June 26, 2024

DiaMedica Therapeutics Announces Expansion of DM199 (Rinvecalinase Alfa) Program Into Preeclampsia

- **Preeclampsia Program to be Initiated with a Phase 2 Investigator-sponsored Trial Beginning in Q4 2024**
- **Key Proof-of-Concept Results Expected in the First Half of 2025**
- **Management will Host a Conference Call Thursday, June 27, 2024 at 8:00 AM Eastern Time / 7:00 AM Central Time to Discuss Preeclampsia**
- **Company to Host Preeclampsia Key Opinion Leader Event July 29, 2024**

MINNEAPOLIS--(BUSINESS WIRE)-- DiaMedica Therapeutics Inc. (Nasdaq: DMAC), a clinical-stage biopharmaceutical company focused on developing novel treatments for severe ischemic diseases, today announced that it plans to expand its DM199 (rinvecalinase alfa; recombinant human tissue kallikrein-1 (rhKLK1)) clinical development program into preeclampsia. Preeclampsia is a life-threatening pregnancy-associated vascular disorder characterized by new onset hypertension with proteinuria, and/or end organ dysfunction, and poses significant risks to both mother and baby. There are no approved therapeutics for preeclampsia in the U.S. or Europe.

“Multiple lines of evidence demonstrate that DM199 can lower blood pressure, and unlike contra-indicated small molecule anti-hypertensives, DM199 is a large molecule protein that has been shown to not cross the placental barrier in animals, potentially creating a significant safety advantage in pregnancy disorders,” commented Rick Pauls, DiaMedica’s President and Chief Executive Officer. He added, “The planned trial is highly capital efficient, enrolling up to 120 participants for an estimated cost of approximately $1.5 million, and has the potential to provide robust proof of concept.”

DM199 for Preeclampsia: Scientific Rationale and Clinical/Preclinical Support

DM199 has the potential to lower blood pressure, enhance endothelial health, and improve perfusion to maternal organs and the placenta. This mode of action is believed to occur through the increased production of endothelial nitric oxide, prostacyclin, and endothelial-derived hyperpolarizing factors (EDHFs). These pathways are typically depressed or impaired in preeclampsia. DM199 holds the potential to be disease modifying for preeclampsia patients if it can effectively increase placental perfusion and reduce placental hypoxia, a significant contributor to the pathophysiology of preeclampsia.

DM199 has demonstrated blood pressure reductions in multiple prior studies. New results from analysis of overall participants with elevated blood pressure (baseline systolic blood pressure ≥ 130 mmHG) from the DM199 Phase 2 REDUX clinical trial in three types of chronic kidney disease (CKD) which demonstrated a statistically significant reduction in systolic blood pressure (SBP) at day 95:

REDUX Phase 2 CKD Trial Results: Baseline SBP*

	SBP ≥130 mmHg	SBP ≥140 mmHg	SBP ≥150 mmHg
Day 95 Change from Baseline	-7.7 mmHg	-12.6 mmHg	-22.1 mmHg
P-value (Student's T-Test)	0.011	0.004	0.003
Number of Participants	47	31	15

*Includes participants from all cohorts

DiaMedica has also completed studies on fertility, embryofetal development and pre- and post-natal development in animal models, which support the potential safety in pregnant humans. DiaMedica recently completed a placental transfer study in pregnant rats in which DM199 did not cross the placental barrier. Specifically, DM199 was detectable in the maternal blood, but undetectable in the fetal blood.

"With scientific evidence that KLK1 is key to endothelial health, I am optimistic about the potential of DM199 to reverse disease severity in addition to improving blood pressure control," commented Professor Stephen Tong, MD, PhD, Obstetrics and Gynaecology and Professor at Mercy Hospital for Women and Co-Director of Mercy Perinatal at The University of Melbourne. He further commented, "if DM199 can also open up maternal blood vessels to improve blood flow to the placenta, it may serve as a disease-modifying therapy for preeclampsia. Additionally, it could address fetal growth restriction, a separate yet related pregnancy disorder that is more prevalent and currently has no FDA-approved therapeutics."

The Phase 2 Investigator-Sponsored Trial in Preeclampsia and Fetal Growth Restriction

Up to 90 women with preeclampsia, and potentially 30 subjects with fetal growth restriction, will be evaluated with the first subject anticipated to be enrolled in the fourth quarter of 2024, pending regulatory approval. Part 1A topline study results are anticipated in the first half of 2025, which will demonstrate whether DM199 is safe, lowers blood pressure, and dilates intrauterine arteries to increase placental blood flow.

This Phase 2 open-label, single center, single-arm, safety and pharmacodynamic, proof-of-concept, investigator-sponsored study of DM199 in treating preeclampsia will be conducted at the Tygerberg Hospital, Cape Town, South Africa (SA), under the direction of Catherine Cluver, MD, PhD, Professor of Maternal/Fetal Medicine, Stellenbosch University, Stellenbosch, SA, in collaboration with DiaMedica. "Women suffering from preeclampsia have few therapeutic options. Controlling hypertension and reducing organ damage and premature delivery is a key goal. DM199 holds promise as a novel medication and we look forward towards evaluating its potential benefits in managing patients with preeclampsia," said Professor Cluver.

