Corporate Presentation

July 2025

DiaMedica THERAPEUTICS

Transforming Care for Preeclampsia and Stroke

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," "could," "seek," "might," "project," "target," "aim" 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 of 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, uncertainties relating to risks and uncertainties relating to DiaMedica's clinical expansion into preeclampsia, the ability of its physician collaborators to successfully conduct a Phase 2, proof-of-concept trial of DM199 as a treatment for preeclampsia, DiaMedica's reliance on its physician collaborators and the ability of other investigators to repeat the interim top-line results; 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 preeclampsia or ReMEDy2 trials; DiaMedica's plans to develop, obtain regulatory approval for its DM199 product candidate for the treatment of preeclampsia and acute ischemic stroke and its expectations regarding the benefits of and potential market size for DM199 in these indications; DiaMedica's ability to conduct successful clinical testing of DM199 within its anticipated parameters, including targeted enrollment numbers, costs and timeframes, and, with respect to the ReMEDy2 trial, the adaptive design and the possibility that other aspects of the trial could change depending upon additional input from the FDA and the blinded interim analysis; the potential impact of ongoing hospital and medical facility staffing shortages on DiaMedica's clinical 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 acute ischemic stroke and/or 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, 2024, 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, 2025.

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OUR MISSION

Life-transforming Therapy

for Patients with Severe Ischemic Diseases

01 Preeclampsia (PE)

02 Acute Ischemic Stroke (AIS)

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Company Overview

Cash: $37 million
(March 31, 2025)

Runway into Q3 2026*
No warrants and no debt

**As of 5/14/2025 conference call*

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

- Recombinant KLK1 (rhKLK1) protein with FDA Fast-Track Designation
- IP until '39 (+ potential 5-year ext.) & expected 12 years regulatory exclusivity
- >300 patients have been dosed with DM199 across multiple studies

Preeclampsia (PE) and Fetal Growth Restriction (FGR)

- $5B+ U.S. market opportunity for Early-Onset PE and FGR
- No FDA approved treatment options
- Phase 2 PE interim results: DM199 significantly lowered blood pressure and dilated intrauterine arteries without crossing the placental barrier
- DM199 is a potential disease-modifying therapy aimed at increasing placental perfusion, reducing blood pressure and improving endothelial function

Acute Ischemic Stroke (AIS)

- >$10 billion US market opportunity
- ~80% of patients have no treatment options today[1, 2]
- Extensive clinical data supporting KLK1 efficacy and safety in AIS patients
  - Increases collateral circulation in the penumbra following stroke
  - DM199 showed encouraging Phase 2 efficacy and safety data
  - Human urinary KLK1 (HUK) treats up to 1 million patients/year in China[3]

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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/S1474-4422(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/Techpool website: http://www.techpool.com.cn/press/r/5ddf3ed2535416541805af75 ; 3. 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/cthn-st75

DiaMedica Pipeline

COMPOUND	INDICATION	PRECLINICAL / PHASE 1 / PHASE 2 / PHASE 2/3	UPCOMING MILESTONES
DM199 (rinvecalinase alfa) Recombinant KLK1	**Preeclampsia**	Phase 2*: Part 1A Dose-Selection / Part 1B Expansion Cohort	Part 1A ✓
		Phase 2*: Parts 2 & 3 Expected Management Study	FPI 2025
	Fetal Growth Restriction	Phase 2 Study	FPI 2025
	Acute Ischemic Stroke	ReMEDy2 Pivotal Phase 2/3 Study	Anticipated **Interim Analysis 1H '26***
DM300 Recombinant serine protease inhibitor	**Severe Acute Pancreatitis**		

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* Investigator sponsored trial

Preeclampsia

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Early-Onset PE and FGR: Severe Conditions with a $5B+ U.S. Market

Disease Overview

- **Preeclampsia (PE):** A life-threatening high blood pressure disorder accompanied by multi-system organ damage that occurs only during pregnancy.
  - Early onset PE is a severe sub-type that occurs before 34 weeks of pregnancy where **50% of deliveries are driven by refractory hypertension despite maximal intervention**[6].
  - There are currently **no disease modifying therapies** approved for PE.
- **Fetal Growth Restriction (FGR)**: A condition where a baby is not growing as expected, often due to **preeclampsia** or other complications.

Annual Incidence in U.S.

325,000+
FGR & PE[1,2]

~200,000
PE[2]

~30,000
Early onset PE[3,4]

+

~20,000
Early onset FGR[5]*

INITIAL TARGETS

*FGR Only

1. Baschat et al. (2021). FIGO initiative on fetal growth: Best practice advice for screening, diagnosis, and management of fetal growth restriction. *International Journal of Gynecology & Obstetrics*, 152(S1), 3-12.
2. Chappell, L. C., et al. (2021). Pre-eclampsia. The Lancet, 398(10297), 341–354.
3. Teka, H., et al. (2023). Clinical presentation, maternal-fetal, and neonatal outcomes of early-onset versus late onset preeclampsia-eclampsia syndrome in a teaching hospital in a low-resource setting: A retrospective cohort study. PloS one, 18(2), e0281952.
4. E., G., Akurati, et al. (2018). Early onset and late onset preeclampsia-maternal and perinatal outcomes in a rural teritiary health center. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 7(6), 2266–2269.
5. Dall'Asta, A., et al. (2017). Early onset fetal growth restriction. Maternal health, neonatology and perinatology, 3, 2.
6. Paidas, M. J., et al. (2020). Prospective, randomized, double-blind, placebo-controlled evaluation of the pharmacokinetics, safety, and efficacy of recombinant antithrombin versus placebo in preterm preeclampsia. American Journal of Obstetrics & Gynecology, 223(5), 739.e1-739.e13.

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Limited and Insufficient Preeclampsia Treatments – A Major Unmet Need

- **There are no disease modifying agents currently available for preeclampsia**
- ***First-line antihypertensives, ACE inhibitors and ARBs, are CONTRAINDICATED in pregnancy***

Medication	Drug	Comments
Anti-Hypertensives	**Alpha-blocker** **Beta-blocker** **Calcium Channel blockers**	Reduce blood pressure and stroke risk Do **not** improve systemic endothelial dysfunction
Anti-Seizure	**Magnesium Sulphate**	Reduce risk of seizure (eclampsia)
Fetal Lung Maturity	**Corticosteroids**	Prepare the baby for early birth

The only cure for preeclampsia is delivery of the fetus and placenta

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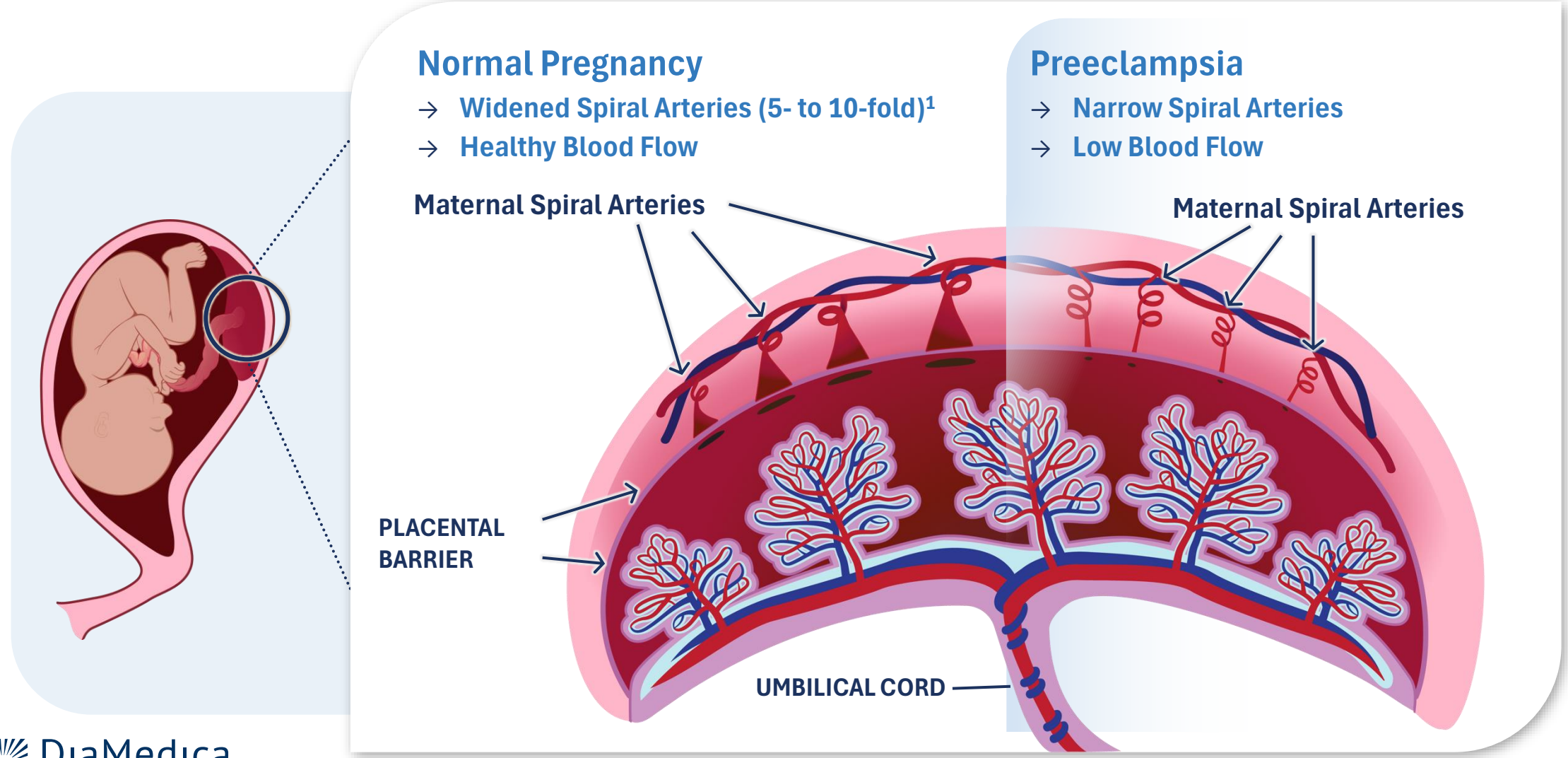
Stage 1 of Preeclampsia: Placental Disease

Inadequate spiral artery development in the first trimester leads to placental hypoxia



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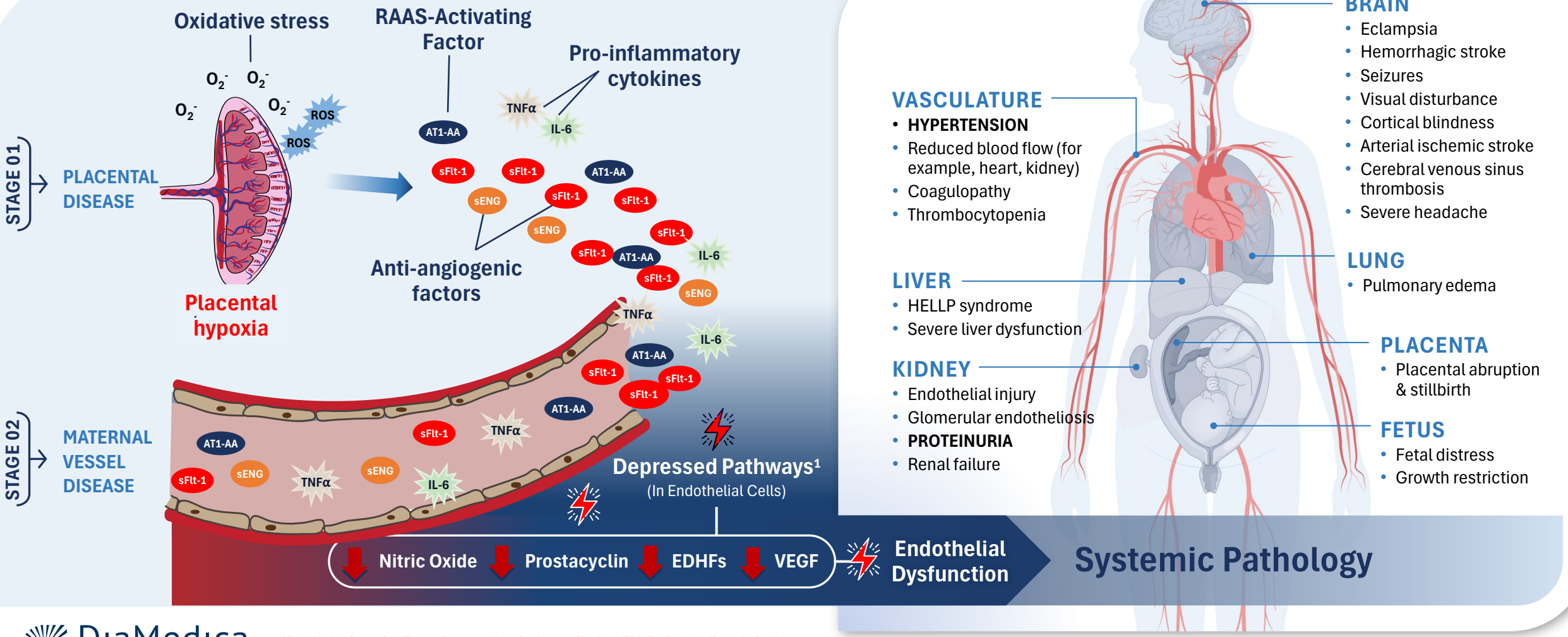
1. Staff, A. C., et al. (2022). Failure of physiological transformation and spiral artery atherosis: their roles in preeclampsia. *American journal of obstetrics and gynecology*, *226*(2S), S895–S906. https://doi.org/10.1016/j.ajog.2020.09.026

