

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 26, 2024

DIAMEDICA THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

British Columbia, Canada
(State or other jurisdiction
of incorporation)

001-36291
(Commission
File Number)

Not Applicable
(IRS Employer
Identification No.)

301 Carlson Parkway, Suite 210
Minneapolis, Minnesota
(Address of principal executive offices)

55305
(Zip Code)

(763) 496-5454
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Voting common shares, no par value per share	DMAC	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On June 26, 2024, DiaMedica Therapeutics Inc. (the “Company”) made available an investor presentation in connection with the announcement of its plans to expand its clinical trials into preeclampsia, a life-threatening, pregnancy-associated, vascular disorder characterized by new onset hypertension with proteinuria, and/or end organ dysfunction (the “Investor Presentation”). The Investor Presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and the information set forth therein is incorporated herein by reference and constitutes a part of this Item 7.01.

Representatives of the Company intend to use the Investor Presentation in connection with presentations at investor conferences, meetings and in other forums. The Company intends to disclose the information contained in the Investor Presentation, in whole or in part, and with updates and possibly modifications, in connection with presentations to investors, analysts and others and on its corporate website.

The information contained in Item 7.01 to this Current Report on Form 8-K and Exhibit 99.1 hereto is summary information that is intended to be considered in the context of the Company’s United States Securities and Exchange Commission (the “SEC”) filings and other public announcements that the Company may make, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this Item 7.01 and Exhibit 99.1 hereto, although it may do so from time to time as its management believes is warranted. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosure. By filing this report and furnishing this information, the Company makes no admission as to the materiality of any information contained in this Item 7.01, including Exhibit 99.1 hereto.

The information contained in this Item 7.01 and Exhibit 99.1 hereto shall not be deemed to be “filed” with the SEC for purposes of Section 18 of the United States Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference into any registration statement or other document filed by the Company under the United States Securities Act of 1933, as amended, or the Exchange Act, except as may be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On June 26, 2024, the Company announced that it plans to expand its clinical trials into preeclampsia. The press release is attached as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K 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 Current Report on Form 8-K, the words "anticipates," "believes," "look forward," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "hope," "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 Current Report on Form 8-K include statements regarding the Company's planned clinical expansion into preeclampsia. Such statements and information reflect management's current view and the Company 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 the Company'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; the Company'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; the Company'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 the Company's business and clinical trials, including its ability to meet its site activation and enrollment goals; the Company's reliance on collaboration with third parties to conduct clinical trials; the Company'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 the Company's annual report on Form 10-K for the fiscal year ended December 31, 2023, quarterly report on Form 10-Q for the quarterly period ended March 31, 2024, and subsequent reports filed with the U.S. Securities and Exchange Commission. The forward-looking information contained in this Current Report on Form 8-K represents the Company's expectations as of the date of this Current Report on Form 8-K 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 the Company may elect to, it does not undertake to update this information at any particular time except as required in accordance with applicable laws.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Investor Presentation issued by DiaMedica Therapeutics Inc. on June 26, 2024 (furnished herewith)
99.2	Press Release dated June 26, 2024 announcing clinical expansion into preeclampsia
104	The Cover Page from this Current Report on Form 8-K, formatted in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DIAMEDICA THERAPEUTICS INC.

By: /s/ Scott Kellen

Scott Kellen

Chief Financial Officer and Secretary

Date: June 26, 2024

Corporate Presentation

June 2024



DiaMedica
THERAPEUTICS

Transforming Care for Stroke and Preeclampsia



Cautionary Note Regarding Forward-Looking Statements

This presentation 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 presentation, the words "estimate," "believe," "anticipate," "intend," "expect," "plan," "continue," "potential," "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 reflect management's current plans, objectives, market opportunity and other estimates, expectations and intentions, benefits and potential of DM199 and anticipated timing of future events and involve assumptions that may never materialize or may prove to be incorrect and inherently involve significant risks and uncertainties, including factors beyond DiaMedica's control that could 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 effects of the protocol amendments to increase the probability of clinical success and streamline the site selection and activation process in the ReMEDy2 trial; the possibility of additional future adverse events associated with or unfavorable results from DiaMedica's ongoing or future trials; 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 PE 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 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 planned clinical trials and obtain regulatory approvals for DM199 for acute ischemic stroke and/or PE, 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 U.S. Securities and Exchange Commission filings, including its most recent quarterly report on Form 10-Q for the quarterly period ended March 31, 2024.

Other risk and uncertainties of which DiaMedica is not currently aware may also affect the Company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. All forward-looking statements contained in this presentation speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. DiaMedica undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.



OUR MISSION

Life-transforming Therapy

for Patients with Severe Ischemic Diseases

- 01 Acute Ischemic Stroke (AIS)
(Non-eligible for tPA or thrombectomy)
- 02 Preeclampsia (PE)

No FDA Approved
Therapeutics

Company Overview

Cash: \$46 million
(as of March 31, 2024)

Lead Program: DM199 - Novel, Late-Stage Biologic Therapy

- › Recombinant KLK1 (rhKLK1) protein with FDA Fast-Track Designation
- › Enrolling pivotal AIS Phase 2/3 trial and planning preeclampsia Phase 2 trial

Acute Ischemic Stroke (AIS)

- › >\$10 billion US market opportunity
- › ~80% of patients have no treatment options today^{1,2}
- › Extensive clinical data supporting KLK1 safety and efficacy in AIS patients
 - Increases collateral circulation in the penumbra
 - Encouraging Phase 2 efficacy and safety data for DM199
 - Up to 1 million treated/year with human urinary KLK1 (HUK) in China³

Preeclampsia (PE) - Hypertensive Disorder of Pregnancy

- › Estimated multi-billion dollar US market opportunity
- › US has highest maternal death rate among high-income nations³
- › Potential disease modifying therapy
 - Strong evidence that DM199 lowers blood pressure
- › Key safety advantage: Unlike most-prescribed anti-hypertensives, DM199 is not expected to cross placental barrier due to its large molecular size



Sources: 1. Fassbender, K., et al (2013). Streamlining of prehospital stroke management: the golden hour. *The Lancet Neurology*, 12(6), 585-586. doi: 10.1016/S1473-4422(13)70078-5; 2. Kansagra AP, et al. Trends in Mechanical Thrombectomy for AIS in the US: A Nationwide Analysis from 2012 to 2016. *Stroke*. 2019;50(3):570-577. doi:10.1161/STROKEAHA.118.023600; 3. Shanghai Pharma/Tecpool website: <http://www.techpool.com.cn/press/5d83ed2235416641805a7f5>; 3. Manira Z, Gunja et al., Insights into the U.S. Maternal Mortality Crisis: An International Comparison (Commonwealth Fund, June 2024). <https://doi.org/10.26099/cfm.st75>

