May 13, 2020

DiaMedica Announces Positive Results in Top-Line Data From the Phase II ReMEDy Acute Ischemic Stroke Study

- ***DM199 Met Primary Safety and Tolerability Endpoints in ReMEDy Study Top-Line Data***
- ***Demonstrated Therapeutic Effect in Participants Not Pre-Treated With Mechanical Thrombectomy***
- ***Reduced Risk of Recurrent Stroke***
- ***Results Consistent With Clinical Studies of Approved Urinary Derived KLK1 in China***
- ***Improvement in eGFR for Pre-Defined Chronic Kidney Disease Sub-Group***

Company to discuss top-line data during its scheduled first quarter financial results conference call tomorrow at 8:00 am Eastern Time

MINNEAPOLIS--(BUSINESS WIRE)-- DiaMedica Therapeutics Inc. (Nasdaq: DMAC), a clinical-stage biopharmaceutical company developing novel treatments for neurological disorders and chronic kidney disease, announced today that DM199, a drug intended to restore KLK1 levels and the body's natural ability to regulate blood flow and reduce inflammation after an acute ischemic stroke (AIS), met primary safety and tolerability endpoints in the ReMEDy phase II study. Further, no DM199-related serious adverse events were noted in the study. According to top-line phase II results, there was also a demonstrated therapeutic effect in participants who received tissue plasminogen activator (tPA) prior to enrollment, but not in participants receiving mechanical thrombectomy.

The ReMEDy study enrolled 92 participants to assess DM199, a recombinant form of human tissue Kalikrein-1 (KLK1), a serine protease, or protein, which plays a critical role in local blood flow regulation and in reducing inflammation, in the treatment of participants who experienced an AIS. AIS occurs when a clot blocks blood flow through a brain artery and represents approximately 85% of all strokes in the United States. According to the U.S. Centers for Disease Control and Prevention (CDC), there are approximately 690,000 acute ischemic strokes in the United States annually, one quarter of which are recurrent strokes, or strokes occurring in people who have had a previous stroke.

Ninety-one (91) of the 92 ReMEDy study enrolled participants were evaluable for safety in this multi-center, double-blind, randomized, placebo-controlled study. Participants were enrolled within 24 hours of stroke symptom onset and received an initial administration of DM199 or placebo as an intravenous infusion, followed by subcutaneous injections every three days over the following three weeks.

Prior to enrollment, 44 of the 91 evaluable patients (48%) received a mechanical thrombectomy, a treatment indicated for those who have a large vessel occlusion and can be

treated within six 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 the study (48%) and a disproportionate distribution 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 noted above, 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% 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% reduction.

DM199 vs. Palliative Therapies and/or tPA

	NIHSS Outcomes at 90 Days			
	0-1	**2-8**	**≥ 9**	**Death**
Placebo (n=21)	14%	57%	5%	24%
DM199 (n=25)	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 on placebo resulting in participant death.

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

- Increased nitric oxide (+105%) and prostaglandin E2 (+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.

DiaMedica is also developing DM199 for the treatment of chronic kidney disease (CKD). Accordingly, changes in the estimated glomerular filtration rate (eGFR), a measure of kidney function, were analyzed in participants with eGFR <70 mL/Min/1.73^2 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. Further the Company noted that eGFR at day 22 increased by at least 2 mL/Min in 77% of DM199 participants compared to 20% in placebo (p=0.007). DM199 is currently being evaluated in the REDUX phase II study for CKD.

	eGFR Mean Δ from Baseline (mL/Min/1.73^2)	
	Day 22 (Last Dose)	**Day 56** (Off Treatment)
Placebo	+0.84 (n=15)	-0.24 (n=12)
DM199	+7.5 (n=13)	+5.8 (n=12)
Group Difference	**+6.6**	**+6.1**

“These findings are consistent with Chinese data on the urine-derived form of KLK1 and 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 acute ischemic stroke,” said Professor Bruce Campbell, BMedSc, PhD, FRACP, FAHMS Neurologist, Head of Stroke Department of Neurology at the Royal Melbourne Hospital.

DiaMedica’s President and CEO, Rick Pauls, said: “Very few patients have a treatment option for AIS today. Approximately 10% of patients receive tPA or mechanical thrombectomy and we are developing DM199, with a 24 hour therapeutic treatment window, to significantly expand the proportion of patients who have access to effective and safe treatment.” Mr. Pauls continued, “It’s also very encouraging to see data suggesting that DM199 treatment may mitigate the adverse impact of ischemic stroke on kidney function, a significant but poorly understood comorbidity in many stroke victims.”

