February 20, 2025

# DiaMedica Therapeutics Announces Publication of DM199's Mechanism of Action for the Treatment of Acute Ischemic Stroke (AIS) in the Journal Stroke

**Scientific insight into DM199's mechanism for increasing collateral circulation and salvaging brain tissue at-risk from infarction**

MINNEAPOLIS--(BUSINESS WIRE)-- DiaMedica Therapeutics Inc. (Nasdaq: DMAC), a clinical-stage biopharmaceutical company focused on developing novel treatments for severe ischemic diseases, today announced the peer-reviewed publication entitled: *Recombinant human tissue kallikrein-1 for treating acute ischemic stroke and preventing recurrence* (Kasner, et al.) which is now available online and is scheduled for print publication in the February 2025 issue of *Stroke*.

The article describes the mechanism of action of DM199 (rinvecalinase alfa), a recombinant form of human tissue kallikrein-1, and its scientific rationale in the Company's ongoing Phase 2/3 trial for acute ischemic stroke (ReMEDy2 Trial). DM199, a bradykinin-producing enzyme, represents a promising potential treatment for AIS by enhancing collateral circulation and stimulating angiogenesis and cellular repair mechanisms. In animal studies of acute stroke, bradykinin B2 receptor expression on brain endothelial cells in the ischemic region increased 36-fold. In this environment, newly generated bradykinin from DM199 induces potent local vasodilation and improves brain perfusion through three synergistic signaling pathways downstream of the B2 receptor. Due to DM199's preferential effect on ischemic tissue, systemic adverse effects such as hypotension can be avoided with proper dosing. Beyond its initial vasodilatory effects through recruitment of preexisting collaterals, DM199 also promotes long-term improvements in brain perfusion by facilitating new blood vessel formation. With an extended course of therapy following AIS, these multifaceted effects may further reduce the risk of stroke recurrence.

"The prior Phase 2 ReMEDy1 trial demonstrated that DM199 treatment had a favorable impact on clinical outcomes in AIS patients who were not eligible for mechanical thrombectomy," said lead author Scott Kasner, MD, Chief of the Division of Neurology and Professor of Neurology at the University of Pennsylvania and ReMEDy2 principal investigator. "This publication provides valuable scientific insight into how DM199 may improve clinical outcomes in AIS, offering a novel approach to enhancing blood flow in stroke treatment."

**About the Acute Ischemic Stroke Phase 2/3 ReMEDy2 Trial**

The ReMEDy2 trial is a Phase 2/3 adaptive design, randomized, double-blind, placebo-controlled trial studying the use of the Company's product candidate, DM199, to treat acute

ischemic stroke patients. The trial is intended to enroll between 300 and 728 patients at up to 100 sites globally. Patients enrolled in the trial will be treated for three weeks with either DM199 or placebo, beginning within 24 hours of the onset of AIS symptoms, with the final follow-up at 90 days. The trial excludes patients who received mechanical thrombectomy (MT) or participants with large vessel occlusions in the intracranial carotid artery or the M1 segment for the middle cerebral, vertebral or basilary arteries or those that are otherwise eligible for MT. Participants treated with tissue plasminogen activator (tPA) or tenecteplase (TNK), thrombolytic agents intended to dissolve blood clots, are eligible for participation if they continue to experience a persistent neurological deficit after receiving thrombolytic treatment and meet all other trial criteria. DiaMedica believes that the proposed trial has the potential to serve as a pivotal registration study of DM199 in this patient population.

**About DM199**

DM199 (rinvecalinase alfa) is a recombinant form of human tissue kallikrein-1 (rhKLK1) in clinical development for acute ischemic stroke and preeclampsia. KLK1 is a serine protease enzyme that plays an important role in the regulation of diverse physiological processes via a molecular mechanism that increases production of nitric oxide, prostacyclin and endothelium-derived hyperpolarizing factors. In the case of AIS, DM199 is intended to enhance blood flow and boost neuronal survival in the ischemic penumbra by dilating arterioles surrounding the site of the vascular occlusion and inhibition of apoptosis (neuronal cell death) while also facilitating neuronal remodeling through the promotion of angiogenesis.

**About DiaMedica Therapeutics Inc.**

DiaMedica Therapeutics Inc. is a clinical stage biopharmaceutical company committed to improving the lives of people suffering from serious ischemic diseases with a focus on acute ischemic stroke and preeclampsia. DiaMedica's lead candidate DM199 is the first pharmaceutically active recombinant (synthetic) form of the KLK1 protein, an established therapeutic modality in Asia for the treatment of acute ischemic stroke, preeclampsia and other vascular diseases. For more information visit the Company's 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 "anticipates," "believes," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "should," or "will," 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 potential of DM199 to successfully treat AIS. 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, risks and uncertainties relating to the timing of ReMEDy2 trial site activations and enrollment, regulatory applications and related filing and approval timelines; the possibility of additional future adverse events associated with or unfavorable results from the ReMEDy2 trial; risks and uncertainties relating to the clinical expansion into preeclampsia and the DM199 Phase 2 trial for preeclampsia, including timing of results; 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 acute ischemic stroke and preeclampsia and its expectations regarding the benefits of DM199; DiaMedica's ability to conduct successful clinical testing of DM199 and within its anticipated parameters, site activations, enrollment numbers, costs and timeframes; the adaptive design of the ReMEDy2 trial and the possibility that the targeted enrollment and other aspects of the trial could change depending upon certain factors, including additional input from the FDA and the blinded interim analysis; the perceived benefits of DM199 over existing treatment options; the potential direct or indirect impact of COVID-19, hospital and medical facility staffing shortages, and worldwide global supply chain shortages on DiaMedica's business and clinical trials, including its ability to meet its site activation and enrollment goals; 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 current and planned clinical trials and obtain regulatory approvals for DM199 for acute ischemic stroke and preeclampsia, 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, 2023 and subsequent reports filed with the U.S. Securities and Exchange Commission, including its most recent quarterly report on Form 10-Q for the quarterly period ended September 30, 2024. 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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Scott Kellen
Chief Financial Officer
Phone: (763) 496-5118
skellen@diamedica.com

**For Investor Inquiries:**
Mike Moyer
Managing Director, LifeSci Advisors, LLC
mmoyer@lifesciadvisors.com

Source: DiaMedica Therapeutics Inc.