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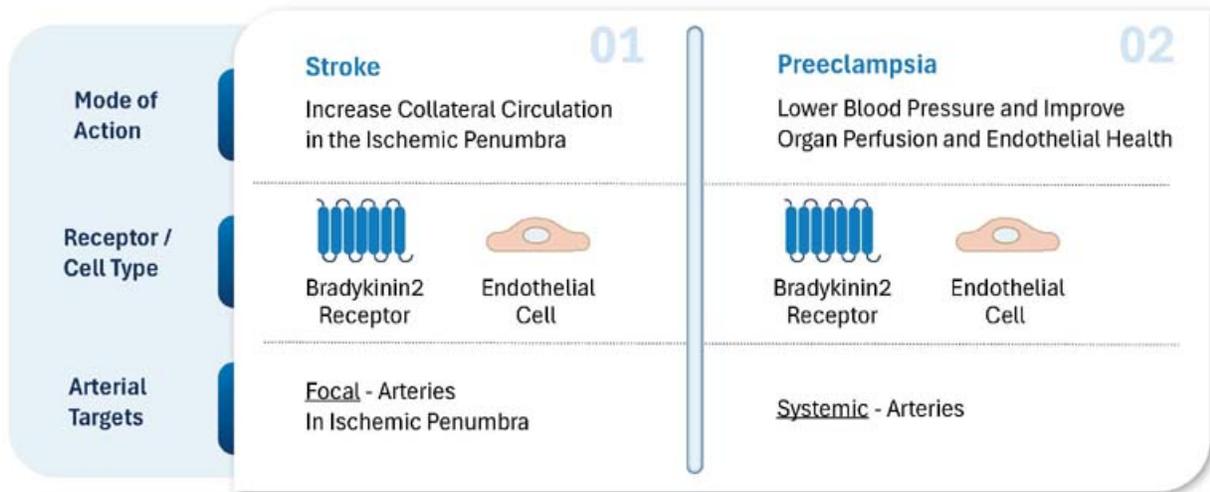
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DiaMedica Pipeline

COMPOUND	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 2/3	UPCOMING MILESTONES
DM199 (Rinvecalinase alfa) Recombinant KLK1	Acute Ischemic Stroke 	ReMEDy2 Study				Anticipated Interim Enrollment Q1 '25
	Preeclampsia Fetal Growth Restriction 	DM199 for Pregnancy Complications				Anticipated Proof of Concept Data in 1H '25
DM300 Recombinant serine protease inhibitor	Severe Acute Pancreatitis 					

DM199: One Target, Dual Impact – BK2 Receptor Activation in Stroke and PE

Both disease processes improved through increased blood flow to ischemic tissue





ReMEDy2
Phase 2/3 Trial

Acute Ischemic Stroke



DiaMedica
THERAPEUTICS



High Unmet Need in Acute Ischemic Stroke

>7.5 million acute ischemic strokes globally⁵

DM199 US Estimated Market Opportunity = \$10+ Billion

Low Treatment Rates

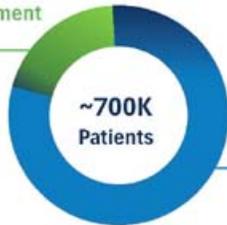
US Annual Acute Ischemic Strokes^{1,2,3}



20%

Active Treatment

<140K Patients



80%

of Patients with No Treatment Options

>500K Patients

Limited Treatment Options

0

No New Pharmaceuticals Approved in Over 25 Years

~10%

tPA / Thrombolytic



~10%

Mechanical Thrombectomy



1st line^{3,4}

Supportive Care Only



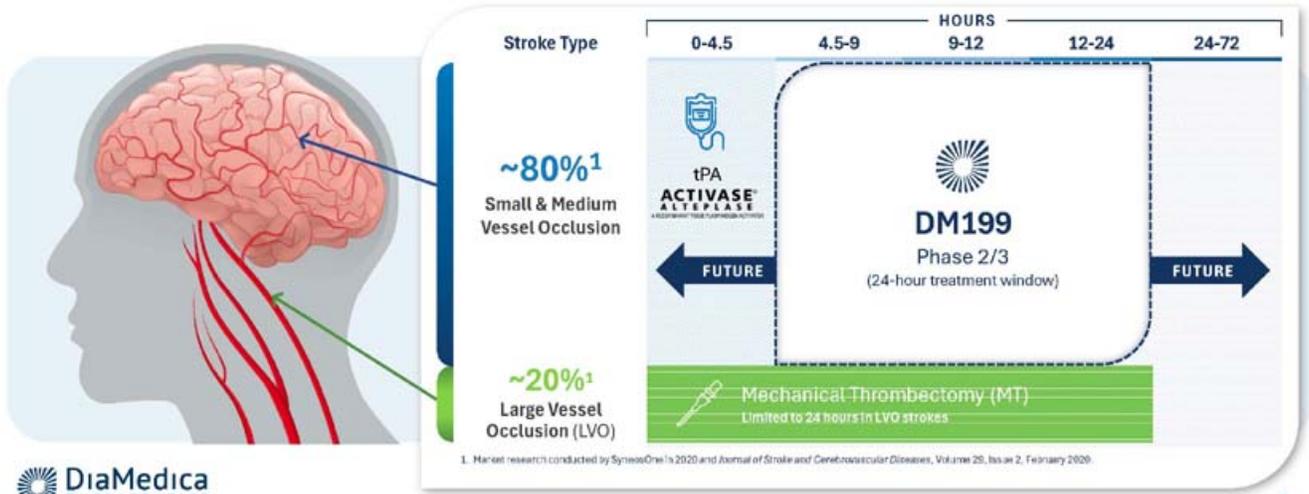
DM199 Initial Target

Sources: 1. Et al., American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation. 2017 Mar 7;135(10):e146-e603. PMID: 28122895; 2. American Stroke Association; 3. Fastbender, K., et al. (2013). Streamlining of prehospital stroke management: the golden hour. The Lancet Neurology, 12(6), 585-586. doi: 10.1016/S1474-4422(13)70078-5; 4. Karsaga AP, Goyal MS, Harrison S, Albers GW. Trends in Mechanical Thrombectomy for Acute Ischemic Stroke in the United States: A Nationwide Analysis from 2012 to 2016. Stroke. 2018;50(3):570-577. doi:10.1161/STROKEAHA.118.023600; 5. World Stroke Organization Global Fact Sheet 2022

DM199 Initial Target in AIS – Significant Whitespace Opportunity

>500k patients in the U.S. with no treatment option

- > The 4.5-hour time window for tPA treatment significantly limits patient eligibility
- > ~90%¹ of patients can reach the hospital emergency department within 24 hours



Human Urinary KLK1 (HUK): Safe and Efficacious Treatment for AIS

HUK guided DM199 development, informing optimal dosing, target patients, & treatment protocols

> HUK for AIS:

- Marketed by Shanghai Pharmaceuticals under Kailikang®.
- Ameliorates neurological symptoms with few adverse events.¹

> Up to 1 million AIS patients treated yearly in China

- Included in National Basic Medical Insurance in 2020.²

> >200 clinical studies demonstrating efficacy including:

- Improved stroke patient outcomes: mRS, NIHSS and BI.
- MRI Imaging: ↑ blood flow, ↑ blood vessels, ↓ ischemia in the penumbra, and ↓ infarct size.
- Reduced stroke recurrence.

1. *Journal of International Medical Research*, 48(3) 1-10, 2020; <https://journals.sagepub.com/doi/full/10.1177/0300060520943452>
2. Shanghai Pharma/Technoo; website: <http://www.technoo.com.cn/jress/j/5683e82535436541805af75>



Meta Analysis



Journal of International Medical Research
48(3) 1-10
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DOI: 10.1177/0300060520943452
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Efficacy and safety of human urinary kallidinogenase for acute ischemic stroke: a meta-analysis

Abstract

Objective: Human urinary kallidinogenase (HUK) is a glycoprotein extracted from human urine that is used to treat stroke by triggering positive regulation of the kallikrein-kinin system. Our aim was to evaluate the efficacy and safety of HUK treatment for acute ischemic stroke.

