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DiaMedica Therapeutics Announces Addition of Stroke Recurrence as a Second Independent Primary Endpoint in ReMEDy2 Phase 2/3 AIS Trial

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 and Drug Administration (FDA) has accepted and concluded that DiaMedica “may proceed” with the proposed clinical investigation using its amended protocol adding stroke recurrence as a second independent primary endpoint to its Phase 2/3 ReMEDy2 trial evaluating DM199 for acute ischemic stroke (AIS). The FDA’s acceptance of the amendment allows the Company to evaluate the effects of DM199 on both physical recoveries post AIS and the rate of recurrent AIS, as two separate independent primary endpoints, with each statistically powered for success. There are no changes in treatment, duration, or study population of the trial as part of this protocol amendment.

ReMEDy2 is a Phase 2/3 adaptive design, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of DM199 for the treatment of AIS, now addressing both stroke recovery and stroke recurrence. The trial is studying AIS in a patient population for whom thrombolysis and/or a catheter-based procedure, mechanical thrombectomy, are not medically appropriate or available due to constraints of clot location, comorbidity risks or time from estimated onset of stroke, which represents approximately 80% of all AIS patients. Stroke recovery is defined as patients with excellent functional outcomes at Day 90 as assessed via the modified Rankin Scale (mRS) with scores of 0 or 1, on a scale from 0-6. Recurrent AIS will be evaluated based upon the proportion of patients who experience a recurrent AIS by Day 90.

Approximately 25% of the 795,000 acute ischemic strokes that occur each year in the U.S. are recurrent. The rationale for adding stroke recurrence to the ReMEDy2 trial as an independent primary endpoint is based on data obtained from DiaMedica’s prior ReMEDy Phase 2 study in AIS. In that study, 45 patients received placebo and 46 were treated with DM199. During the 90-day follow-up period, recurrent ischemic stroke occurred in 6 patients (13.3%) of the placebo arm versus none in the DM199 arm (P=0.012). Moreover, 4 (66%) of the recorded strokes in the placebo arm were fatal. When excluding patients pre-treated with mechanical thrombectomy, recurrent ischemic stroke occurred in 4 patients (19.0%; N=21) of the placebo arm, all of which were fatal, versus none in the DM199 arm (0%; N=25) (P=0.037).

“The medical need to develop new and better treatments for AIS is clear," commented Rick Pauls, Chief Executive Officer of DiaMedica. “Based upon our encouraging clinical experience in our Phase 2 study, we are very pleased to be formally elevating AIS

recurrence to a primary endpoint in our ReMEDy2 study. This provides another pathway to potential success in this trial, but more importantly, underscores the importance of evaluating DM199's potential to reduce AIS patients' risk of suffering a recurrent stroke which is often more disabling and fatal."

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, among other things, increases production of nitric oxide and prostaglandin. KLK1 deficiency may play a role in multiple vascular and fibrotic diseases such as stroke, chronic kidney disease, retinopathy, vascular dementia and resistant hypertension where current treatment options are limited or ineffective. DiaMedica is the first company to have developed a pharmaceutically active recombinant form of the KLK1 protein. The KLK1 protein, in forms 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 acute ischemic stroke and chronic kidney disease.

About Acute Ischemic Stroke and Stroke Recurrence

Stroke is characterized by the rapidly developing loss of brain function due to a blockage of blood flow in the brain. As a result, the affected tissues of the brain becomes inactive and may eventually die. AIS is characterized by interruption of the blood supply by a blood clot (ischemia). Risk factors for stroke include, among other things, advanced age, hypertension (high blood pressure), previous stroke or transient ischemic attack (TIA), diabetes, high cholesterol, cigarette smoking, atrial fibrillation, physical inactivity and obesity.

According to the U.S. Centers for Disease Control:

- Every year in the United States, approximately 795,000 people experience a stroke (ischemic or hemorrhagic). Approximately 610,000 of these are first events and approximately 25%, or 185,000, are recurrent stroke events.
- Approximately one of every 20 deaths in the United States is caused by stroke and is the fifth leading cause of death. On average, someone in the United States has a stroke every 40 seconds and someone dies from a stroke every four minutes.
- Stroke is the leading cause of serious long-term disability and reduces mobility in more than half of stroke survivors aged 65 and over.
- Risk of having a first stroke is nearly twice as high for African Americans as for Caucasians, and African Americans have the highest rate of death due to stroke.

About DiaMedica Therapeutics Inc.

DiaMedica Therapeutics Inc. is a clinical stage biopharmaceutical company committed to improving the lives of people suffering from serious diseases. DiaMedica's lead candidate DM199 is the first pharmaceutically active recombinant (synthetic) form of the KLK1 protein, an established therapeutic modality for the treatment of acute ischemic stroke and chronic kidney disease. For more information visit our website at 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," "potential," "continue," "look forward," "will," "may" 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, and the timing and requirements of its clinical programs, including its Phase 2/3 trial for DM199 in patients with AIS, which DiaMedica believes 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 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 and its trials; 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 chronic kidney disease, 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 as filed with the U.S. Securities and Exchange Commission (SEC) and subsequent SEC filings. 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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