Stage 2 of Preeclampsia: Endothelial Dysfunction & Maternal Disease

Noxious factors released from the ischemic placenta cause endothelial dysfunction



AT1-AA = Angiotensin II Type 1 Receptor Agonist Autoantibody | EDHF = Endothelium-derived hyperpolarizing factor | sFlt-1 = Soluble fms-like tyrosine kinase-1 | sENG = Soluble endoglin | IL-6 = Interleukin 6 | ROS = Reactive oxygen species | TNF-α = Tissue necrosis factor alpha

Adapted from: *Nature Reviews Disease Primers | (2023) 9:8 1*

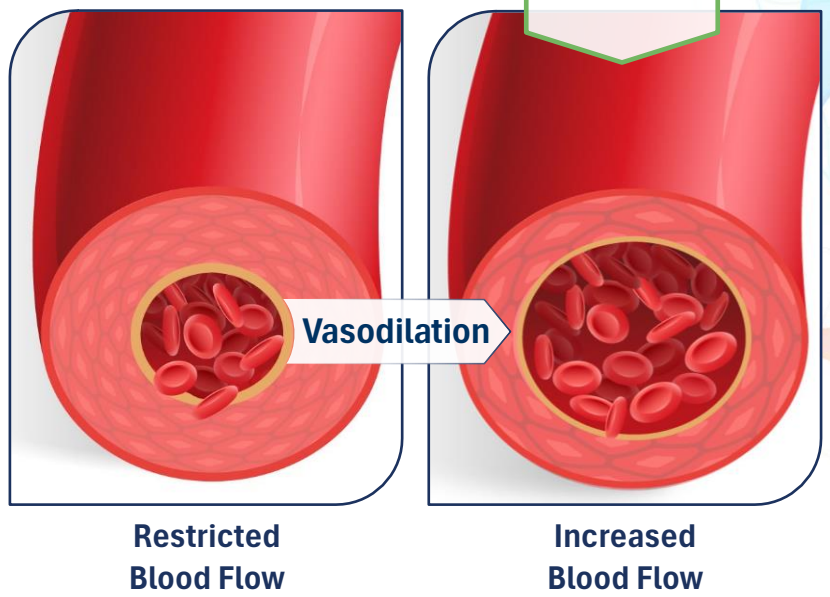
DM199 May Offer a Disease-Modifying Solution for Preeclampsia

DM199 produces all three major endothelial derived vasodilating factors through the bradykinin pathway

DM199 may address root causes of PE by improving:

- **Rapid and durable blood pressure control** through enhanced vasodilation, with the potential to prolong pregnancy, reduce neonatal complications, and lower maternal stroke risk
- **Placental perfusion** by dilating uterine arteries and promoting formation of new blood vessels, accelerating fetal growth
- **Endothelial health** through increased NO signaling and transactivation of VEGF bypassing the sFLT1 blockade

While offering a key safety benefit: Avoid crossing the placental barrier



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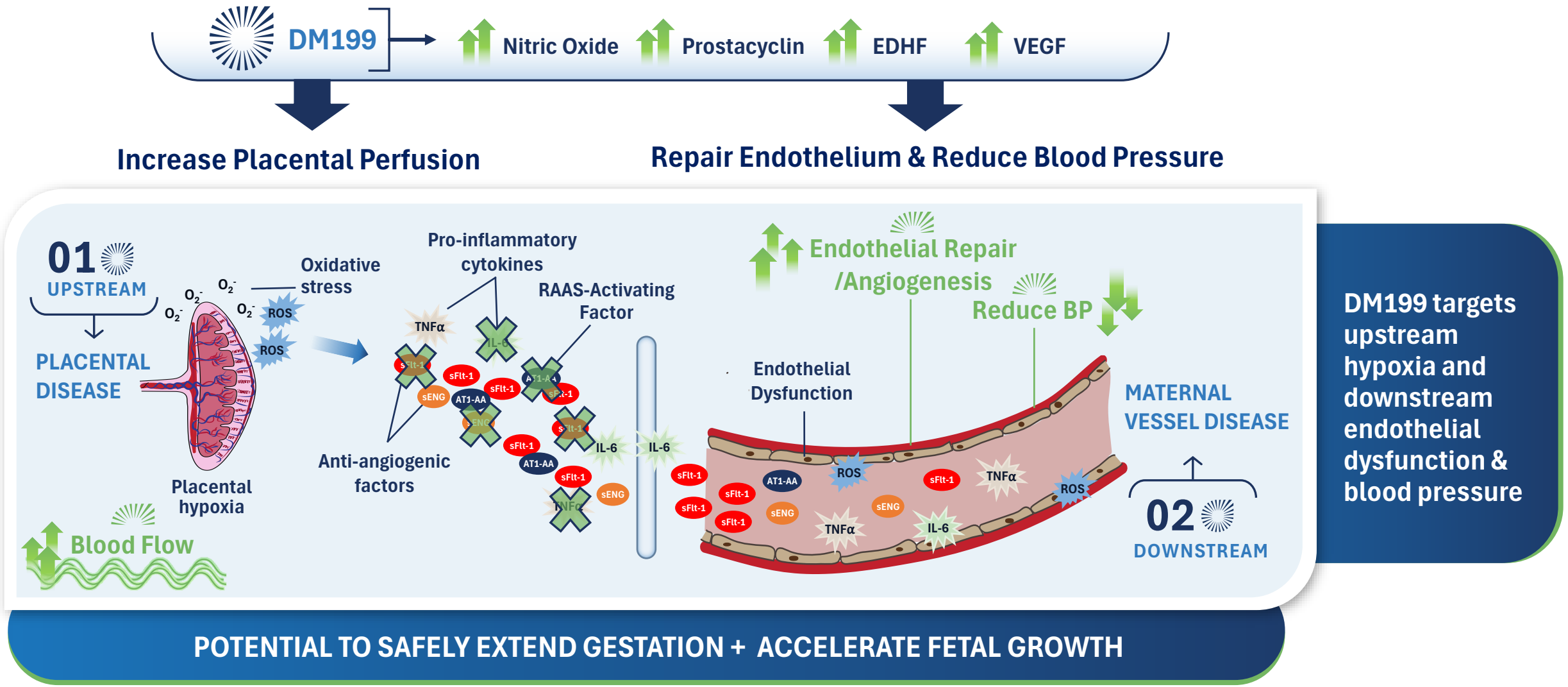
NO: Nitric Oxide
VEGFR2: Vascular Endothelial Growth Factor Receptor 2
cGMP: Cyclic Guanosine Monophosphate
cAMP: Cyclic Adenosine Monophosphate

DM199 Preeclampsia Potential Mode of Actions



DM199 targets upstream hypoxia and downstream endothelial dysfunction & blood pressure

POTENTIAL TO SAFELY EXTEND GESTATION + ACCELERATE FETAL GROWTH

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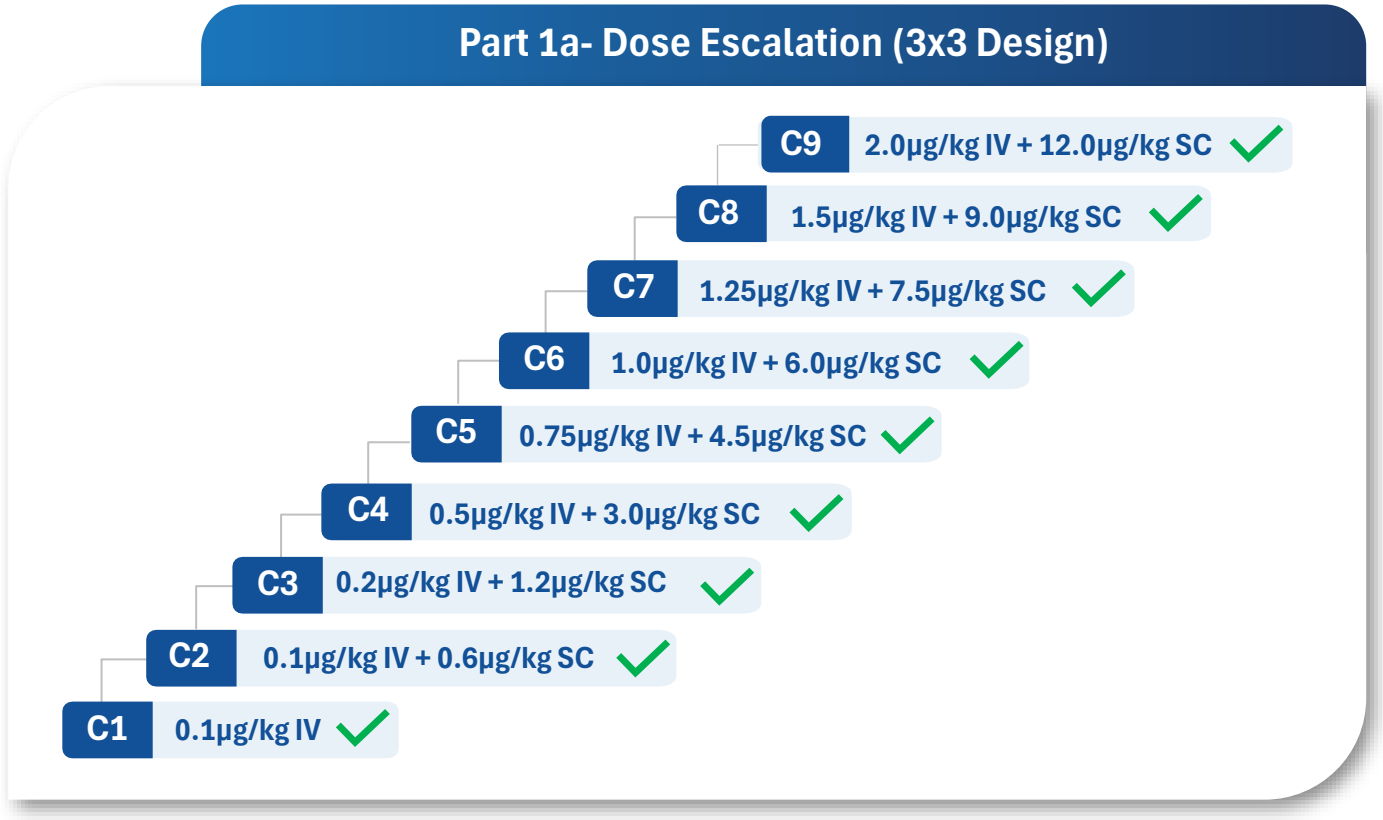
1. Goulopoulou, S. Maternal Vascular Physiology in Preeclampsia. *Hypertension*. 2017;70:1066-1073 https://doi.org/10.1161/HYPERTENSIONAHA.117.08821

DM199 Preeclampsia Phase 2 IST Trial – Part 1a

Women planned for delivery within 72 hours



- Study designed to assess DM199 placental transfer with minimal fetal exposure and to evaluate early blood pressure effects. Repeated dosing avoided to prevent prolonged fetal exposure if transfer occured. Limited dosing (one each IV & SC) minimized fetal exposure risk during this assessment.

Part 1 Overview

- 27-42 weeks gestation (singleton)
- >150 systolic blood pressure
  - Receiving standard of care
- <72 hours scheduled for delivery

Study Groups

- *1a.* Up to 30 preeclampsia participants
  - Ascending dose study identifying the optimal, medically relevant dose based on BP reductions
- *1b.* 30 preeclampsia participants. Expansion cohort at dose identified in 1A

Primary Endpoints:

- Safety and tolerability
  - Includes results of placental crossing analysis/assay
- Lower blood pressure

Key Exploratory Endpoint

- Dilation of uterine arteries (Doppler)

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Interim Phase 2 (Part 1a) Results

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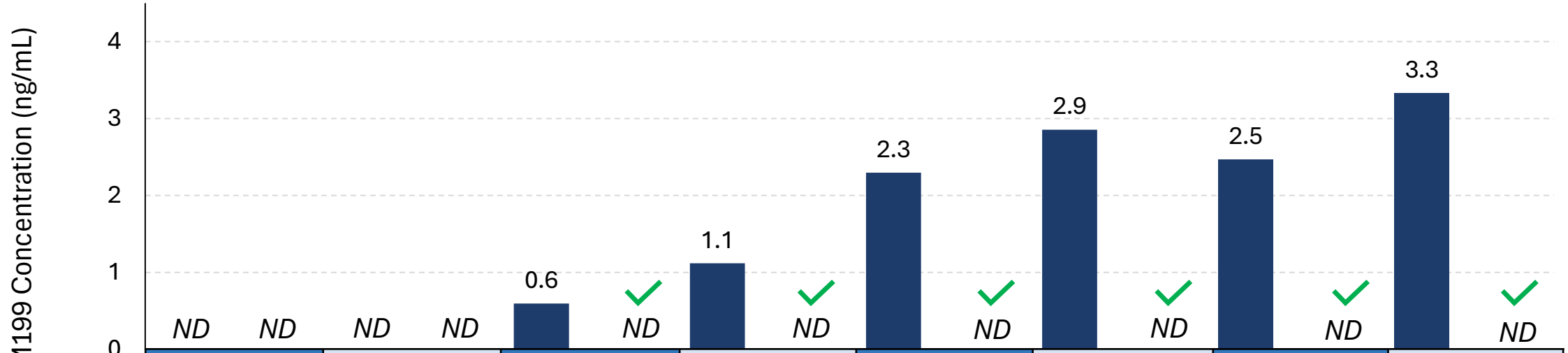
DM199 Was NOT Detected in Umbilical Cord Blood in Any Dose Cohort

- At delivery, DM199 was not detected in any cord blood samples, while a clear dose-dependent increase in DM199 was observed in maternal plasma.
- Data suggests DM199 does **not cross the placental barrier**, a potentially unique safety advantage.