Methods: We searched the online databases PubMed, Embase, Cochrane Library, Google Scholar, and China National Knowledge Infrastructure (CNKI) for papers published between January 2015 and December 2019. The quality of each trial was assessed using the Cochrane Reviewers' Handbook. Randomized controlled trials of HUK in patients with acute ischemic stroke were included.

Results: Sixteen trials with 1326 participants were included. The HUK injection groups had more neurological improvement than the control groups in National Institutes of Health Stroke Scale scores (mean difference, -1.65; 95% confidence interval [CI], -2.12 to -1.71) and clinical efficacy (1.30; 95% CI, 1.21 to 1.41). Subgroup analysis indicated that age may influence heterogeneity. Eleven trials reported adverse effects and there were no significant differences between the control and HUK groups (risk difference, 0.01; 95% CI, -0.02 to 0.04).

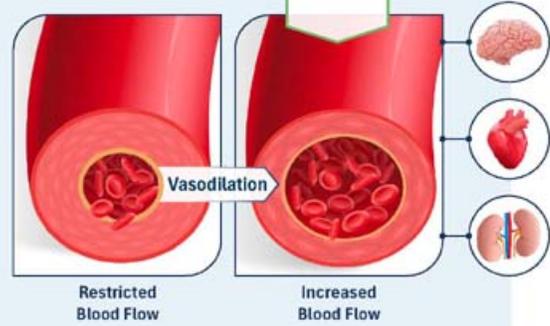
Conclusions: HUK ameliorates neurological symptoms in stroke patients with few adverse effects. Further high-quality, large-scale randomized trials are needed to confirm these results.

DM199 (rhKLK1 – Rinvcalinase Alfa) Novel Mechanism of Action

Increased perfusion and other cardiovascular benefits

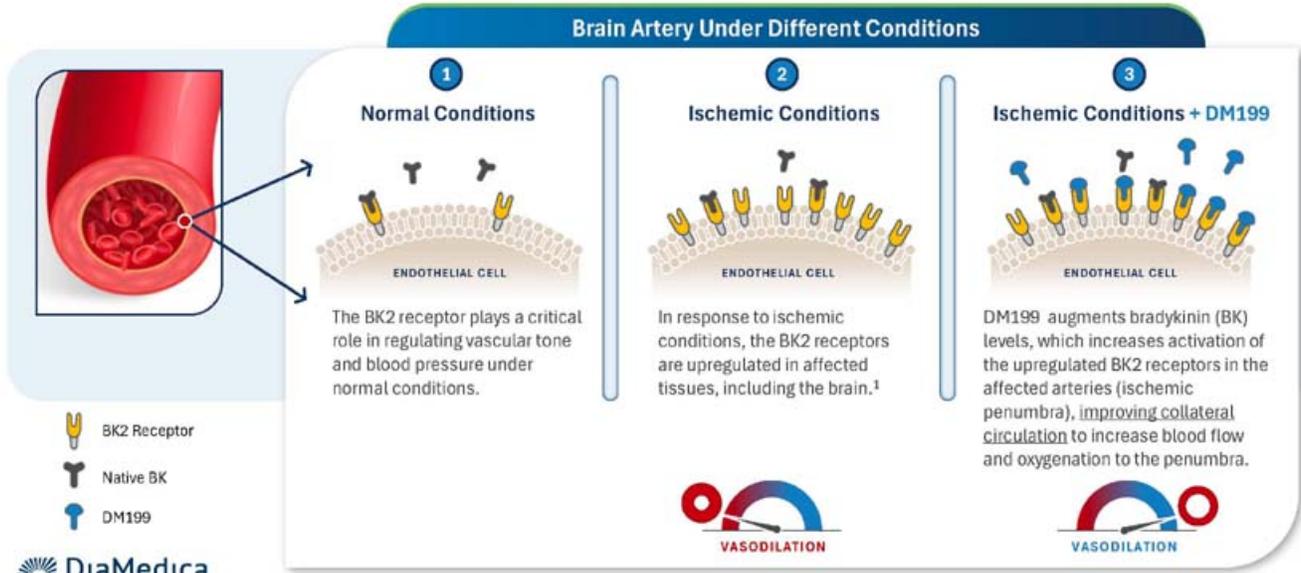


- > KLK1 is made predominately in kidneys (present also in the vasculature and brain) and circulates in the blood.
- > KLK1 acts on low molecular weight kininogen to produce bradykinin.
- > KLK1 is the main bradykinin forming enzyme within organs and blood vessels during resting conditions.¹
 - ACE is the main kinin-inactivating enzyme in the circulation.
- > Bradykinin binds to bradykinin 2 receptors (BK2R) on arterial endothelium to release nitric oxide (NO) & prostacyclin (PGI₂).
- > Increased NO and PGI₂ via cGMP and cAMP, respectively, relax arterial smooth muscle cells driving vasodilation.



Ischemia Naturally Induces Upregulation of Bradykinin 2 (BK2) Receptors

DM199 enhances BK2 receptor activation to promote focal vasodilation in the penumbra



¹ PLOS ONE, June 18, 2018; <https://doi.org/10.1371/journal.pone.0198053>

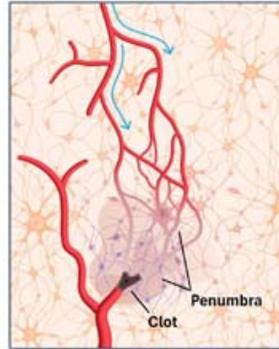
DM199 (rhKLK1): Improve Collateral Circulation in Acute Ischemic Stroke

Novel mechanism with potential to improve stroke outcomes & reduce risk of stroke recurrence

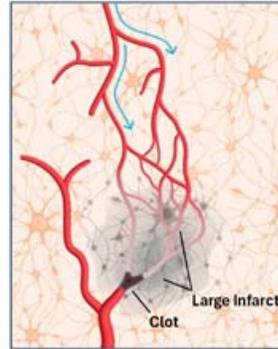
DM199 does **not** need to pass the blood-brain barrier to deliver therapeutic benefit.

DM199 facilitates release of endothelial nitric oxide and prostacyclin to preferentially vasodilate arteries in the ischemic penumbra and increase collateral blood flow.