The detailed results of the ReMEDy trial has been accepted for E-Poster discussion at the joint European Stroke Organisation and World Stroke Organization Conference (ESO-WSO 2020), to be held in Vienna, Austria on November 7, 2020 and will also be submitted for publication.

DiaMedica intends to request a meeting with the FDA to define the development program leading to a path to commercialization for acute ischemic stroke.

Conference call and webcast information

DiaMedica will host a live conference call and webcast on Thursday May 14, 2020 at 7:00 am Central Time to discuss the top-line phase II data.

Conference Call details:

Date: Thursday, May 14, 2020
Time: 7:00 AM CT / 8:00 AM ET
Web access: https://event.on24.com/wcc/r/2158468/5BAA62D375A1F892573859D379BAF858
Dial In: (833) 502-0492 (domestic)
(778) 560-2558 (international)
Conference ID: 8757888

Interested parties may access the conference call by dialing in or listening to the simultaneous webcast. Listeners should log on to the website or dial in 15 minutes prior to the call. The webcast will remain available for play back on DiaMedica's website, under investor events and presentations, following the earnings call and for 12 months thereafter. A telephonic replay of the conference call will be available until May 21, 2020, by dialing (800) 585-8367 (US Toll Free), (416) 621-4642 (International), replay passcode 8757888.

About DM199

DM199 is a recombinant (synthetic) form of the human serine protease, KLK1. The KLK1 protein plays an important role in the regulation of diverse physiological processes including blood flow, inflammation, fibrosis, oxidative stress and neurogenesis via a molecular mechanism that increases production of nitric oxide and prostaglandin. KLK1 deficiency may play a role in multiple vascular and fibrotic diseases such as chronic kidney disease, retinopathy, stroke, vascular dementia and resistant hypertension where current treatment options are limited or ineffective. DiaMedica is the first company to have developed a recombinant form of the KLK1 protein. The KLK1 protein, produced from porcine pancreas and human urine, has been used to treat patients in Japan, China and Korea for decades. DM199 is currently being studied in patients with chronic kidney disease and patients with acute ischemic stroke.

About DiaMedica Therapeutics Inc.

DiaMedica Therapeutics Inc. is a clinical stage biopharmaceutical company focused on developing novel treatments for neurological and kidney diseases. DiaMedica's common shares are listed on The Nasdaq Capital Market under the trading symbol "DMAC."

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and forward-looking information that are based on the beliefs of management and reflect management's current expectations. When used in this press release, the words "may," "expects," "intends," "estimates", "believes", "anticipates", "plans", "continue," "will", or "should", the negative of these words or such variations thereon or comparable terminology and the use of future dates are intended to identify forward-looking statements and information. The forward-looking statements and information in this press release include statements regarding, but not limited to, the anticipated clinical benefits and success of DM199; the safety and efficacy of DM199; the assessment of the data from the ReMEDy study and the future publication and sharing of the full study results, and regulatory path forward. By their nature, forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause actual results, performance or achievements, or other future events, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Applicable risks and uncertainties include, among others, the

possibility of unfavorable results from additional clinical trials of DM199 or from subsequent analysis of existing data from the ReMEDy study or existing or new data received from additional ongoing and future studies of DM199; the risk that existing preclinical and clinical data may not be predictive of the results of ongoing or later clinical trials; DiaMedica's ability to conduct successful clinical testing of DM199 and within its anticipated parameters, costs and timeframes; the perceived benefits of DM199 over existing treatment options; the potential direct or indirect impact of the COVID-19 pandemic on DiaMedica's business; its reliance on collaboration with third parties to conduct clinical trials; its ability to continue to obtain funding for its operations, and the risks identified under the heading "Item 1.A. Risk Factors" in DiaMedica's annual report on Form 10-K for the fiscal year ended December 31, 2019 as filed with the SEC on March 23, 2020 and subsequent SEC filings by DiaMedica. The forward-looking information contained in this press release represents the expectations of DiaMedica as of the date of this press release and, accordingly, is subject to change after such date. Readers should not place undue importance on forward-looking information and should not rely upon this information as of any other date. While DiaMedica may elect to, it does not undertake to update this information at any particular time except as required in accordance with applicable laws.

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