Average Plasma DM199 Concentrations (Maternal and Cord Blood Samples At Delivery)



	C1[1] & C2		C3		C4		C5		C6		C7		C8		C9[2]	
	Mom	*Cord*	*Mom*	*Cord*	*Mom*	*Cord*	*Mom*	*Cord*	*Mom*	*Cord*	*Mom*	*Cord*	*Mom*	*Cord*	*Mom*	*Cord*
IV Dose(µg/kg)	*0.1 µg/kg*		*0.2 µg/kg*		*0.5 µg/kg*		*0.75 µg/kg*		*1.0 µg/kg*		*1.25 µg/kg*		*1.5 µg/kg*		*2.0 µg/kg*	
SC Dose(µg/kg)	*0.6 µg/kg*		*1.2 µg/kg*		*3.0 µg/kg*		*4.5 µg/kg*		*6.0 µg/kg*		*7.5 µg/kg*		*9.0 µg/kg*		*12.0 µg/kg*	

ND: Non-detectable concentrations – lower limit of quantification is <0.5 ng/mL IV= Intravenous SC=Subcutaneous

1. Did not receive SC dose
2. Data cut for placental transfer was 6/27/25 to allow for sample shipment and analysis. Results for the final C9 patient, enrolled on 7/1/25, are not available

DM199 Was Generally Safe and Well Tolerated

- No serious TEAEs were reported in response to any dose

Maternal Treatment-Emergent Adverse Events

TEAE	N=28 [n(%)]	Dose Cohorts
Nausea	4 (14%)	C8 (n=2), C9 (n=2)
Headache	3 (11%)	C3 (n=1), C6 (n=2)
Flushing	1 (4%)	C9

Expected Events Of Preeclampsia (per protocol definition)

Expected Event	N=28 [n(%)]	Dose Cohorts
Postpartum Hemorrhage	4 (14%)	C3 (n=2), C4 (n=1), C8 (n=1)
Eclampsia	1 (4%)	C1
HELLP Syndrome	1 (4%)	C4
Pulmonary Edema	1 (4%)	C9

- No events of hypotension
- No patient paused or discontinued treatment
- No induction of early labor

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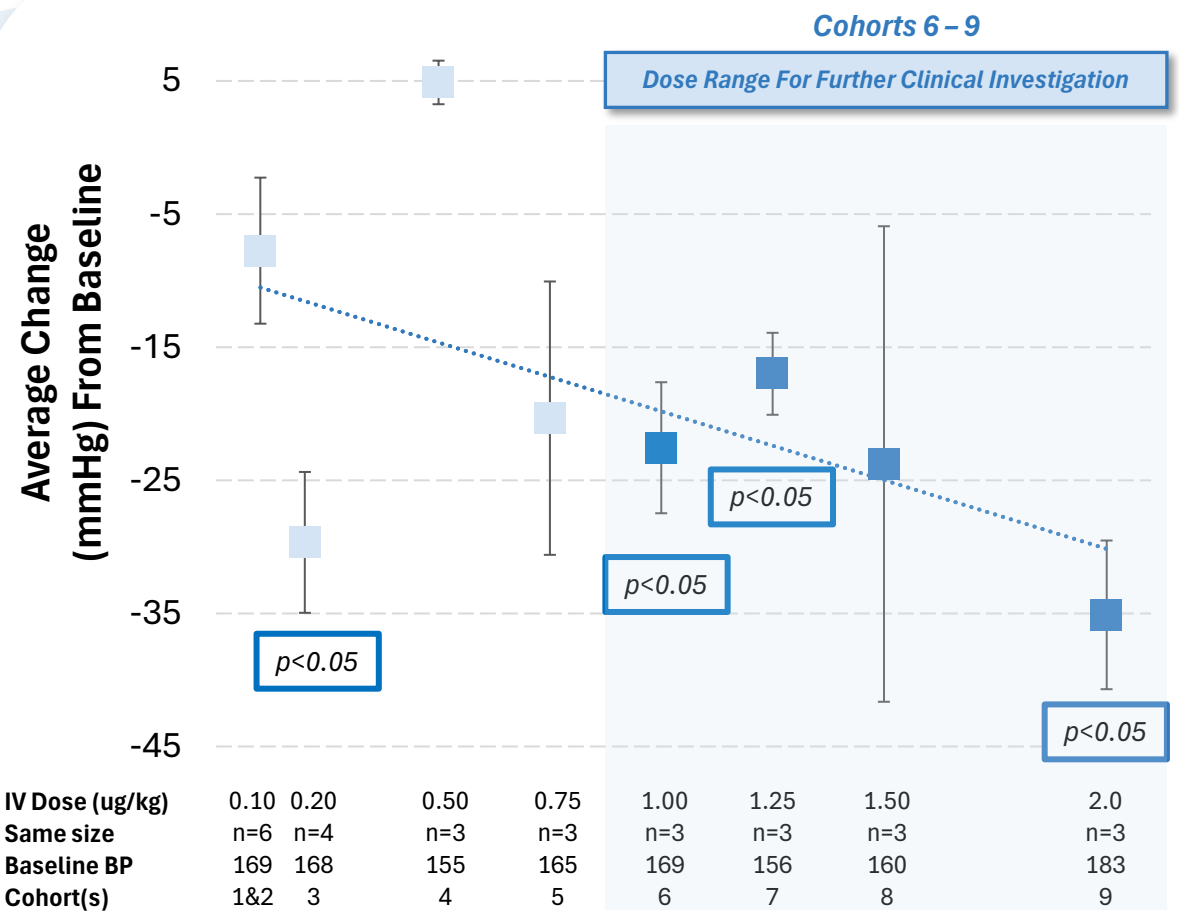
TEAE: Treatment Emergent Adverse Event

Blood Pressure Was Reduced at Prespecified 5-Minute Post-Infusion Endpoint

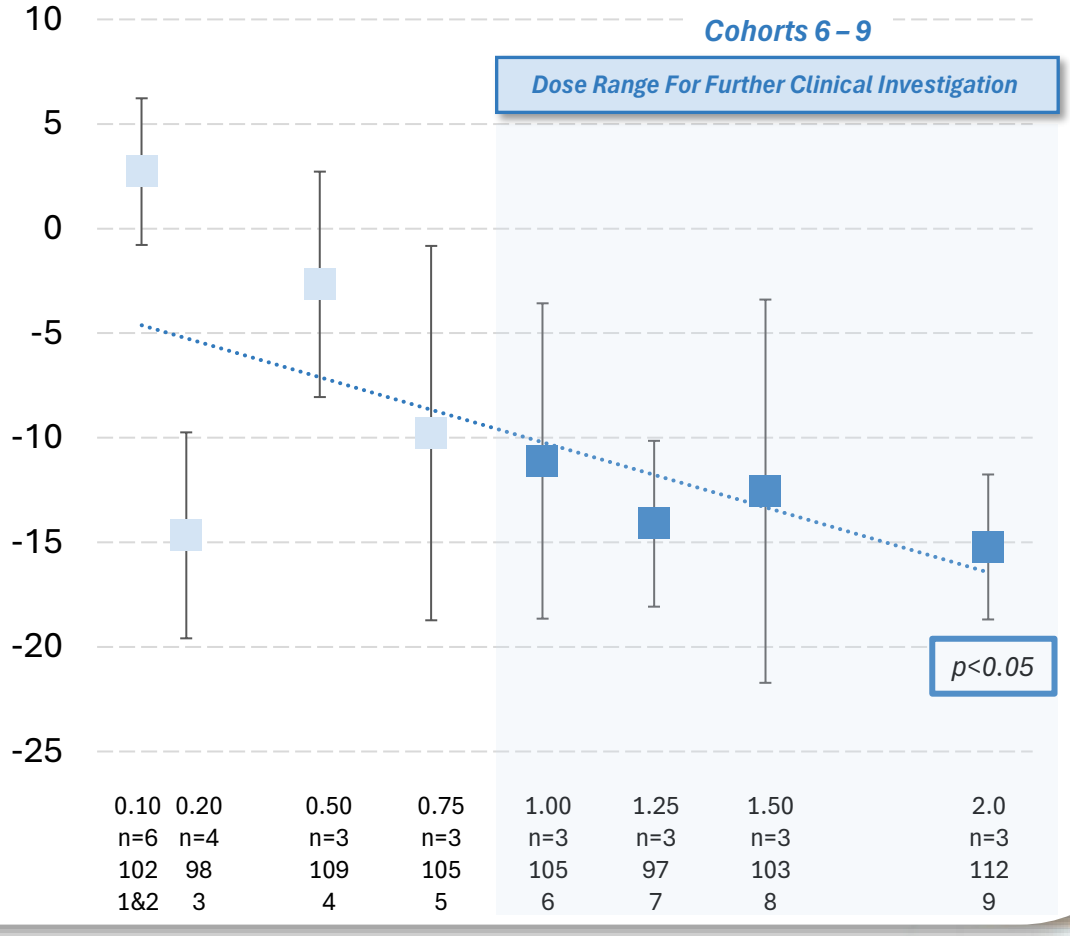
Pooled Cohorts C6–C9 achieved statistically significant reductions in SBP (-25 mmHg) and DBP (-15 mmHg)

Systolic



IV Dose (ug/kg)	0.10	0.20	0.50	0.75	1.00	1.25	1.50	2.0
Same size	n=6	n=4	n=3	n=3	n=3	n=3	n=3	n=3
Baseline BP	169	168	155	165	169	156	160	183
Cohort(s)	1&2	3	4	5	6	7	8	9

Diastolic



IV Dose (ug/kg)	0.10	0.20	0.50	0.75	1.00	1.25	1.50	2.0
Same size	n=6	n=4	n=3	n=3	n=3	n=3	n=3	n=3
Baseline BP	102	98	109	105	105	97	103	112
Cohort(s)	1&2	3	4	5	6	7	8	9

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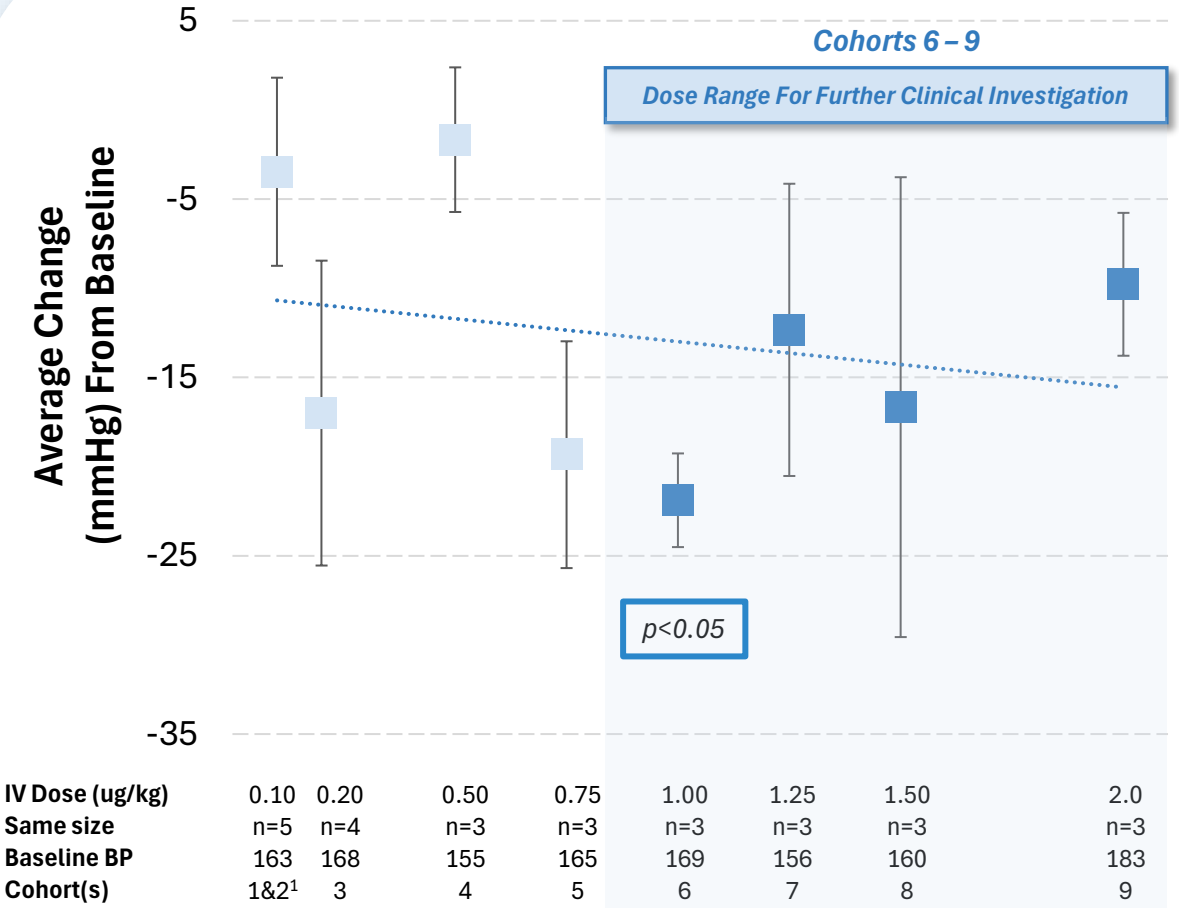
Mean ± SEM presented| Paired T-test vs. baseline| best-fit line based on mean values
No patients received short-acting BP meds during these time points

