive protein (CRP) of (-70%), a blood marker of inflammation, at 90 days. CRP decreased significantly vs. baseline (p<0.05), but was not statistically significant vs. placebo. The change in the placebo group was not statistically significant vs. baseline (p>0.05).
  - Reduction in elevated glucose levels in participants with type 2 diabetes, as defined by a blood glucose level >7 mmol/l (n=14), an average decrease of 1.9 mmol/l (p=0.06) in blood glucose levels of participants on active therapy was observed at day 22. In comparison, participants in the placebo group (n=16) showed an average increase of 0.08 mmol/l (p=0.94) at day 22.
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Changes in the eGFR, a measure of kidney function, were also analyzed in participants with eGFR <70 mL/Min/1.732 at baseline, which indicates the presence of CKD. Participants receiving DM199 exhibited a marked increase in eGFR at days 22 (last dose) and 56 (34 days post-treatment), as shown in the table below. eGFR at day 22 increased by at least 2 mL/Min in 77% of DM199 participants compared to 20% in placebo (p=0.007).

	eGFR Mean Δ from Baseline (mL/Min/1.732)	
	Day 22 (Last Dose)	Day 56 (Off Treatment)
<b>Placebo</b>	+0.84 (n=15)	-0.24 (n=12)
<b>DM199</b>	+7.5 (n=13)	+5.8 (n=12)
<b>Group Difference</b>	<b>+6.6</b>	<b>+6.1</b>

We believe these findings from our Phase II ReMEDy trial, which are consistent with Chinese data on the urine-derived form of KLK1, provide a signal that recombinant human KLK1 appears safe and may have promise as a new tool for physicians who have limited options for the treatment of patients suffering AIS and may also mitigate the adverse impact of ischemic stroke on kidney function.

#### Potential DM199 Commercial Advantages

The growing understanding of KLK1's role in human health and its use in Asia as an approved therapeutic treatment highlights two important potential commercial advantages for DM199:

- KLK1 treatments currently sold in Japan, China and Korea** Research has shown that patients with low levels of KLK1 are associated with a variety of diseases related to vascular dysfunction, such as CKD, AIS, retinopathy and hypertension. Clinical trial data with human urine and porcine derived KLK1 has demonstrated statistically significant clinical benefits in treating a variety of patients with KLK1 compared to placebo. These efficacy results are further substantiated by established markets in Japan, China and Korea for pharmaceutical sales of KLK1 derived from human urine and porcine pancreas. We estimate that millions of patients have been treated with these forms of KLK1 in Asia. Altogether, we believe this supports a strong market opportunity for a synthetic version of KLK1 such as DM199.
  - KLK1 treatment has had limited side effects and has been well tolerated to date** KLK1 is naturally produced by the human body; and, therefore, the body's own control mechanisms act to limit potential side effects. The only notable side effect observed in our clinical trials was orthostatic hypotension, or a sudden drop in blood pressure, which was only seen at doses ten to twenty times higher than our anticipated therapeutic dose levels. Moreover, routine clinical use of KLK1 treatment in Asia we understand has been well-tolerated by patients for several decades. In 2017, we completed a clinical trial comparing the pharmacokinetic profile of DM199 to the human urinary form of KLK1 (Kailikang), which showed DM199, when administered in intravenous form, had a similar pharmacokinetic profile. Further, when DM199 was administered subcutaneously, DM199 demonstrated a longer acting pharmacokinetic profile, superior to the intravenously administered Kailikang and DM199.
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In addition, we believe there are also significant formulation, manufacturing, regulatory and other advantages for our synthetic human KLK1 drug candidate DM199:

- **Potency and Impurity Considerations.** KLK1 derived from human urine or porcine pancreas may contain impurities, endotoxins, and chemical byproducts due to the inherent variability of the isolation and purification process. We believe that this creates the risk of inconsistencies in potency and impurities from one production run to the next. However, we expect to produce a consistent formulation of KLK1 that is free of endotoxins and other impurities.
- **Cost and Scalability.** Large quantities of human urine and porcine pancreas must be obtained to derive a small amount of KLK1. This creates potential procurement, cost and logistical challenges to source the necessary raw material, particularly for human urine sourced KLK1. Once sourced, the raw material is processed using chemicals and costly capital equipment and produces a significant amount of byproduct waste. Our novel recombinant manufacturing process utilizes widely available raw materials and can be readily scaled for commercial production. Accordingly, we believe our manufacturing process will have significant cost and scalability advantages.
- **Regulatory.** We are not aware of any attempts by manufacturers of the urine or porcine based KLK1 products to pursue regulatory approvals in the United States. We believe that this is related to challenges presented by using inconsistent and potentially hazardous biomaterials, such as human urine and porcine pancreas, and their resulting ability to produce a consistent drug product. Our novel recombinant manufacturing process utilizes widely available raw materials which we believe provides a significant regulatory advantage, particularly in regions such as the United States, Europe and Canada, where safety standards are high. In addition, we believe that DM199 could qualify for 12 years of data exclusivity under the Biologics Price Competition and Innovation Act of 2009, which was enacted as part of the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010.

## **Our Strategy**

We aim to become a leader in the discovery, development and commercialization of recombinant proteins for the treatment of severe and life-threatening diseases. To achieve this goal, we are pursuing the following strategies:

- Complete our ongoing Phase II studies for DM199 in CKD patients;
- Commence a Phase III study for DM199 in AIS patients;
- Explore potential new indications for DM199; and
- Leverage our experience and technologies to develop new recombinant therapies and programs.

## **Our Team**

We have assembled a seasoned management team with extensive experience in drug discovery, development and manufacturing. Our Chief Executive Officer, Rick Pauls, MBA, is a successful venture capitalist and formerly the Co-Founder and Managing Director of CentreStone Ventures Inc., a life sciences venture capital fund which made early investments in DiaMedica. Our Chief Medical Officer, Harry Alcorn Jr., Pharm. D, has more than 30 years' experience planning, operating, and executing clinical development programs across a range of diseases including kidney disease, diabetes, and cardiovascular disease, and most recently served as Chief Scientific Officer of DaVita Clinical Research. Our Vice President, Regulatory Affairs, Sydney Gilman, Ph.D., has more than 30 years' experience in drug research, regulatory affairs and quality assurance, including six years as a chemistry reviewer in FDA's Center for Drug Evaluation and Research. Edward Calamai, our consulting head of manufacturing, has over 30 years' experience guiding manufacturing operations, including senior positions at Sensu and Seragen. Dr. Calamai is currently the Managing Partner at PM&C Associates, a company he co-founded in 2001. Our Chief Financial Officer, Scott Kellen, CPA, brings over two decades of operational and corporate finance expertise including an extensive background working with publicly-traded healthcare and biotechnology companies.

### Updated Certain Risk Factor Disclosure

*Investing in our common shares involves a high degree of risk. Before investing in our common shares, you should carefully consider the risks described below, together with all of the other information contained in this prospectus supplement and the accompanying prospectus and incorporated by reference herein and therein, including from our Annual Report on Form 10-K for the year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the period ended March 31, 2020, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC. Some of these factors relate principally to our business and the industry in which we operate. Other factors relate principally to your investment in our securities. The risks and uncertainties described therein and below are not the only risks facing us. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also materially and adversely affect our business and operations.*

#### Risks Related to Our Business and Our Industry

***The recent and ongoing COVID-19 pandemic could significantly disrupt our clinical trials and, therefore, our receipt of necessary regulatory approvals could be delayed or prevented.***

The COVID-19 pandemic is having a severe effect on the clinical trials of many drug candidates. Some trials have been merely delayed, while others have been cancelled. The extent to which the COVID-19 pandemic may impact our ongoing and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration and geographic reach of the outbreak, the severity of COVID-19, and the effectiveness of actions to contain and treat COVID-19. To date, the COVID-19 pandemic has caused significant delays in the enrollment of participants. The continued spread of COVID-19 could cause us to experience additional disruptions that could severely impact our business and clinical trials, including:

- additional delays or difficulties in enrolling and/or retaining participants in our clinical trials;
  - delays or difficulties in the initiation of additional clinical sites in the event that the current clinical sites are unable to recruit sufficient participants or at an acceptable rate;
  - delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in shipping that may affect the transport of clinical trial materials;
  - changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
  - inability of participants to comply with clinical trial protocols, impede participant movement or interrupt healthcare services;
  - interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
  - risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could result in participants dropping out of the trial, missing scheduled doses or follow-up visits or failing to follow protocol or otherwise impact the results of the clinical trial, including by increasing the number of observed adverse events;
  - delays in receiving authorizations from local regulatory authorities to initiate our planned clinical trials;
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- delays in necessary interactions with local regulatory authorities, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

As a result, the expected timeline for data readouts of our clinical trials and certain regulatory filings may be negatively impacted, which would adversely affect our ability to initiate required phase III studies, obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our financial results.

***We have conducted and may in the future conduct clinical trials for our product candidate outside the United States, and the FDA may not accept data from such trials.***

We have conducted and may in the future conduct clinical trials for our product candidate outside the United States. For example, we conducted our ReMEDy Phase II clinical trial in Australia. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data by the FDA is subject to certain conditions, and there can be no assurance that the FDA will accept data from the clinical trial we conducted in Australia or clinical trials we may conduct outside the United States in the future. For example, the clinical trial must be conducted in accordance with good clinical practices (GCP) requirements, and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. In addition, when studies are conducted only at sites outside the United States, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, which would likely require us to conduct additional clinical trials.

If the FDA does not accept data from the clinical trial we conducted in Australia, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay aspects of our business plan, including the development and commercial launch of our DM199 product candidate. In addition, the conduct of clinical trials outside the United States also exposes us to additional risks, including risks associated with the following:

- foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schemes;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment, and storage requirements;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

#### **Risks Related to Our Common Shares and this Offering**

***Our management will have broad discretion and flexibility as to how to use the net proceeds from this offering and may use the net proceeds in ways with which you disagree or which may not prove effective.***

We currently intend to use the net proceeds from this offering as discussed under “Use of Proceeds” in this prospectus supplement. We have not allocated specific amounts of the net proceeds from this offering for any of the purposes set forth in that section. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds of this offering. You will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the net proceeds are being used appropriately. It is possible that the net proceeds will be invested in a way that does not yield a favorable, or any, return for us. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flow.

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***Purchasers of common shares in this offering will experience immediate and substantial dilution in the book value of their investment. You may experience further dilution upon exercise of our outstanding options and warrants.***

The public offering price per common share in this offering is higher than the net tangible book value per common share before giving effect to this offering. Accordingly, if you purchase common shares in this offering, you will incur immediate substantial dilution of approximately \$      per share, representing the difference between the public offering price of \$      per common share, and our as adjusted net tangible book value per share as of March 31, 2020. In addition, if outstanding options or warrants are exercised, you could experience further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section in this prospectus entitled "Dilution."

***Our common share price has been volatile and may continue to be volatile.***

Our common shares trade on the Nasdaq Capital Market under the trading symbol "DMAC." 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 our R&D and clinical activities including the timing of costs for manufacturing DM199 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. As a result of this volatility, you may not be able to sell your common shares at or above the public offering price.

***We do not have a very active trading market for our common shares, and one may never develop.***

Our common shares commenced trading in the United States on the Nasdaq Capital Market in December 2018. Previously our shares traded in Canada on the TSX Venture Exchange. We do not have a very active trading market for our common shares, and one may never develop, even after this offering. Although we anticipate a more active trading market for our shares will develop after this offering, we can give no assurance that this will occur or that an active trading market will be sustained following this offering. If an active market for our common shares does not develop, it may be difficult for you to sell our common shares you purchase in this offering at a favorable price or at all.