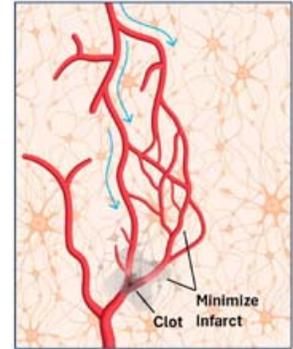
Early Stroke



No DM199 treatment



DM199 treatment

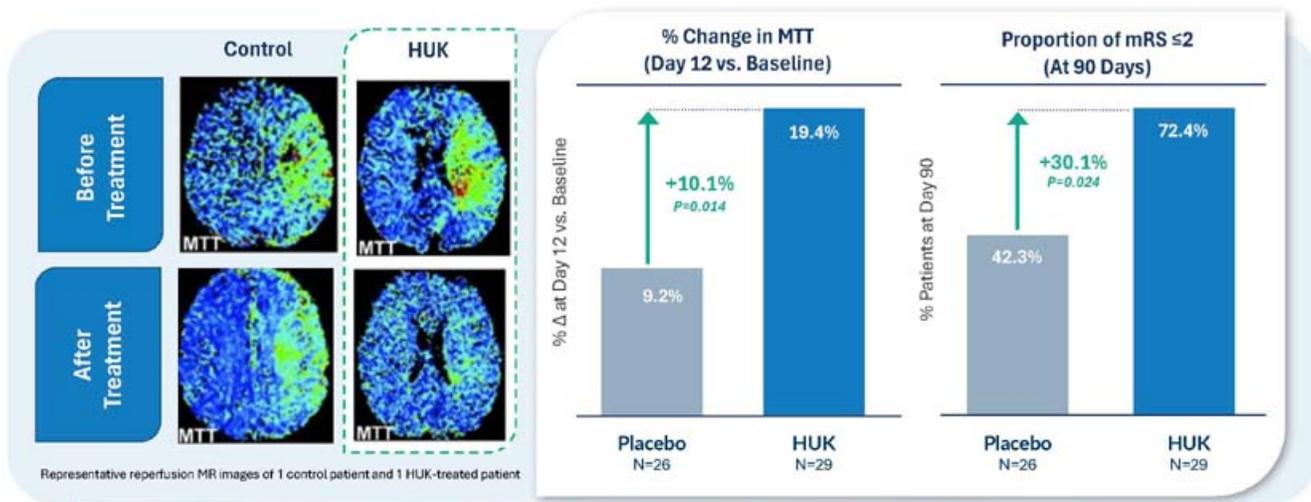


› **Improve stroke outcomes –**
save cerebral tissue in the ischemic penumbra
reducing the size and impact of the stroke

› **Reduce risk of stroke recurrence –**
improved collateral blood flow reduces the
risk of arterial re-occlusion (stroke)

Human Urinary KLK1 (HUK) Improved Cerebral Blood Flow and Stroke Outcomes

MTT (Mean Transit Time) assesses blood flow velocity in the brain of AIS patients



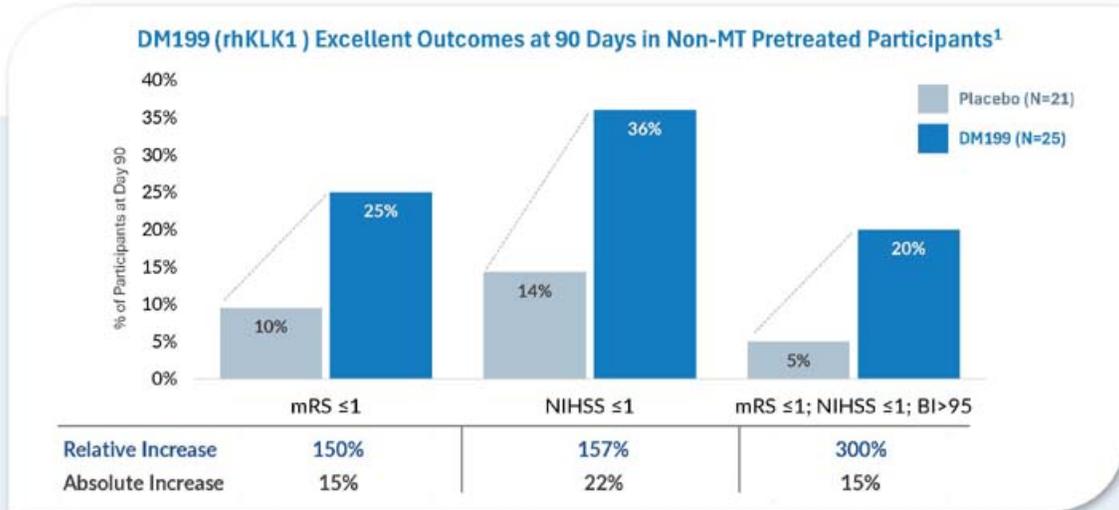
Improved relative MTT associated with favorable functional outcome OR=0.483 95% CI (0.243-0.960) p=0.038¹



Journal of Stroke and Cerebrovascular Diseases, Vol. 24, No. 8 (August), 2015: pp 1730-1737
 1. Based on univariate regression analysis per 20% improvement

DM199(rhKLK1) Phase 2 Results: Improved Excellent Outcomes in Non-MT Subgroup

Patient population closely aligns with ReMEDy2 Phase 2/3 trial



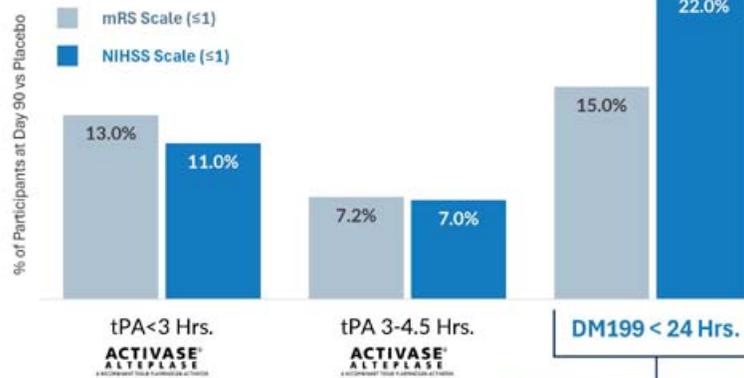
DM199 (rhKLK1) Phase 2 AIS Results Compared with Published tPA Data

Clinically relevant outcomes with DM199 extending treatment window 5X longer

- > tPA (Activase®) approved for AIS in 1996
 - Narrow 4.5-hour treatment window with greater efficacy ≤3 hours
 - ↑5.8% intracranial hemorrhage
- > No other FDA approved therapeutics
- > Human Urinary KLK1 (**Kailikang®**) improvement in excellent outcomes studies comparable to **DM199** Phase 2 trial

Comparison of Improvements in % of Participants with Excellent Outcomes (NIHSS ≤1 and mRS ≤1) vs Placebo

(DM199 and tPA analysis excludes MT treated participants)