Blood Pressure Was Reduced at Prespecified 30-Minute Post-Infusion Endpoint

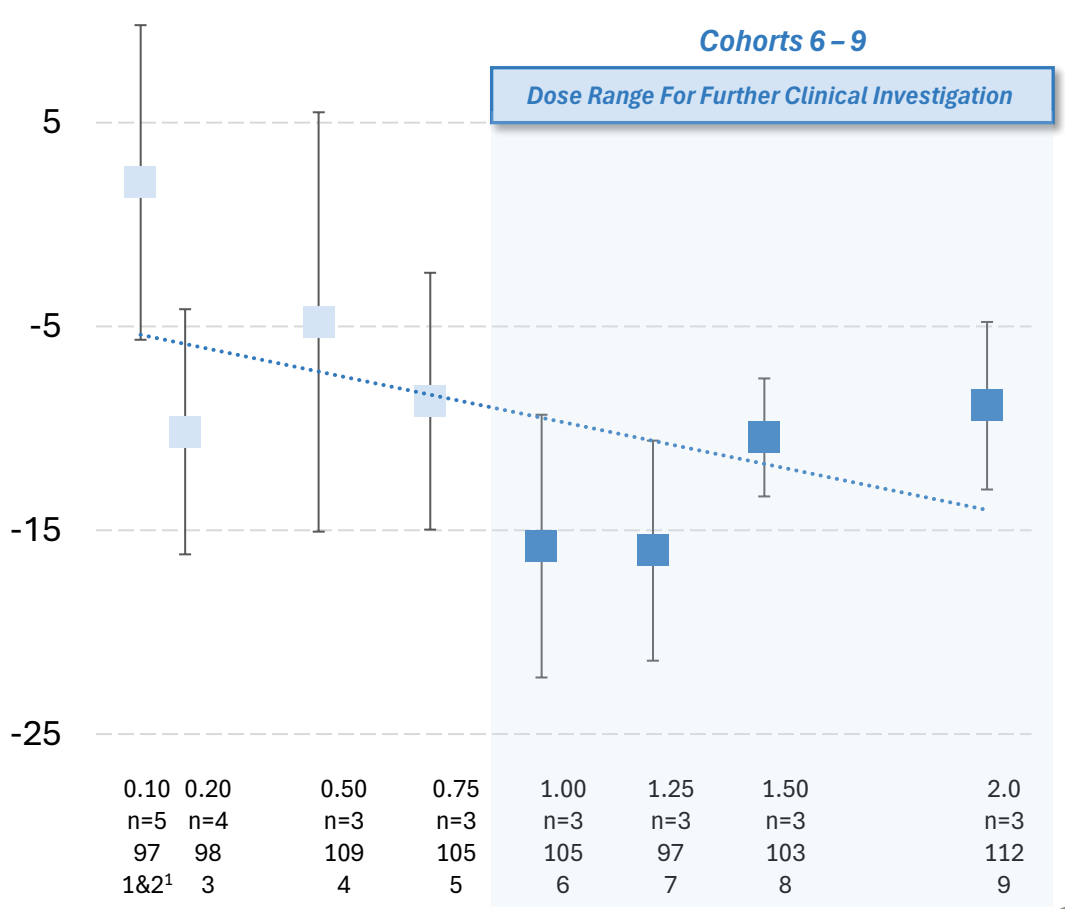
Pooled Cohorts C6–C9 achieved statistically significant reductions in SBP (-15 mmHg) and DBP (-13 mmHg)

Systolic



IV Dose (ug/kg)	0.10	0.20	0.50	0.75	1.00	1.25	1.50	2.0
Same size	n=5	n=4	n=3	n=3	n=3	n=3	n=3	n=3
Baseline BP	163	168	155	165	169	156	160	183
Cohort(s)	1&2[1]	3	4	5	6	7	8	9

Diastolic



0.10	0.20	0.50	0.75	1.00	1.25	1.50	2.0
n=5	n=4	n=3	n=3	n=3	n=3	n=3	n=3
97	98	109	105	105	97	103	112
1&2[1]	3	4	5	6	7	8	9

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Mean ± SEM presented | Paired T-test vs. baseline | best-fit line based on mean values

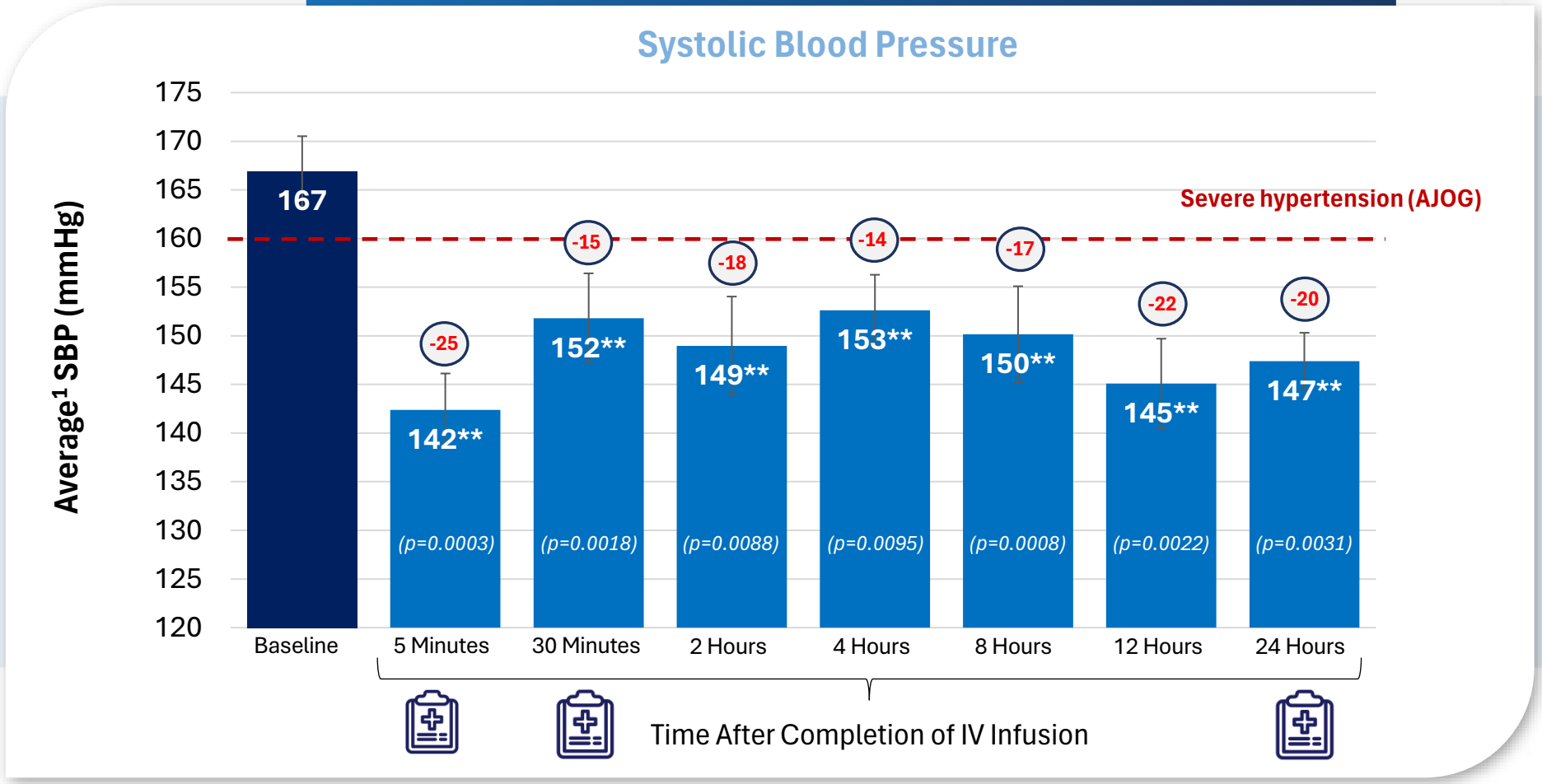
No patients received short-acting BP meds during these time points

1. Excludes Patient 1 due to delivery occurring 15 minutes after infusion completion (emergency c-section)

DM199 Drove Statistically Significant Systolic Blood Pressure Reduction

Pooled analysis of Cohorts 6 to 9

1.0-2.0 µg/kg IV (Cohorts 6-9) n=12[2]



Mean ± SEM presented | Paired T-test vs. baseline: *p<0.05 | **p<0.01

1. Average of three consecutive readings per timepoint
2. Patients in cohorts 6–8 (n=9) did not receive any short-acting antihypertensive medications after DM199 administration. Patients in cohort 9 (n=3) received short-acting BP medications at various time points after the 30-minute measurement but prior to the 24-hour assessment.

Note: measurement timepoints presented as scheduled. Actual measurement times varied

Prespecified Primary Endpoint

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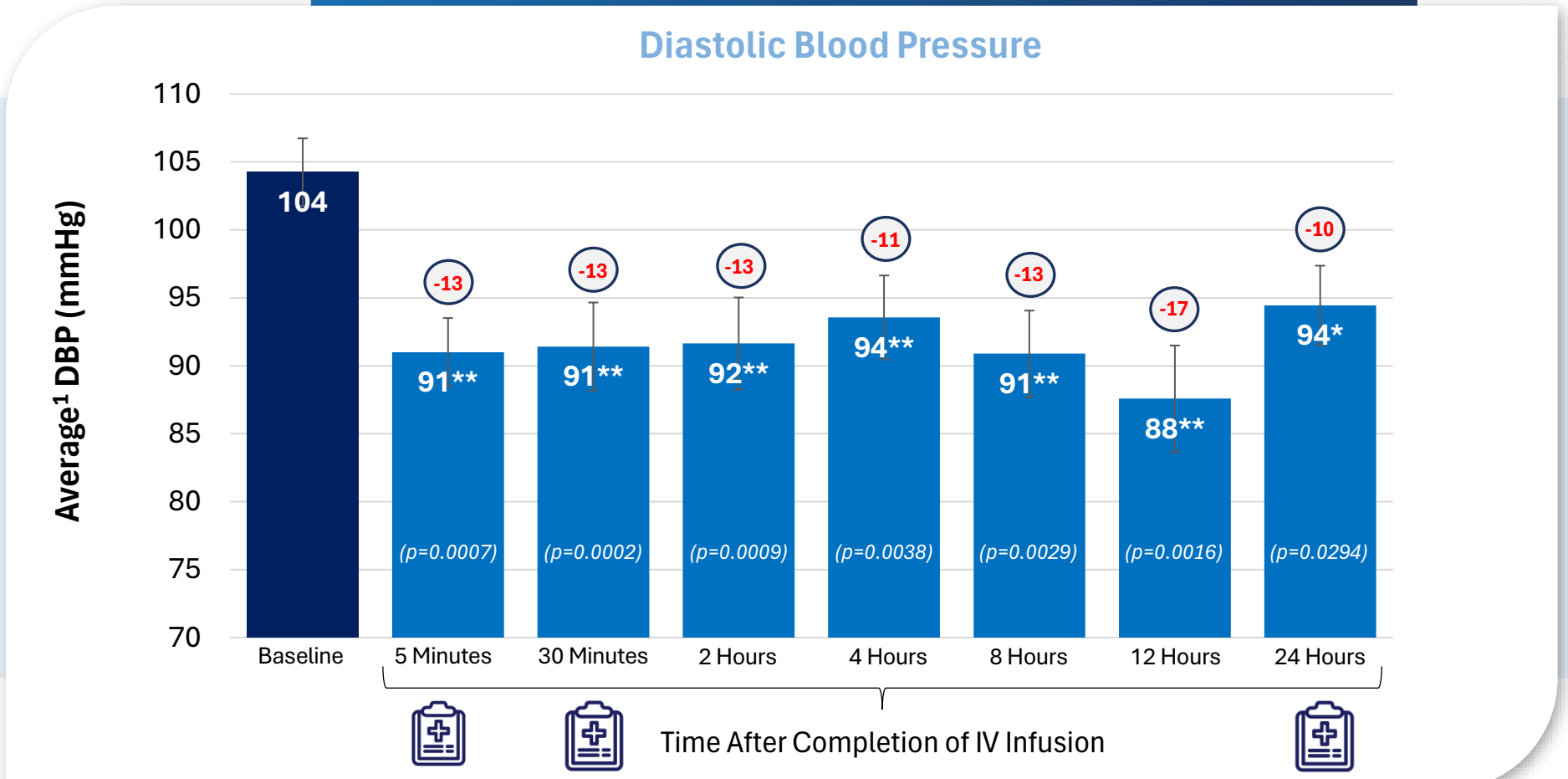
DM199 Drove Statistically Significant Diastolic Blood Pressure Reduction