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

Future dilution will likely occur due to anticipated future equity issuances by us. To the extent we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our shareholders will be diluted. In addition, as of March 31, 2020, we had outstanding warrants to purchase 255,000 common shares, options to purchase 1,181,309 common shares, deferred share units representing 21,183 common shares and 1,363,700 common shares reserved for future issuance in connection with future grants under the DiaMedica Therapeutics Inc. 2019 Omnibus Incentive Plan. If these or any future outstanding warrants, options, or deferred share units are exercised or otherwise converted into our common shares, our shareholders will experience additional dilution.

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***If there are substantial sales of our common shares or the perception that such sales could occur, the market price of our common shares could decline.***

Sales of substantial numbers of our common shares or the perception that such sales could occur 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.

***We could be subject to securities class action litigation, which is expensive and could divert management attention.***

In the past, securities class action litigation has often been brought against a company following a decline or increase in the market price of its securities or certain significant business transactions. We may become involved in this type of litigation in the future, especially if our clinical trial results are not successful or we enter into an agreement for a significant business transaction. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business. This is particularly true in light of our limited securities litigation insurance coverage.

***If securities or industry analysts do not publish research or reports about our business, or publish negative reports about our business, the market price of our common shares and trading volume could decline.***

The market price and trading volume for our common shares in the United States after this offering will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will continue to cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our common shares or change their opinion of our common shares, the market price of our common shares would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause the market price of our common shares or trading volume to decline.

***We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to us as such may make our common shares less attractive to our shareholders and investors.***

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We may remain an emerging growth company until December 31, 2023, the last day of the fiscal year following the fifth anniversary of our first sale of common shares pursuant to a registration statement under the Securities Act of 1933, as amended (the Securities Act) or until such earlier time as we have more than \$1.07 billion in annual revenue, the market value of our common shares held by non-affiliates is more than \$700 million or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (Section 404) not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a non-binding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. Our shareholders and other investors may find our common shares less attractive as a result of our reliance on these exemptions. If some of our shareholders or other investors find our common shares less attractive as a result, there may be a less active trading market for our common shares, and the trading price of our common shares may be more volatile.

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We are also a “smaller reporting company” under the federal securities laws and, as such, are subject to scaled disclosure requirements afforded to such companies. For example, as a smaller reporting company, we are subject to reduced executive compensation disclosure requirements.

Our shareholders and investors may find our common shares less attractive as a result of our status as an “emerging growth company” and “smaller reporting company” and our reliance on the reduced disclosure requirements afforded to these companies. If some of our shareholders or investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and the market price of our common shares may be more volatile.

***Our inability to comply with Nasdaq’s continued listing requirements could result in our common shares being delisted, which could affect the market price and liquidity of our common shares and reduce our ability to raise capital.***

We are required to meet certain qualitative and financial tests to maintain the listing of our common shares on the Nasdaq Capital Market. If we do not maintain compliance with Nasdaq’s continued listing requirements within specified periods and subject to permitted extensions, our common shares may be recommended for delisting (subject to any appeal we would file). No assurance can be provided that we will comply with these continued listing requirements. If our common shares were delisted, it could be more difficult to buy or sell our common shares and to obtain accurate quotations, and the price of our common shares could suffer a material decline. Delisting would also impair our ability to raise additional capital.

***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 or other investors could lose confidence in our financial reporting, which would harm our business and could negatively impact the market 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 or other investors could lose confidence in our financial reporting, which would harm our business and could negatively impact the market price of our common shares. As a result of our limited administrative staffing levels, internal controls that rely on segregation of duties in many cases are not possible. Due to resource constraints and the present stage of our development, we do 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, we are 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 generally accepted accounting principles in the United States, 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.

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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 shareholder or other investor confidence in the reliability of our consolidated financial statements, harm our business and negatively impact the market price of our common shares.

Pursuant to Section 404, we are required to furnish a report by our management regarding our internal control over financial reporting, and if we become an accelerated filer under the federal securities laws, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***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 common shares. There is no present intention by our Board of Directors to pay dividends on our common shares. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, appreciation, if any, in the market price of our common shares will be your sole source of gain for the foreseeable future.