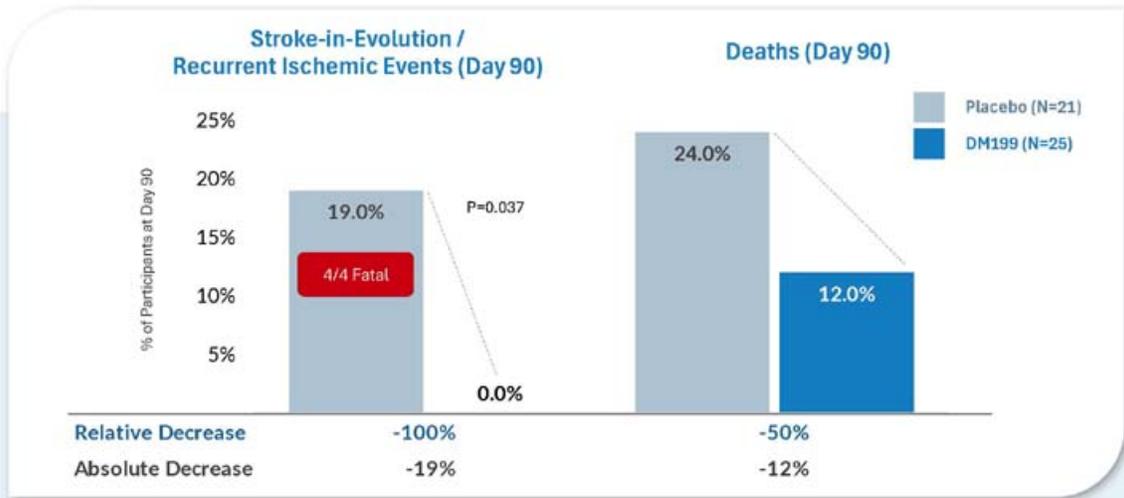
5X time expansion vs. tPA

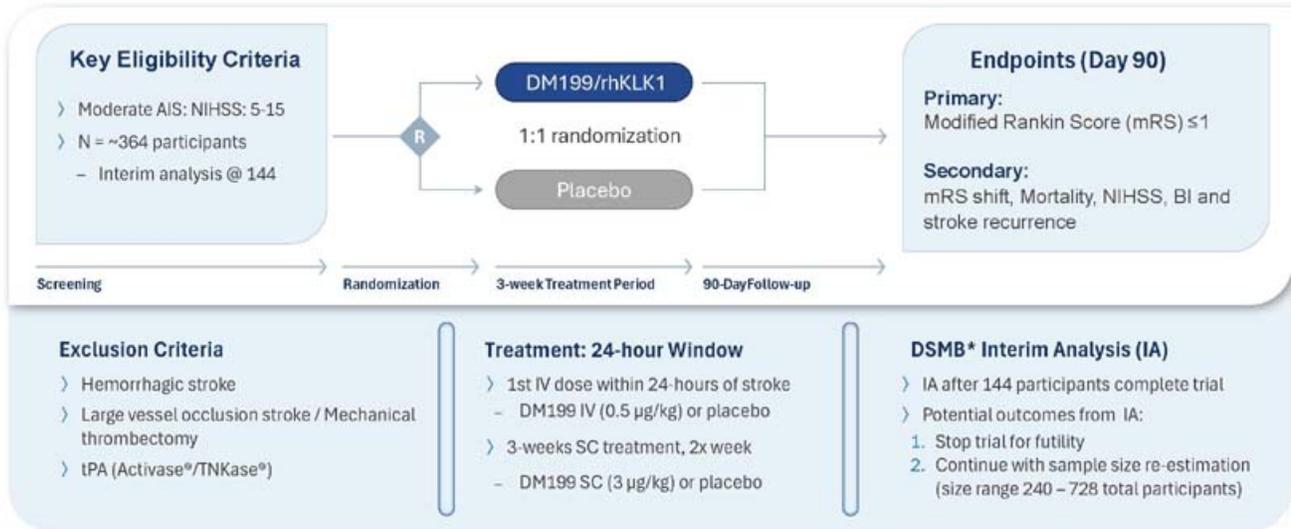


1. N Engl J Med 1995; 333:1501-1508; and N Engl J Med 2008 Sep 25; 359(13):1317-2; associated with 5.8% absolute increase in intracranial hemorrhage, Phase 3 N=333
 2. N Engl J Med 2008 Sep 25; 359(13):1317-2; associated with 9.4% absolute increase in intracranial hemorrhage, N=821
 3. Globaldata report July 2018: Acute Ischemic Stroke: Global Drug Forecast and Market Analysis to 2027

DM199 (rhKLK1) Phase 2 AIS Results: Reduced Stroke Recurrence & Deaths

Supporting secondary endpoints in non-MT pretreated subgroup





Preeclampsia



Preeclampsia: Significant Unmet Medical Need

No FDA approved therapies for preeclampsia



Disease Overview

- › Preeclampsia is a life-threatening high blood pressure disorder that occurs only during pregnancy and the postpartum period.
- › Preeclampsia and related hypertensive disorders of pregnancy are usually marked by a rapid spike in blood pressure, potentially causing seizures, stroke, multiple organ failure, and even death of the mother and/or baby.
- › The only way to stop disease progression is to deliver the fetus and placenta, **often prematurely**

Market Opportunity

- › Preeclampsia and related hypertensive disorders of pregnancy affect 5-8% of all births in the U.S., impacting approximately 180,000 to 300,000 patients annually^{1,2}
- › Pre-term preeclampsia (<34 weeks gestation) is among the most severe subtypes of preeclampsia, and there are up to 30,000 patients annually in the U.S.³ (has qualified for orphan designation)
- › DiaMedica is initially targeting preterm preeclampsia

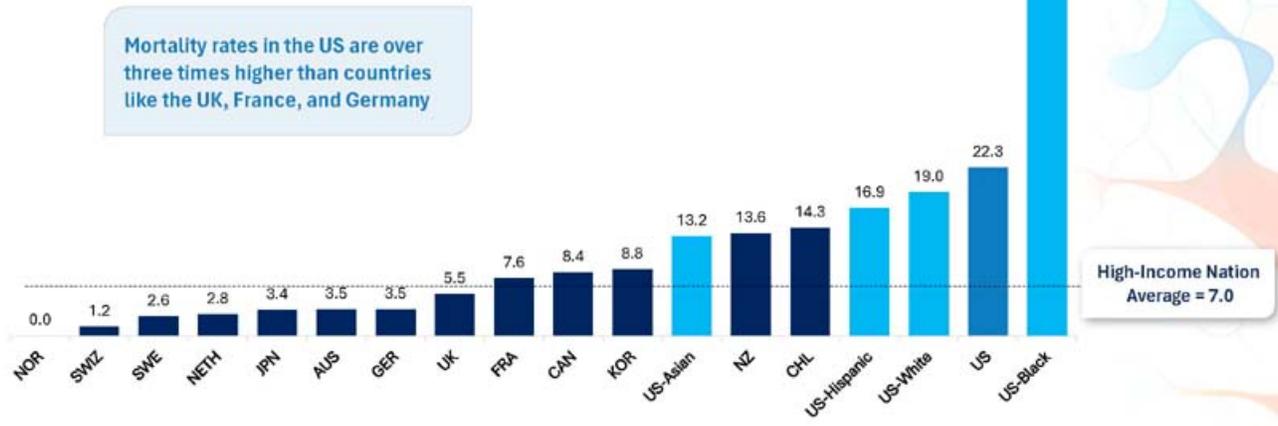


1. Preeclampsia Foundation, "What is Preeclampsia" Accessed June 10, 2024. <https://www.preeclampsia.org/what-is-preeclampsia>
2. Centers for Disease Control and Prevention. [n.d.]. Births and natality. National Center for Health Statistics.
3. Dimitriadis, E., Rahnik, D.L., Zhou, W. et al. Pre-eclampsia. *Nat Rev Dis Primers* 9, 8 (2023). <https://doi.org/10.1038/s41572-023-00417-6>

US Has Highest Maternal Death Rate Among High-Income Nations

US Black women disproportionately impacted - mortality rate >7x High-Income Nation average

Maternal deaths per 100,000 live births



Munira Z. Gunja et al., *Insights into the U.S. Maternal Mortality Crisis: An International Comparison* (Commonwealth Fund, June 2024). <https://doi.org/10.26099/cftrn-s175>