Pooled analysis of Cohorts 6 to 9

1.0-2.0 µg/kg IV (Cohorts 6-9) n=12[2]



Mean ± SEM presented | Paired T-test vs. baseline: *p<0.05 | **p<0.01

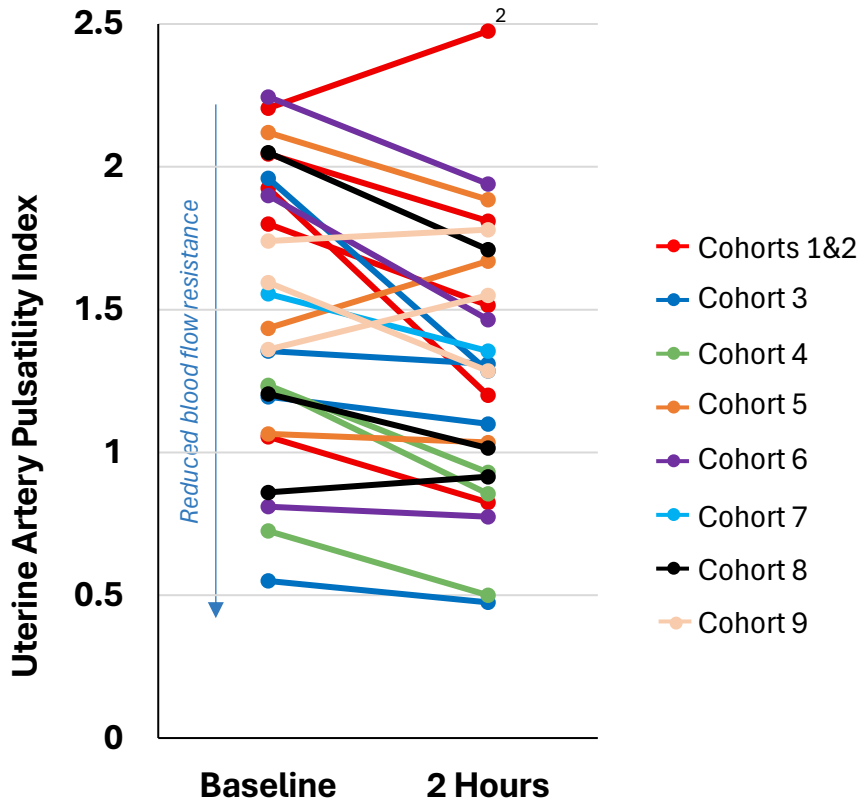
1. Average of three consecutive readings per timepoint
2. Patients in cohorts 6–8 (n=9) did not receive any short-acting antihypertensive medications after DM199 administration. Patients in cohort 9 (n=3) received short-acting BP medications at various time points after the 30-minute measurement but prior to the 24-hour assessment.

Note: measurement timepoints presented as scheduled. Actual measurement times varied

Prespecified Primary Endpoint

DM199 Reduced Uterine Artery Resistance, Suggesting Enhanced Placental Perfusion

Overall[1,2] (n=25)



Geomean % Change[1]	-13.2%
P-value[1]	0.0003

- Dilation of the uterine arteries was assessed by Doppler ultrasound at baseline and two hours after IV infusion
- 13.2% average reduction in blood flow resistance was observed across cohorts (p=0.0003), **suggesting DM199 increased perfusion to the placenta**

Improved perfusion may reduce placental hypoxia, supporting fetal growth and disease modification

1. Measurements not available for one patient in Cohort 1, and two patients in Cohort 7
2. One patient in Cohort 2 (baseline: 2.2, 2hr: 2.5) was crowning (baby's head visible at the vaginal opening) at the time of the 2-hour measurement, potentially impact the 2-hour measurement

Fetal Growth Restriction: DM199's Indication Expansion

Strong mechanistic rationale based on Interim Part 1a PE data

Fetal Growth Restriction is a Major Unmet Medical Challenge

- Placental insufficiency—particularly impaired uteroplacental blood flow—is a core pathophysiologic driver of FGR
- **No approved therapies** to directly treat FGR; current management is limited to monitoring and early delivery
- The Pulsatility Index (PI) in uterine and umbilical arteries is a core diagnostic and prognostic biomarker and is directly correlated with fetal oxygen/nutrient delivery

DM199 Offers the Potential to Improve Uteroplacental Blood Flow

- Like preeclampsia, FGR is often marked by abnormal uterine artery Doppler waveforms:
  - Elevated PI
  - Absent or reversed end-diastolic flow
- DM199 has been shown to dilate intrauterine arteries, resulting in:
  - Improved uteroplacental perfusion
  - Reduced vascular resistance, as quantified by the Pulsatility Index

DM199's efficacy in lowering PI in preeclampsia patients supports its potential in FGR—especially early-onset forms

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DM199 Phase 2 Preeclampsia IST Next Steps

All parts can enroll concurrently

Part 1b (n=30)
Planned Delivery in 72 Hrs

- Recruiting the same population as Part 1a: women with planned delivery within 72 hours and SBP >150 mmHg (27 – 42 weeks GA)
- Participants will receive a single IV/SC dose on Day 1, using the dose identified in Part 1a (no additional doses)
- Primary endpoints: Safety* and lowering blood pressure

Part 2 (n=30)
Expectant Management

- Recruiting women with early onset preeclampsia (GA 27+0 to 32+6) who are candidates for expectant management (prolongation)
- Participants will receive an initial IV/SC dose on Day 1, followed by repeated SC doses until delivery
- Primary endpoints: Safety*, prolongation, change in UACR, need to increase/decrease anti-hypertensive agents

Part 3 (n=30)
Fetal Growth Restriction

- Recruiting women with early onset FGR (GA 27+0 to 32+6), defined as fetal growth <3rd centile, who do not have preeclampsia
- Participants will receive an initial IV/SC dose on Day 1, followed by repeated SC doses until delivery
- Primary endpoints: Safety*, changes in uterine, ophthalmic, and fetal Dopplers, and birthweight centile

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IST = Investigator Sponsored Trial
GA = Gestational Age
*including placental transfer of DM199 (umbilical cord levels after birth)

ReMEDy2

Phase 2/3 Trial

Acute Ischemic Stroke

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High Unmet Need in Acute Ischemic Stroke

>7.5 million acute ischemic strokes occur globally each year[5]

DM199 US Estimated Market Opportunity = $10+ Billion

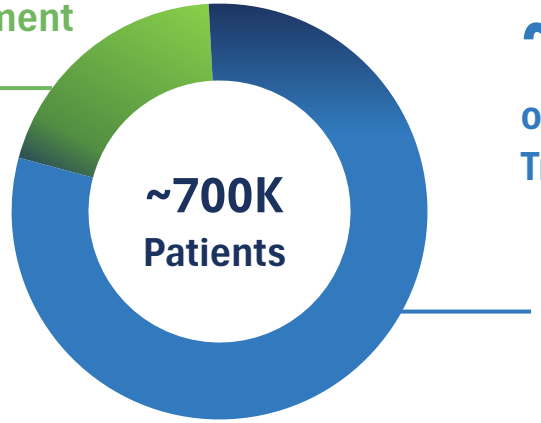
Low Treatment Rates

US Annual Acute Ischemic Strokes[1,2,3]

~20%

Active Treatment

<140K Patients



>500K Patients

~80%

of Patients with No Treatment Options

Limited Treatment Options

0 — **No New Pharmaceuticals Approved in Over 25 Years**

~10% — **tPA / Thrombolytic**

~10% — **Mechanical Thrombectomy**

1st line[3,4]

~80% — **Supportive Care Only**

DM199 Initial Target

Sources:1. Ej etc. 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: 28122885; 2. American Stroke Association; 3. Fassbender, 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. Kansagra AP, Goyal MS, Hamilton S, Albers GW. Trends in Mechanical Thrombectomy for Acute Ischemic Stroke in the United States: A Nationwide Analysis from 2012 to 2016. *Stroke*. 2019;50(3):570-577. doi:10.1161/STROKEAHA.118.023600; 5. World Stroke Organization Global Fact Sheet 2022

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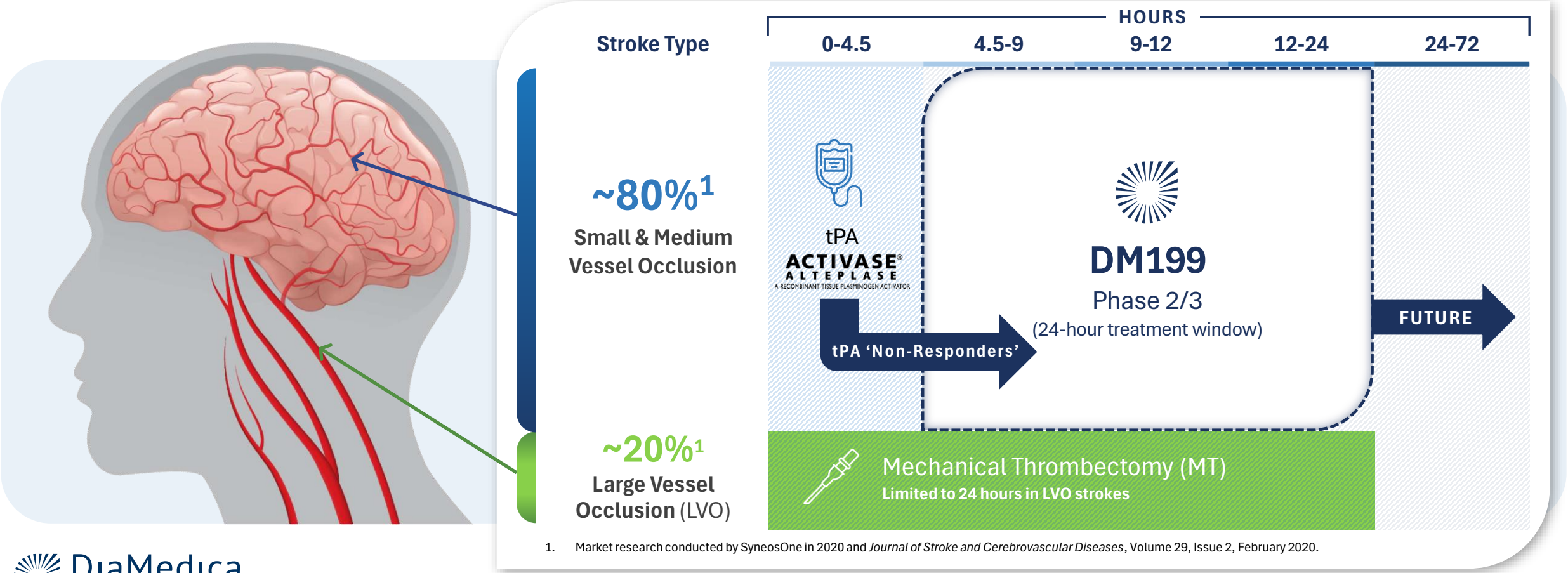
DM199 Initial Target in AIS – Significant Whitespace Opportunity

>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



1. Market research conducted by SyneosOne in 2020 and *Journal of Stroke and Cerebrovascular Diseases*, Volume 29, Issue 2, February 2020.