The planned Phase 2 trial of DM199 for preeclampsia will be conducted in up to three parts as follows:

	Participants	Summary
Part 1	Up to 60	Pregnant woman with preeclampsia between 27 to 42 weeks of gestation and are scheduled to deliver within 72 hours, SBP ≥150 mmHg. Part 1A involves an ascending dose-finding study recruiting up to 30 participants. Part 1B is an expansion cohort of an additional 30 participants at the dose established in Part 1A. Key data from Part 1 will be used to assess safety and tolerability, and to assess whether DM199 acutely lowers blood pressure, acutely dilates intrauterine arteries (measured with Doppler ultrasound), and whether it crosses the placental barrier (measured in cord blood), as well as other disease specific measurements and biomarkers.
Part 2	Up to 30	Pregnant woman with preeclampsia between 27 to 33 weeks gestation in the expectant management setting, aimed at safely prolonging the pregnancy. Key data from Part 2 is expected to include assessments of safety and tolerability, the number of days pregnancy is prolonged, changes in the urinary albumin-to-creatinine ratio over seven days compared to baseline, need to increase or decrease other antihypertensive agents, as well as other disease-specific measurements and biomarkers.
Part 3	Up to 30	Pregnant woman between 26 to 32 weeks of gestation with fetal growth restriction (FGR) but without preeclampsia, contingent upon observing if DM199 can enhance intrauterine blood flow as assessed by Doppler ultrasound evaluation in Part 1. Key data from Part 3 is expected to include changes in uterine artery and ophthalmic arterial blood flow (measured by Doppler ultrasound), birthweight centile and fetal growth trajectory.

The investigators on the study include Catherine Cluver, MD, PhD, Professor of Maternal/Fetal Medicine, Stellenbosch University, Stellenbosch, South Africa, Stephen Tong, MD, PhD, Professor at Mercy Hospital for Women and Co-Director of Mercy Perinatal at The University of Melbourne, and Sue Walker, MD, PhD, Head of the Department of Obstetrics and Gynecology, University of Melbourne, and Director of Perinatal Medicine at Mercy Hospital for Women.

“Gaining access to these leading academics and trailings in the field of preeclampsia is invaluable and underscores the potential of DM199 for treating this grave condition. Additionally, as this is an investigator-sponsored trial, it will not significantly consume DiaMedica’s clinical resources, allowing us to maintain focus on the Remedy AI clinical trial,” commented Lorain Mazurka, MD, DiaMedica’s Chief Medical Officer. “The United States has the highest rate of maternal mortality among high-income nations, and according to the U.S. Centers for Disease Control and Prevention, black women are three times more likely to die during pregnancy than white women. If DM199 can address this unmet need, it would be a significant benefit for these women and their babies.”

More details on DM199 for preeclampsia and fetal growth restriction will be presented at a key opinion leader event to be held on July 29, 2024. Instructions for participating in this event will be provided in the coming weeks.

Conference Call and Webcast Information

DiaMedica Management will host a conference call and webcast to discuss its clinical expansion into preeclampsia on Thursday, June 27, 2024, at 8:00 AM Eastern Time / 7:00 AM Central Time:

Date:	Thursday, June 27, 2024
Time:	8:00 AM ET / 7:00 AM CT
Web access:	https://app.webinar.net/3J46BqeBGXV
Dial In:	(646) 357-8785
Conference ID:	53747

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 playback on the Company’s website, under

investor relations - events and presentations, following the earnings call and for 12 months thereafter. A telephonic replay of the conference call will be available until July 4, 2024, by dialing (888) 660-6345 (US Toll Free) and entering the replay pass code: 53747#.

About Preeclampsia

Preeclampsia is a serious pregnancy disorder that typically develops after the 20th week of gestation, characterized by high blood pressure and damage to organ systems, often the kidneys and liver. Affecting up to 8% of pregnancies worldwide, preeclampsia can pose significant risks to both the mother and baby, including risk of stroke, placental abruption, progression to elecampane, premature delivery, and death. Symptoms may include severe headaches, vision changes, upper abdominal pain and swelling in the hands and face. Delivery of the baby, often very prematurely, is the only available option for stopping the progression of preeclampsia. Women who have had preeclampsia have three to four times the risk of high blood pressure and double the risk for heart disease and stroke.

About DM199 (rinvecalinase alfa)

DM199 is a recombinant (synthetic) form of human tissue kallikrein-1 (rhKLK1) in clinical development for acute ischemic stroke (AI) 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 factor. In the case of AI, 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. In preeclampsia, DM199 is intended to lower blood pressure, enhance endothelial health and improve perfusion to maternal organs and the placenta.

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 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," "can," 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 Company's planned clinical expansion into preeclampsia, the planned DM199 Phase 2 trial for preeclampsia, the receipt of regulatory approvals for such trial, the timing

and costs of such trial, enrollment in such trial, and anticipated clinical benefits and success of DM199. 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 planned clinical expansion into preeclampsia and the planned DM199 Phase 2 trial for preeclampsia; uncertainties relating to the timing of 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; 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, 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 March 31, 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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