Strong Rationale for DM199 in Treating Pregnancy Complications

Potential disease modifying therapy



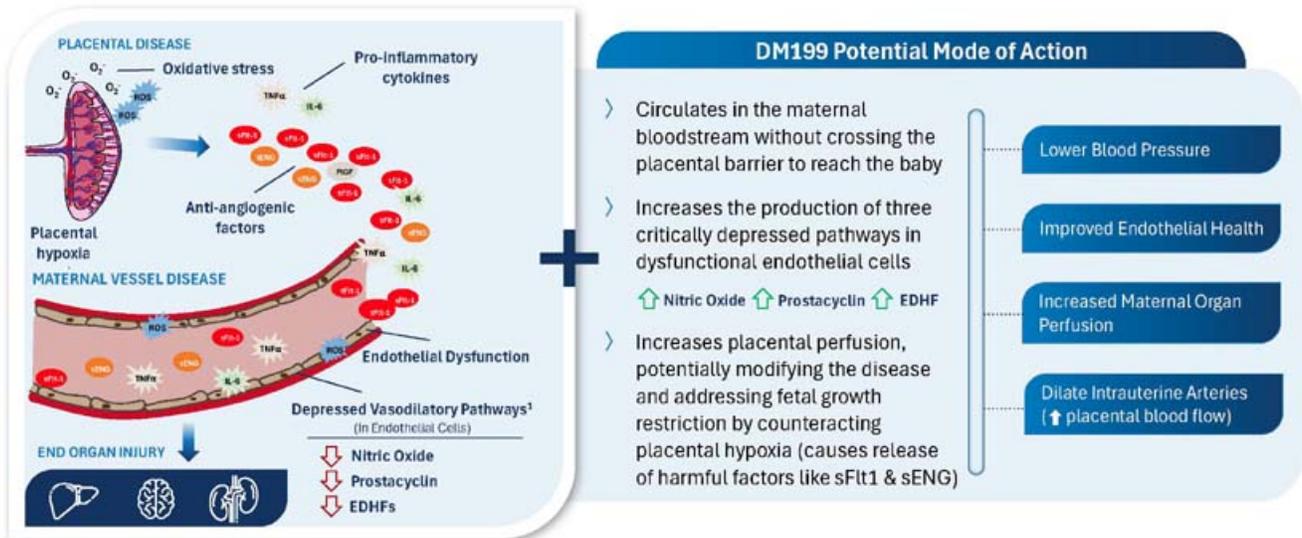
- › DM199's novel MOA addresses several pathophysiological mechanisms of preeclampsia and has the potential to be disease modifying
- › DM199 has not been shown to cross placental barrier
- › Completed full battery of preclinical reproductive toxicology tests which support advancing to human study
- › KLK1 initially discovered as an anti-hypertensive agent
- › Strong reductions in blood pressure in Phase 2 CKD trial
- › DM199 dose limiting tolerability is hypotension
- › A main cause of abnormal placentation and endothelial dysfunction in PE is the reduced bioavailability of nitric oxide¹ – DM199 facilitates the release of endothelial nitric oxide



1. P. Guiray et al. Role of oxidative stress in the dysfunction of the placental endothelial nitric oxide synthase in preeclampsia. *Redox Biology* (2021)

DM199 Mode of Action in Preeclampsia

Targeting both upstream placental hypoxia & downstream endothelial dysfunction and blood pressure

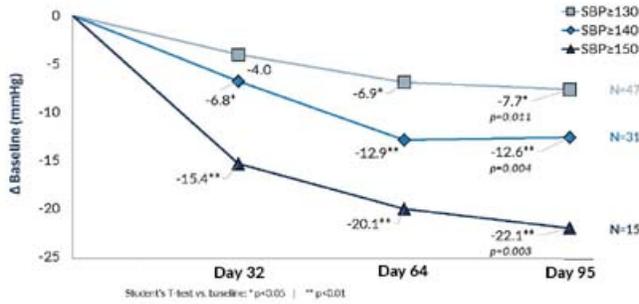


EDHF = Endothelium-derived hyperpolarizing factor sFlt1 = Soluble fms-like tyrosine kinase-1 sENG = Soluble endoglin IL-6 = Interleukin 6 ROS = Reactive oxygen species TNF-α = Tissue necrosis factor alpha

1. Goulopoulou, S. Maternal Vasc. & Plac. Physiology in Preeclampsia. Hypertension. 2017;70:1086-1073
<https://doi.org/10.1161/HYPERTENSIONAHA117.09821>

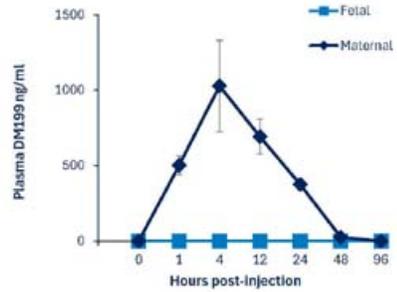
DM199 Shown to Reduce Blood Pressure and Not Cross Placental Barrier

DM199 Phase 2 CKD Trial – Change in Blood Pressure



Statistically significant reductions in systolic blood pressure (SBP) observed in participants with baseline levels ≥ 130 mmHg, with greater reductions seen at higher baseline levels: ≥ 140 mmHg and ≥ 150 mmHg.

Placental Transfer Study*

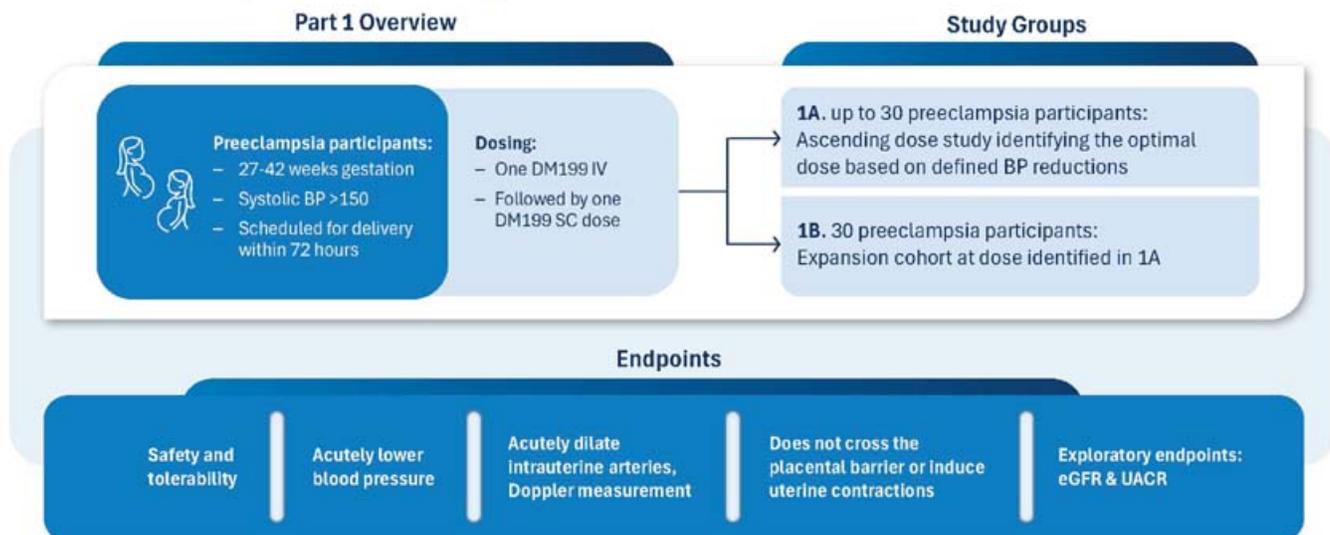


DM199 was not detected in fetal plasma, while a clear dose-response was observed in maternal plasma