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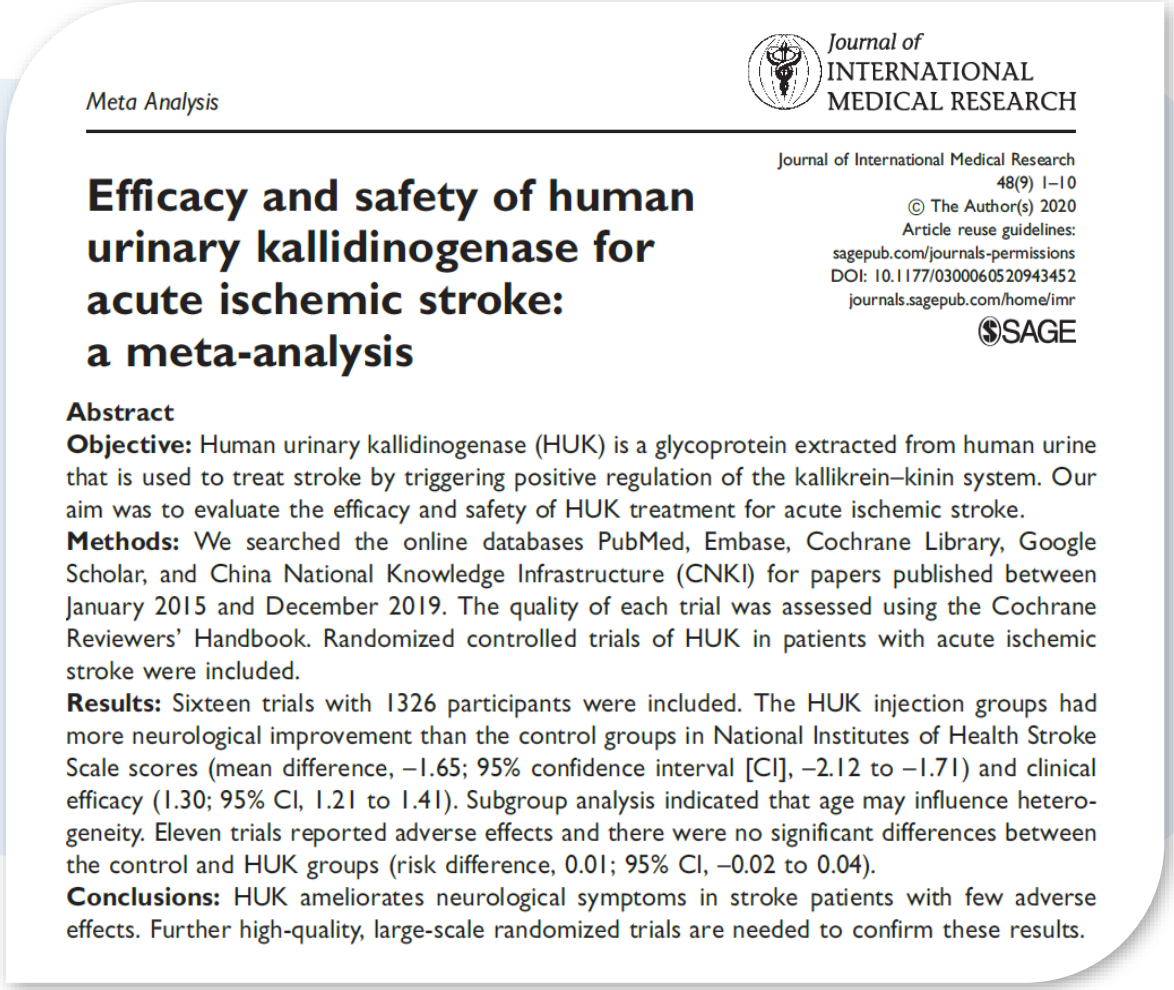
Human Urinary KLK1 (HUK): Safe and Efficacious Treatment for AIS

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



Meta Analysis

Journal of INTERNATIONAL MEDICAL RESEARCH

Efficacy and safety of human urinary kallidinogenase for acute ischemic stroke: a meta-analysis

Journal of International Medical Research
48(9) 1–10

DOI: 10.1177/0300060520943452
journals.sagepub.com/home/imr
SAGE

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.

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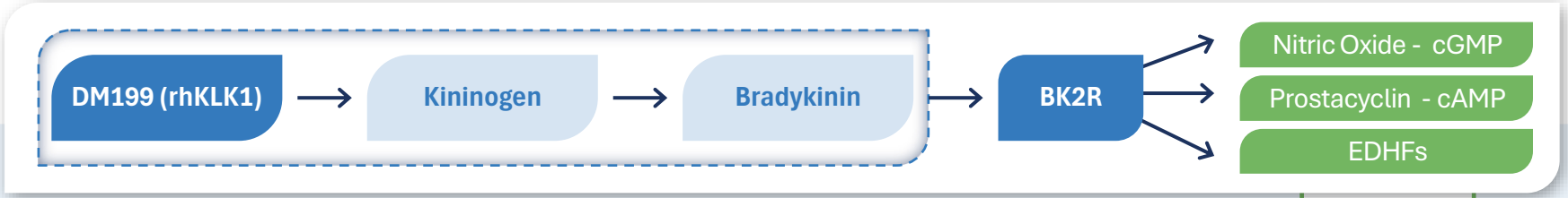
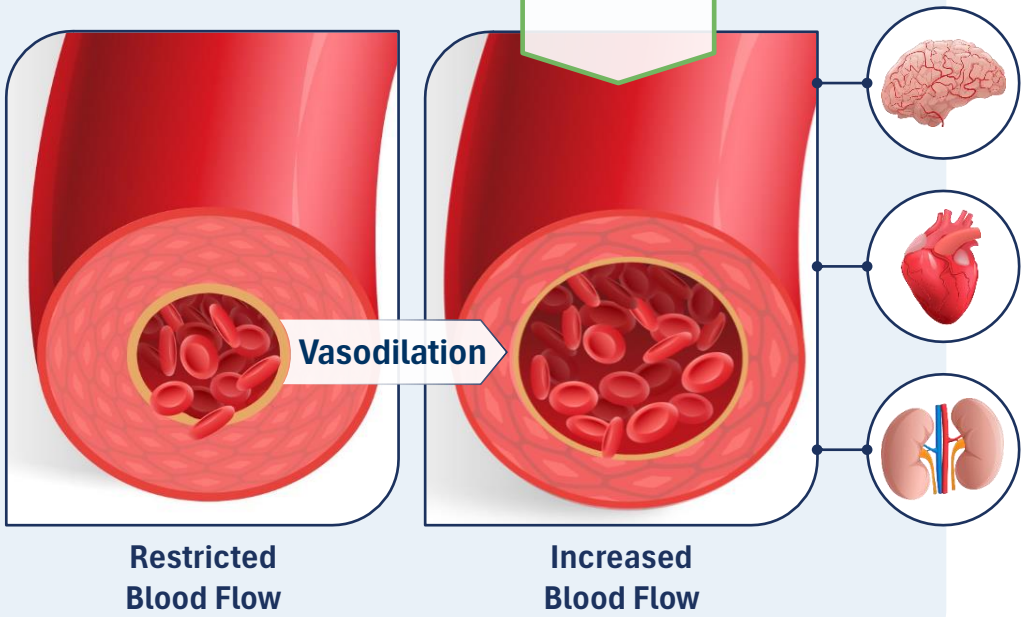
1. Huang Y, et al. (2020). Efficacy and safety of human urinary kallidinogenase for acute ischemic stroke: a meta-analysis. *Journal of International Medical Research*. 2020;48(9).https://journals.sagepub.com/doi/full/10.1177/0300060520943452
2. Shanghai Pharma/Techpool website: http://www.techpool.com.cn/press/r/5ddf3ed2535416541805af75

DM199 (rhKLK1 – rinvecalinase alfa) Novel Mechanism of Action

DM199 produces all three major endothelial derived vasodilating factors



- 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 key vasodilating factors:
  - Nitric oxide (NO)
  - Prostacyclin (PGI_2) and
  - Endothelium-derived hyperpolarizing factors (EDHFs)

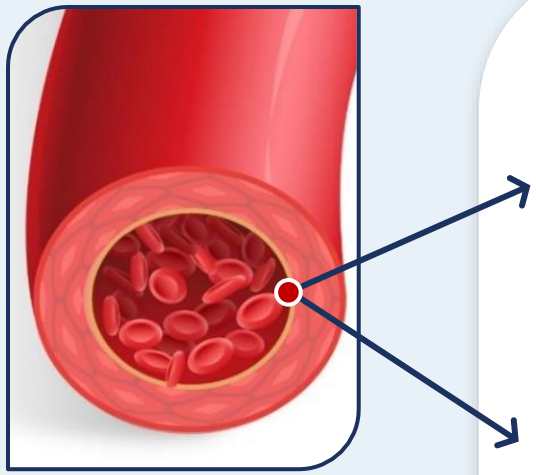


ACE= Angiotensin converting enzyme cGMP = Cyclic guanosine monophosphate cAMP = Cyclic adenosine monophosphate

1. Marin et al. (2019). Kallikrein/K1, Kinins, and ACE/Kininase II in Homeostasis and in Disease Insight From Human and Experimental Genetic Studies, Therapeutic Implication. *Journal of Personalized Medicine*, 9(1), 16.

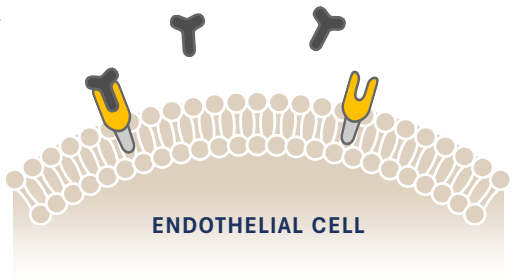
Ischemia Naturally Induces Upregulation of Bradykinin 2 Receptors (BK2R)

DM199 has potential to enhance BK2R activation & promote focal vasodilation in the penumbra



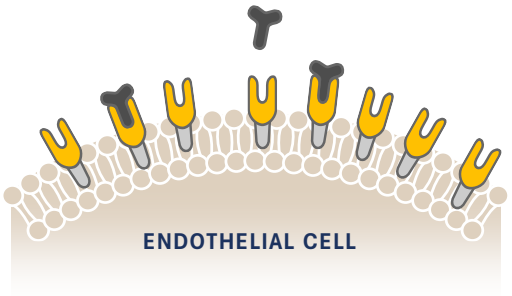
Brain Artery Under Different Conditions

1 Normal Conditions



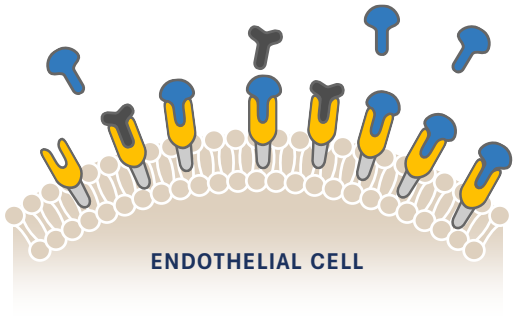
The BK2R plays a critical role in regulating vascular tone and blood pressure under normal conditions.

2 Ischemic Conditions



In response to ischemic conditions, the BK2R are significantly upregulated in affected tissues, including the brain.[1]

3 Ischemic Conditions + DM199



DM199 may augment bradykinin (BK) levels, increasing activation of the upregulated BK2R in the affected arteries (ischemic penumbra) and improving collateral circulation to increase blood flow and oxygenation to the penumbra.


BK2R


Native BK


DM199 BK

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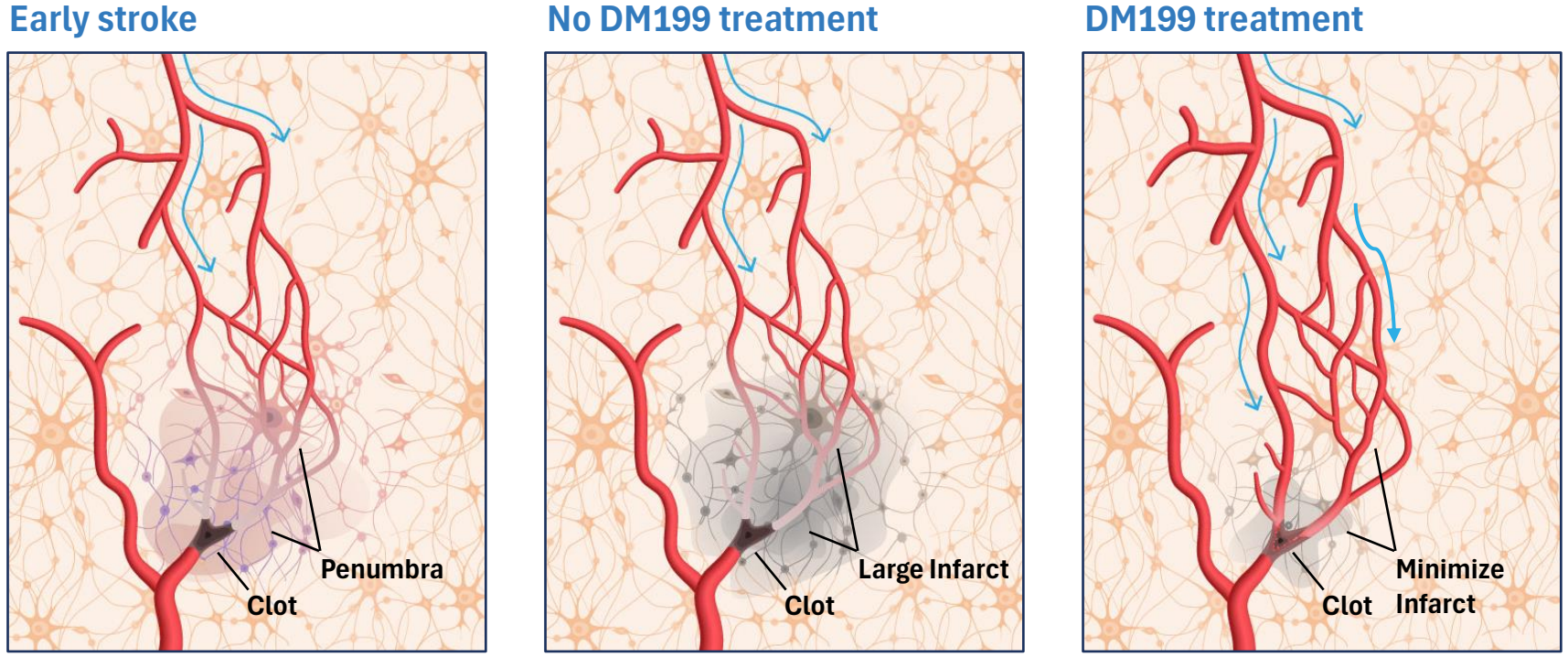
1. *PLOS ONE*, June 18, 2018; https://doi.org/10.1371/journal.pone.0198553

DM199: May 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 **NO, PGI_2 and EDHF** to preferentially vasodilate arteries in the ischemic penumbra and increase collateral blood flow.



