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DiaMedica Therapeutics Announces FDA Clearance of IND Application to Initiate Phase 2/3 Clinical Trial for DM199 for Acute Ischemic Stroke

- ***Initiating ReMEDy2 – Pivotal Phase 2/3 Randomized, Double-Blind, Placebo-Controlled Study***

MINNEAPOLIS--(BUSINESS WIRE)-- DiaMedica Therapeutics Inc. (Nasdaq: DMAC), a clinical-stage biopharmaceutical Company focused on developing novel treatments for neurological disorders and kidney diseases, announced today that the U.S. Food & Drug Administration (FDA) has accepted the Company's Investigational New Drug (IND) application. The Company plans to proceed with a pivotal Phase 2/3 study of DM199 (recombinant human tissue kallikrein-1or KLK1) for the treatment of patients with Acute Ischemic Stroke (AIS).

The upcoming ReMEDy2 Trial follows the Phase 2 study in AIS patients that demonstrated an improvement in stroke outcomes and reduction in stroke recurrence, along with an excellent safety profile. The findings are consistent with a significant body of clinical evidence from the use of the approved urinary-sourced KLK1 (Kailikang®) in China. The upcoming pivotal ReMEDy2 trial will evaluate whether DM199, a recombinant investigational agent, can improve three-month outcomes in AIS patients without other treatment options.

"While we have options to remove or dissolve clots in a small segment of AIS patients, we need novel treatment options for the remaining 80% of stroke patients who often have clinically significant morbidity and mortality following an acute ischemic stroke," said Scott Kasner, M.D., Professor of Neurology and Director of Comprehensive Stroke Center at the University of Pennsylvania. "In the ReMEDy2 Trial, we will be evaluating a mechanism of action with significant rationale and clinical data supporting the hypothesis that restoring low KLK1 levels with DM199 may both improve patient outcomes following a stroke and reduce the number of recurrent strokes."

The ReMEDy2 Trial is a randomized, double-blind, placebo-controlled Phase 2/3 trial with the objective to enroll approximately 350 participants at up to 75 sites. Adult participants must be able to initiate treatment, DM199 or placebo, within 24 hours of AIS onset and who do not have a large vessel occlusion (e.g. patients eligible for mechanical thrombectomy) and/or who do not receive tissue plasminogen activator (tPA). This patient group represents up to 80% of the approximately 700,000 patients who experience an AIS each year in the United States. Participants will be randomized 1:1 to receive either DM199 or placebo and will be treated for 3 weeks with final follow up at day 90. Endpoints will include the modified Rankin Scale (mRS), stroke recurrence, the National Institute of Health Stroke Score (NIHSS) and Barthel Index, deaths, safety and tolerability. The Company plans an interim

analysis to determine whether (i) the study should proceed as planned, (ii) a sample size increase is needed, or (iii) the study should be halted for futility. DiaMedica will remain blinded to the data at the interim.

“The IND clearance of the Phase 2/3 study of DM199 for acute ischemic stroke represents a major milestone for DiaMedica as we work to bring new hope and options to patients who experience an acute ischemic stroke,” said Rick Pauls, President and Chief Executive Officer of DiaMedica. “We look forward to further studying the potential of DM199 and moving closer to providing a much-needed new treatment option for the more than 10 million people globally who experience an acute ischemic stroke each year and do not have a treatment option today.”

About Acute Ischemic Stroke

Acute Ischemic Stroke (AIS) is a serious medical emergency caused by sudden loss of blood flow to an area of the brain, resulting in localized damage to the brain, often causing disability or death. Treatment for AIS is limited to dissolving blood clots with a medication (tissue plasminogen activator) in the first 4.5 hours after stroke onset or physical removal of the blockage (mechanical thrombectomy) up to 24 hours after onset in select patients. Globally, there are approximately 13 million AIS cases with approximately 5 million deaths each year and less than 20% have a treatment option which represents a significant unmet medical need.

About DM199

DM199 is a recombinant (synthetic) form of human tissue kallikrein-1 (KLK1). KLK1 is a serine protease (protein) that 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 South Korea for decades. DM199 is currently being studied in patients with acute ischemic stroke and chronic kidney disease.

About DiaMedica Therapeutics Inc.

DiaMedica Therapeutics Inc. (Nasdaq: DMAC) is a clinical stage biopharmaceutical company focused on developing novel treatments to improve the lives of patients with neurological and chronic kidney diseases. To learn more about DiaMedica, visit www.diamedica.com.

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 “estimate,” “believe,” “anticipate,” “intend,” “expect,”

“plan,” “continue,” “look forward,” “will,” “may,” “potentially” 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 the anticipated clinical benefits and success of DM199, the timing and requirements of its clinical programs, including its anticipated Phase 2/3 trial for DM199 in patients with AIS, which DiaMedica believes will commence in Summer 2021 and has the potential to serve as a pivotal registration study of DM199 in that patient population. Such statements and information reflect management’s current view and DiaMedica undertakes no obligation to update or revise any of these statements or information. 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 DiaMedica’s ongoing or future clinical trials 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 plans to develop, obtain regulatory approval for and commercialize its DM199 product candidate for the treatment of AIS and chronic kidney disease (CKD) and its expectations regarding the benefits of DM199; 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; DiaMedica’s reliance on collaboration with third parties to conduct clinical trials; DiaMedica’s ability to continue to obtain funding for its operations, including funding necessary to complete planned clinical trials and obtain regulatory approvals for DM199 for AIS and CKD, and the risks identified under the heading “Risk Factors” in DiaMedica’s annual report on Form 10-K for the fiscal year ended December 31, 2020. 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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