*Assay values below limit of quantification shown as zero

Planned DM199 Preeclampsia Phase 2 Trial (Tygerberg Hospital in Cape Town, South Africa)*

Part 1: Women planned for delivery in 72 hours

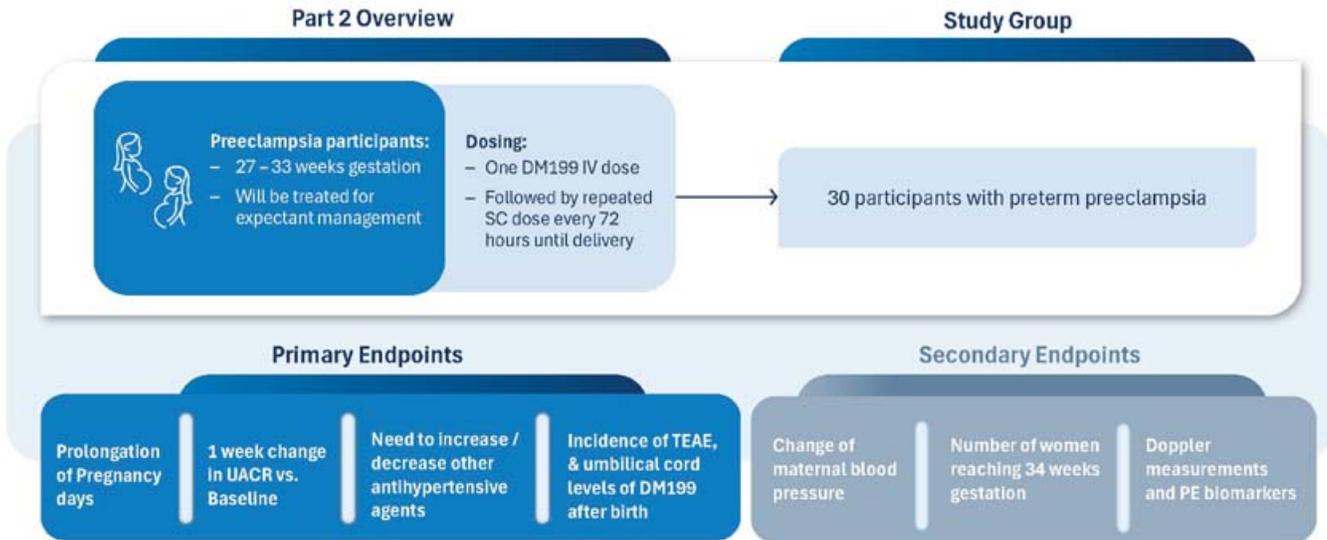


*Subject to final hospital ethics committee and South African Health Products Regulatory Authority approval
BP: Blood pressure; SC: Subcutaneous

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Planned DM199 Preeclampsia Phase 2 Trial*

Part 2: Expectant management



* Subject to final hospital ethics committee and South African Health Products Regulatory Authority approval

TEAE: Treatment Emergent Adverse Event UACR: Urine Albumin-Creatinine Ratio SC: Subcutaneous

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Corporate Summary



DM199 (Rinvecalinase Alfa) Multi-layered IP and Exclusivity Position

Key manufacturing challenges solved: protein activity, stability and economical scale

Protein Development & Trade Secrets

DM199 (rhKLK1): Excellent Enzymatic Activity & Highly Scalable

- › Configuration of high & low molecular weight glycoforms critical for optimal activity
- › Reproducible manufacturing process
- › Modification of 2 inert amino acids enhances manufacturability
- › 5+ companies unsuccessful in moving rhKLK1 proteins to the clinic
- › Numerous key manufacturing steps kept as trade secrets

Patents and Exclusively Licensed Technology

Patents¹

- › **Composition of matter**
 - Issued US/EU (2033)
- › **Formulation, subcutaneous and improved PK**
 - Issued US (2033)
- › **Dosing & route of delivery**
 - Issued US (2038) / pending global

Exclusive license of patented gene expression technology for KLK1

- › Reliable, high-expressing technology
- › Economical, commercial scale/yields

Regulatory Exclusivity

In the US, anticipate 12 years' data exclusivity for biologics

- › Regulatory counsel has confirmed this is a reasonable expectation

Exclusivity protections outside of the U.S. for Biologics:

- › **EMA:** Up to 10 years
- › **Japan:** Up to 8 years



¹ One patent eligible for regulatory patent term extension up to five years

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Leadership

Rick Pauls, President & CEO

CEO of DiaMedica since 2010. Former venture capitalist with two funds, including co-founder and managing director of life sciences fund and early investor in DMAC.

Lorianne Masuoka, MD, Chief Medical Officer

25+ years experience building and expanding high value pipelines in the biopharmaceutical industry that have resulted in drug approvals and strategic alliances, including CMO roles at Epygenix, Marinus, Cubist (Merck) and Nektar.

Scott Kellen, CPA, Chief Financial Officer

25+ years in life sciences industry. CPA (inactive), held senior leadership roles including CFO and COO for several private & public (Nasdaq) companies.

Ambarish Shah, Ph.D., Chief Technology Officer

25+ years experience in CMC leadership roles at Pfizer, GSK, AZ, BMS and CSL Behring, with key contributions to 50+ pipeline drugs and multiple successful BLAs.

Dominic Cundari, Chief Commercial Officer

30+ years pharma experience. Led product launches with tPA (Activase®) for acute ischemic stroke and Lucentis® for retinal diseases at Genentech.

David Wambeke, Chief Business Officer

15+ years life sciences / biotech investment banking experience. Completed more than 100 financings and M&A transactions. US Army Purple Heart Recipient.



Board of Directors

Richard Pilnik, Chairman of the Board

30+ years in executive commercial roles at Eli Lilly, Quintiles. President Vigor Medical Services.

Michael Giuffre, MD

Clinical Professor of Cardiac Sciences and Pediatrics at University of Calgary. CSO, COB of FoodCheck Systems, Inc.

Richard Kuntz, M.D., M.Sc.

25+ years in life sciences most recently serving as Chief Medical Officer and Chief Scientific Officer for Medtronic where he held the position for over ten years.

Tanya Lewis

25+ years in regulatory drug development experience including approvals of five drugs. Most recently Chief Development Operations Officer at Replimune.

James Parsons

20+ years as a life sciences CFO for several companies. Former CFO Trillium Therapeutics (Acquired by Pfizer for ~\$2.2B).

Rick Pauls

See Leadership for details.

Charles Semba, M.D.

20+ years drug development experience at Genentech where he led development of Activase® and Lucentis®, Shire, ForSight VISION5, and Graybug. Currently CMO of Eluminex.