- **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)

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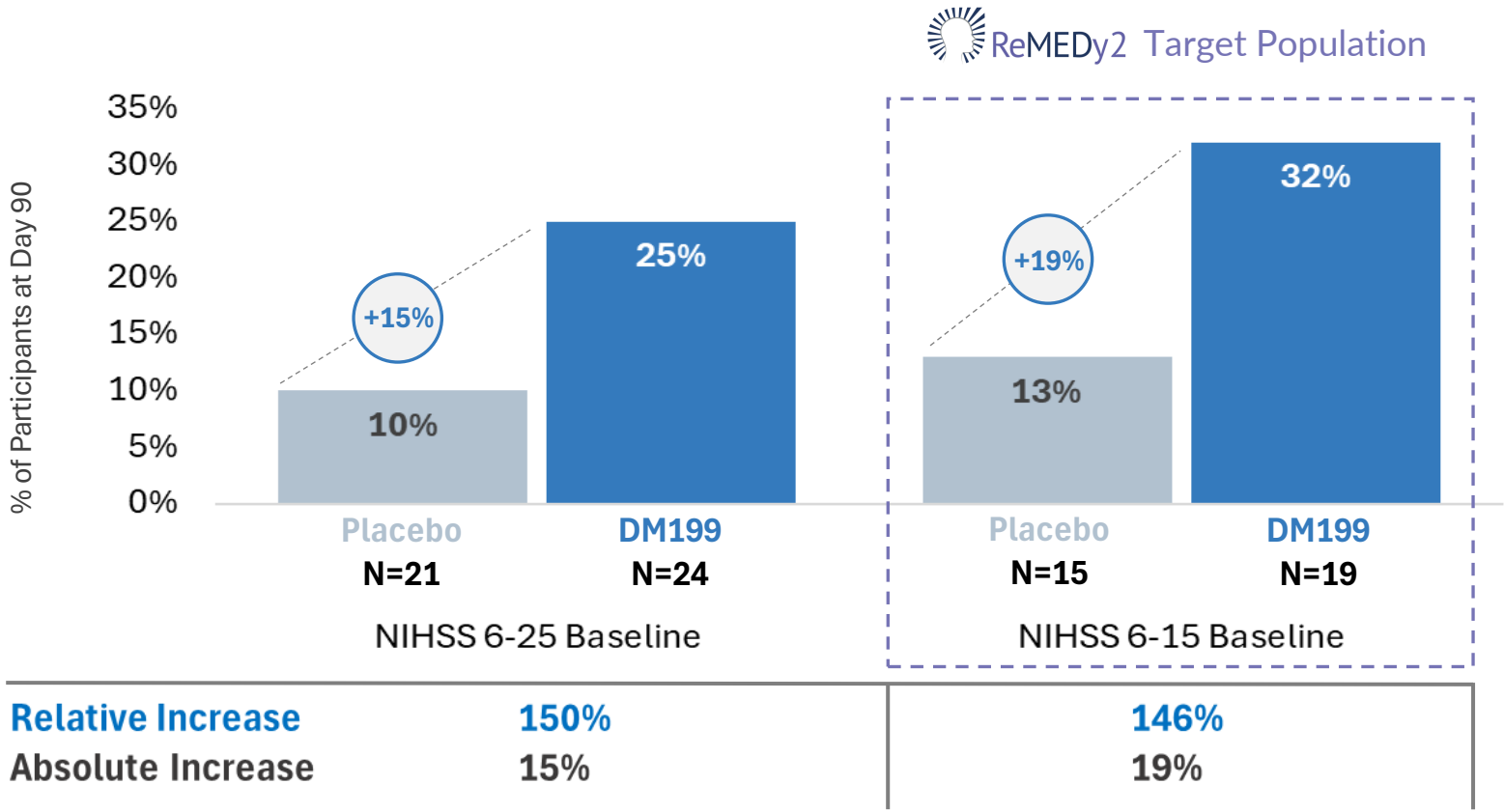
DM199 Phase 2 Results: Improved Excellent Outcomes in Non-MT Subgroup

Patient population closely aligns with ReMEDy2 Phase 2/3 trial

mRS ≤ 1 at 90 Days (Non-MT Participants)



	NIHSS 6-25 Baseline	NIHSS 6-15 Baseline
Relative Increase	150%	146%
Absolute Increase	15%	19%

MT – Mechanical Thrombectomy NIHSS – National Institute of Health Stroke Scale mRS – Modified Rankin Scale BI – Barthel Index

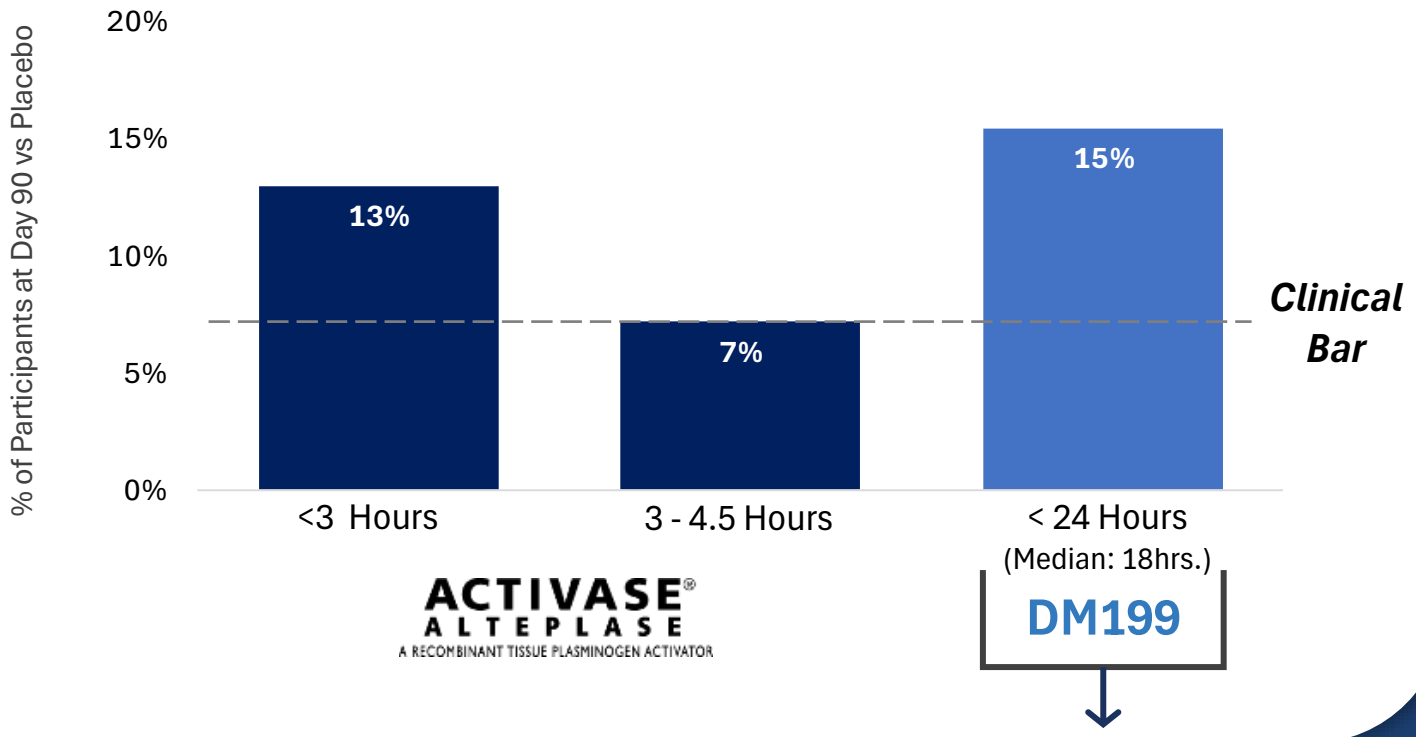
DM199 Phase 2 AIS Results Comparison with tPA Data

Clinically relevant outcomes with DM199 extending treatment window from 4.5 to 24 hours

- **tPA (Activase®)** approved for AIS in 1996
  - Only FDA approved therapeutic
  - 4.5-hour narrow treatment window
    - Greater efficacy ≤3 hours

Comparison of Absolute Improvements in mRS ≤ 1 vs Placebo

(DM199 Phase 2 and tPA analysis; excludes MT treated participants)



1. N Engl J Med 1995; 333:1581-1588; 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 Pivotal Phase 2/3 AIS Trial

ReMEDy2

Overview

- Moderate AIS: NIHSS: 5-15
- Adaptive Design
  - Interim analysis @ N=200
  - Intended to enroll N=~300
- Up to 100 global sites

Endpoints at Day 90

Primary:
Modified Rankin Score (mRS) ≤1

Secondary:
mRS shift, mortality, NIHSS, BI and stroke recurrence

Screening → Randomization → 3-week Treatment Period → 90-Day Follow-up

Exclusion Criteria

- Hemorrhagic stroke
- Received or eligible to receive MT
- Occlusion in the intracranial carotid artery or M1 segment of the middle cerebral, vertebral or basilary arteries
- tPA (Activase®/TNKase®) 'Responders'

Treatment: 24-hour Window

- 1st IV dose within 24-hours of stroke
  - DM199 IV (0.5 µg/kg) or placebo
- 3-weeks SC treatment, 2x week
  - DM199 SC (3 µg/kg) or placebo

DSMB* Interim Analysis (IA)

- IA after 200 participants complete trial
- Potential outcomes from IA:
  1. Stop trial for futility
  2. Continue with sample size re-estimation (size range 300 – 728 total participants)

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* Data Safety Monitoring Board (DSMB)

Corporate Summary

DiaMedica THERAPEUTICS

DM199 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

Patents[1]

- **Composition of matter**
  - Issued US/EU (2033)
- **Formulation, subcutaneous and improved PK**
  - Issued US (2033)
- **Dosing & route of delivery**
  - Issued US (2039) and Australia (2038) / pending global
- **Treating pregnancy disorders**
  - Pending US (2045)

Exclusive License of Patented Gene Expression Technology for rhKLK1

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

Regulatory Exclusivity

U.S.: Anticipate 12 Years' Data Exclusivity for Biologics

- Regulatory counsel has confirmed this is a reasonable expectation

Outside of the U.S. for Biologics Exclusivity Protections:

- **Europe:** Up to 10 years
- **Japan:** Up to 8 years

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

Leadership

Rick Pauls, President & Chief Executive Officer

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.

Alex Aimetti, PhD., Chief Development Officer

15 years executive leadership experience in research, clinical development, and medical affairs. Most recently CSO at Marinus, contributing to the successful development and launch Ztalmy® for rare epilepsy and strategic sale of Company

David Wambeke, Chief Business Officer

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

Board of Directors

James Parsons, Chairman of the Board

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

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.

Rick Pauls

See Leadership for details.

Dan O'Connor

25+ years of experience in the biopharmaceutical industry, including executive leadership positions at Ambrx Biopharma, and ImClone Systems. Most recently, CEO of Ambrx growing the company from a $40 million market cap to being acquired by Johnson & Johnson for $2 billion 14 months later.

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.

DiaMedica THERAPEUTICS

Company Overview

Cash: $37 million
(March 31, 2025)

Runway into Q3 2026*
No warrants and no debt

**As of 5/14/2025 conference call*

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

- Recombinant KLK1 (rhKLK1) protein with FDA Fast-Track Designation
- IP until '39 (+ potential 5-year ext.) & expected 12 years regulatory exclusivity
- >300 patients have been dosed with DM199 across multiple studies

Preeclampsia (PE) and Fetal Growth Restriction (FGR)

- $5B+ U.S. market opportunity for Early-Onset PE and FGR
- No FDA approved treatment options
- Phase 2 PE interim results: DM199 significantly lowered blood pressure and dilated intrauterine arteries without crossing the placental barrier
- DM199 is a potential disease-modifying therapy aimed at increasing placental perfusion, reducing blood pressure and improving endothelial function

Acute Ischemic Stroke (AIS)

- >$10 billion US market opportunity
- ~80% of patients have no treatment options today[1, 2]
- Extensive clinical data supporting KLK1 efficacy and safety in AIS patients
  - Increases collateral circulation in the penumbra following stroke
  - DM199 showed encouraging Phase 2 efficacy and safety data
  - Human urinary KLK1 (HUK) treats up to 1 million patients/year in China[3]

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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/S1474-4422(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/Techpool website: http://www.techpool.com.cn/press/r/5ddf3ed2535416541805af75 ; 3. 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/cthn-st75

Thank You!