Company Overview

Cash: \$46 million
(as of March 31, 2024)

Lead Program: DM199 - Novel, Late-Stage Biologic Therapy

- › Recombinant KLK1 (rhKLK1) protein with FDA Fast-Track Designation
- › Enrolling pivotal AIS Phase 2/3 trial and planning preeclampsia Phase 2 trial

Acute Ischemic Stroke (AIS)

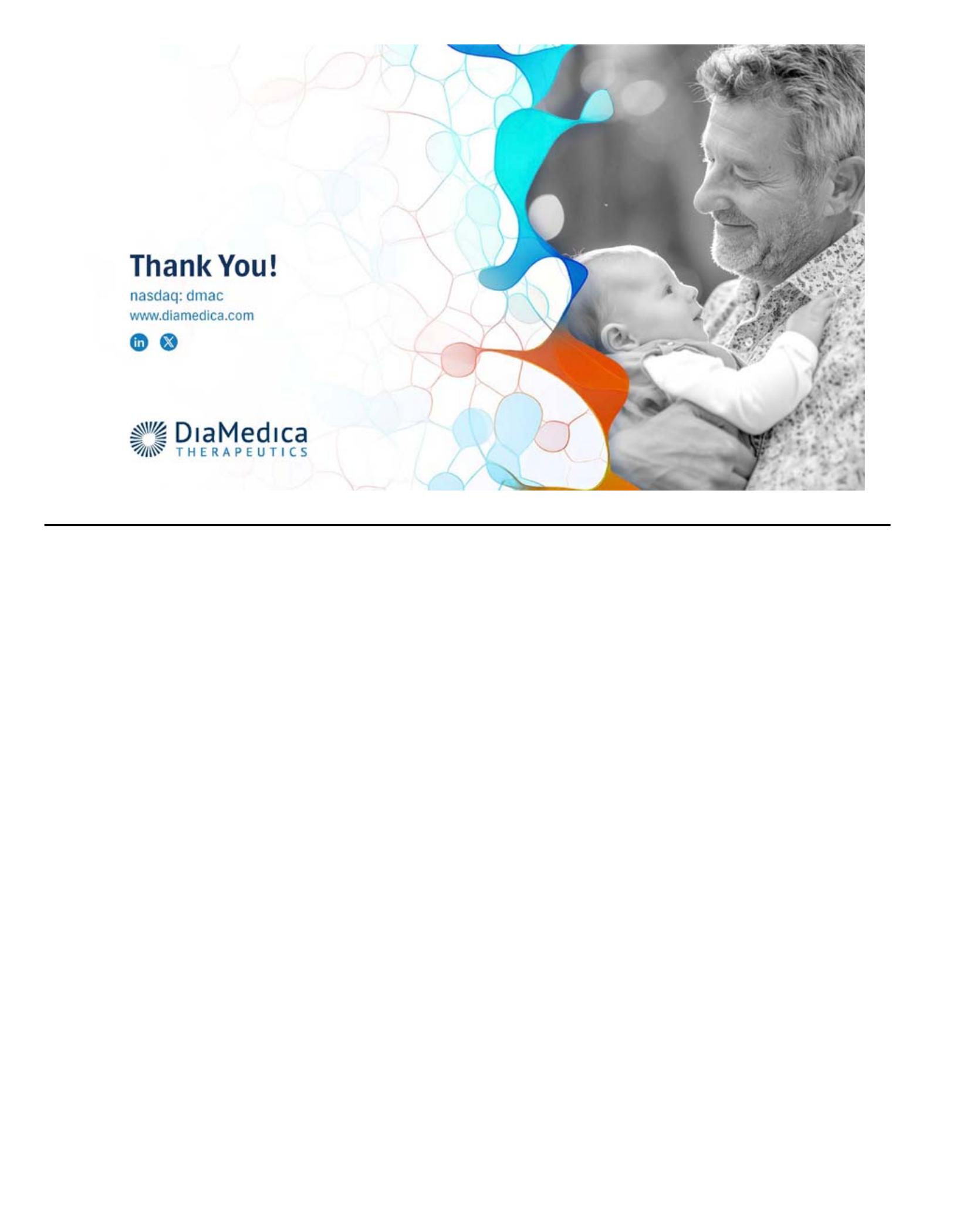
- › >\$10 billion US market opportunity
- › ~80% of patients have no treatment options today^{1,2}
- › Extensive clinical data supporting KLK1 safety and efficacy in AIS patients
 - Increases collateral circulation in the penumbra
 - Encouraging Phase 2 efficacy and safety data for DM199
 - Up to 1 million treated/year with human urinary KLK1 (HUK) in China³

Preeclampsia (PE) / Hypertensive Disorders of Pregnancy

- › Estimated multi-billion dollar US market opportunity
- › US has highest maternal death rate among high-income nations³
- › Potential disease modifying therapy
 - Strong evidence that DM199 lowers blood pressure
- › Key safety advantage: Unlike most-prescribed anti-hypertensives, DM199 is not expected to cross placental barrier due to its large molecular size



Sources: 1. Fassbender, K., et al (2013). Streamlining of prehospital stroke management: the golden hour. *The Lancet Neurology*, 12(6), 585-586. doi: 10.1016/S1473-4222(13)70078-5; 2. Kansagra AP, et al. Trends in Mechanical Thrombectomy for AIS in the US: A Nationwide Analysis from 2012 to 2016. *Stroke*. 2019;50(3):570-577. doi:10.1161/STROKEAHA.118.023600; 3. Shanghai Pharma/Tecpool website: <http://www.techpool.com.cn/press/5d83ed2235416641805a75>; 3. Manira Z, Gunja et al., Insights into the U.S. Maternal Mortality Crisis: An International Comparison (Commonwealth Fund, June 2024). <https://doi.org/10.26099/cfm.st75>



Thank You!

nasdaq: dmac
www.diamedica.com



DM199 Phase 2/3 AIS Trial Adaptations Based on Phase 2 Results



Aligned Study Population to Target Patient Responders from Phase 2 and HUK-Treated Population

- › Greater clinical benefit anticipated in patients who do not receive mechanical thrombectomy and/or tPA and moderate severity strokes

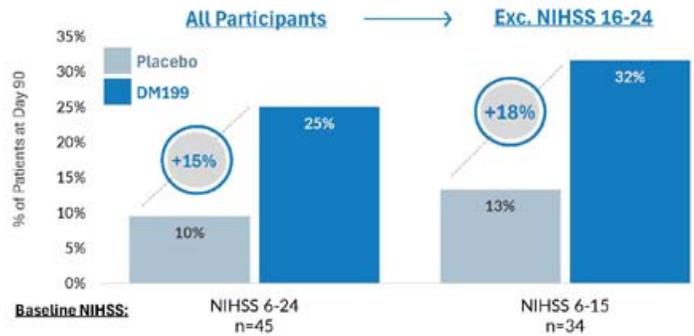
Reduce Baseline Stroke Severity:

- › Greater DM199 treatment effect vs placebo in less severe strokes.
- › Lowered NIHSS baseline inclusion range to 5–15 from 6–25 used in Phase 2 trial

Exclude: MT

- › Once clot is physically removed via catheter, blood flow is re-established and outcomes are very favorable
- › No observed efficacy improvement in DM199 phase 2 AIS mechanical thrombectomy sub-group
 - Genentech’s P3 TIMELESS study of Tenecteplase (tPA) also showed no improvement in MT Participants (May 2023)

% of ReMEDy1 Participants with mRS ≤1 at 90 Days (Non-MT subgroup)^{1,2}



1. One participant on DM199 did not have a day 90 follow-up visit. This participant had a day 22 NIHSS of 1 and has been excluded from the analysis.
 2. Post hoc analysis of participants not receiving mechanical thrombectomy (MT) prior to enrollment in the ReMEDy1 trial.



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, Minnesota – June 26, 2024 (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 Phas 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 Profesor 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 \geq 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 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, Profosor 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 trialists 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 ReMEDy2 AIS clinical trial,” commented Lorianne Masuoka, 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/3J46BqcBGXV>
 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 passcode: 53747#.

About Preeclamsia

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 eclampsia, 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 (AIS) 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 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. 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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