Nasdaq: dmac

www.diamedica.com

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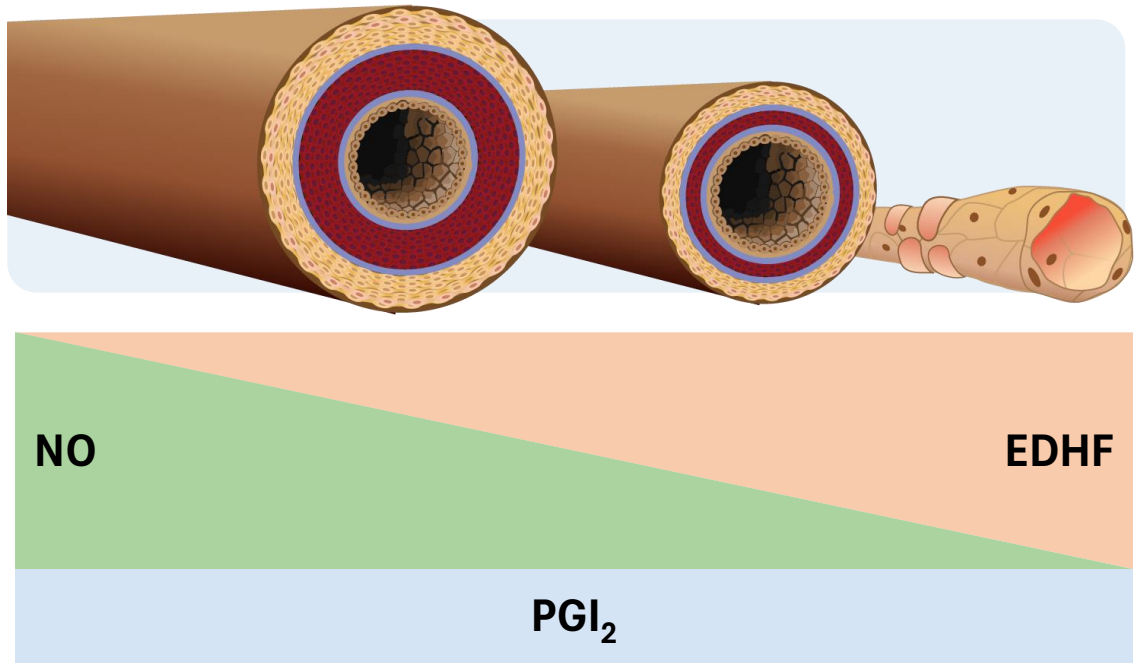
APPENDIX

DiaMedica THERAPEUTICS

Relative Contribution of 3 Major Endothelial Derived Vasodilating Factors[1]

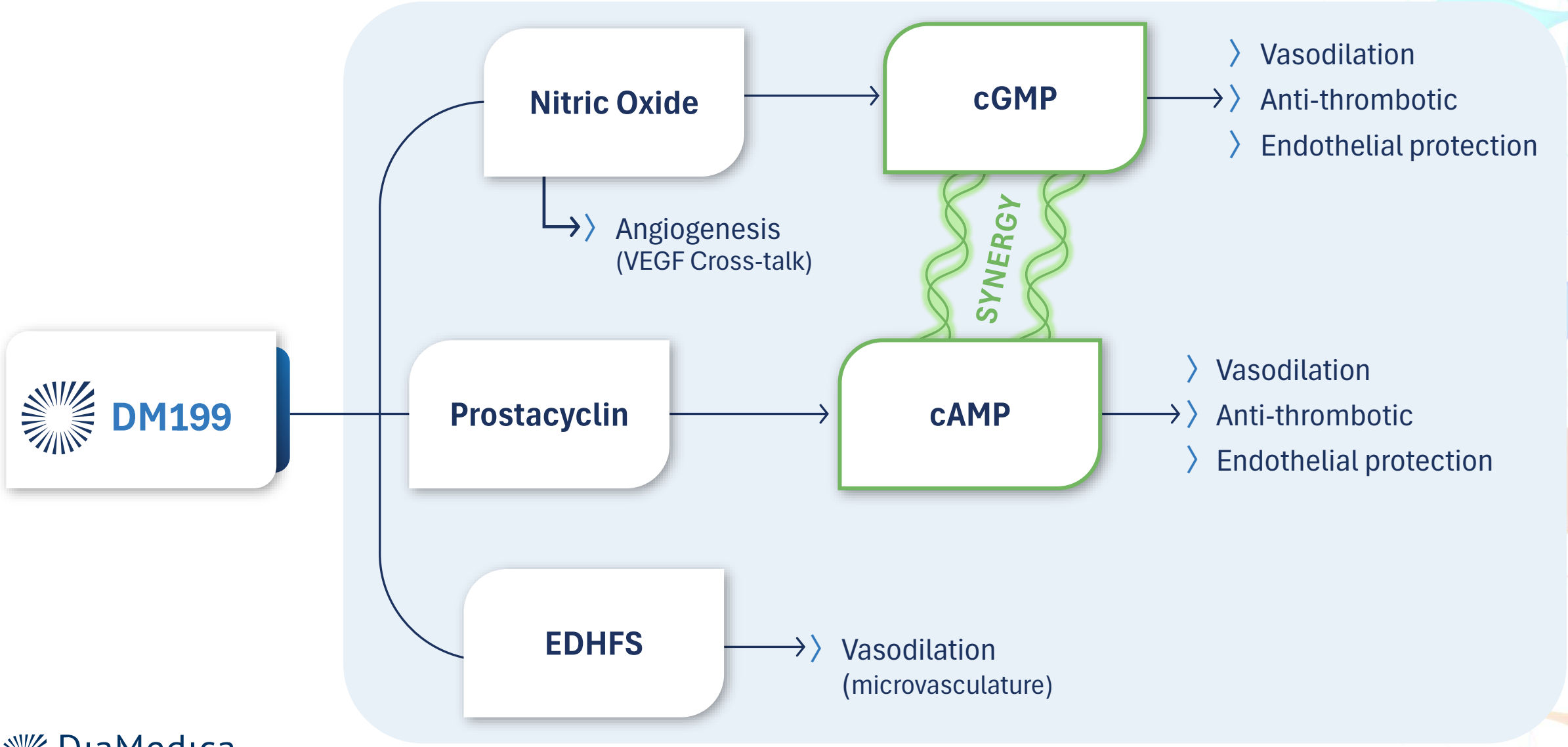
EDHF is critical in microvasculature and compensates when NO and PGI_2 signaling are compromised



- Arterioles are the **primary site of resistance in the vascular tree** and **the most significant contributors to blood pressure**[2]
- Arterioles account for approximately **80% of the total resistance** to blood flow in the body[2]

1. Davis, C. M., Siler, D. A., & Alkayed, N. J. (2011). EDHF in the brain: Influence of sex, vessel size, and disease state. Women's Health (Lond.), 7(3), 293–303. https://doi.org/10.2217/whe.11.26
2. Rahman, M., & Siddik, A. B. (2023, January 13). Anatomy, arterioles. StatPearls. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK555921/

DM199: Enhancing Vascular Health Beyond Blood Pressure Control



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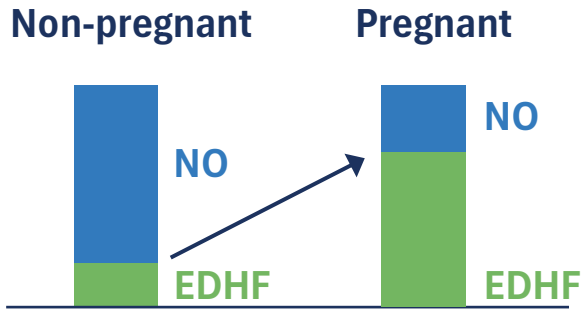
DM199 Targets All 3 Key Vasodilatory Agonists: NO, PGI_2 and EDHF

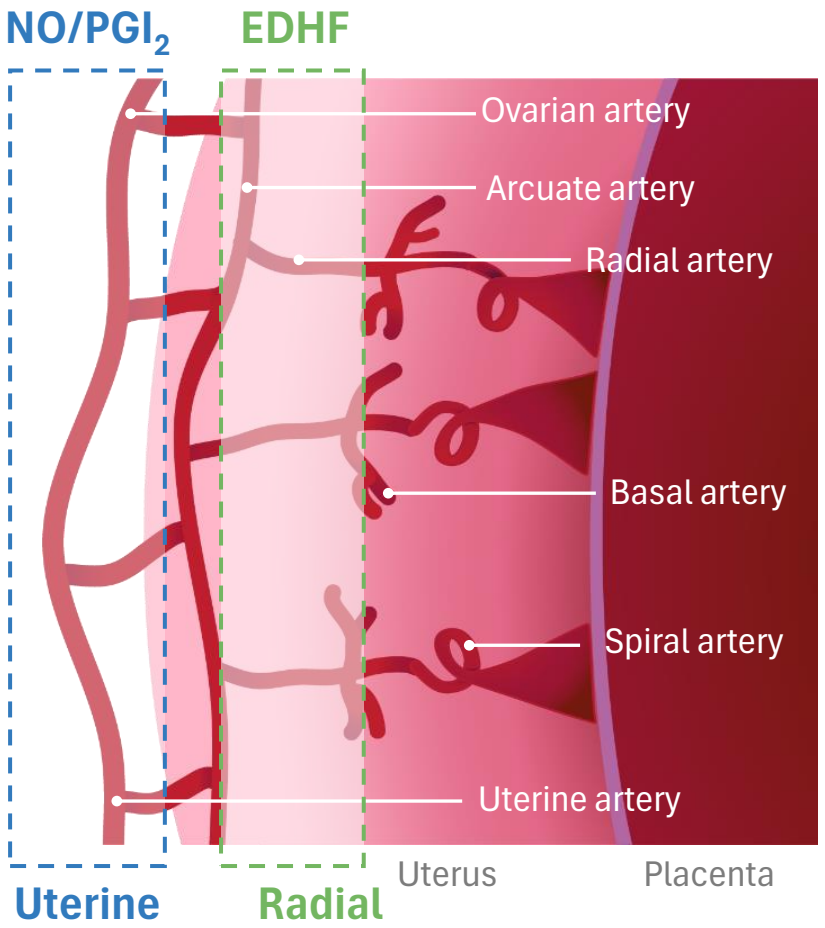
Potential to increase placental perfusion & reduce placental-released noxious factors

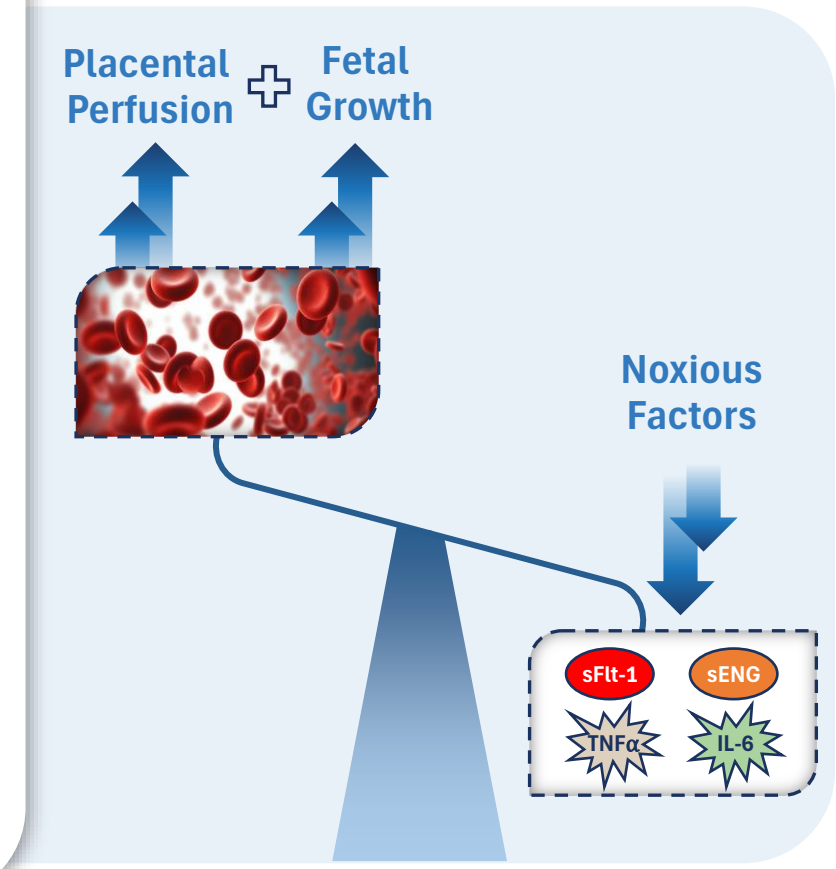
01 UPSTREAM

Vasodilation During Pregnancy Varies by Size and Role of Arteries

- Agonist-induced vasodilation in the main uterine artery relies primarily on NO and PGI_2
- In pregnancy, EDHF becomes the predominant agonist-induced vasodilation pathway in radial arteries







1. Senadheera, S et al. Pregnancy-induced remodeling and enhanced endothelium-derived hyperpolarization-type vasodilator activity in rat uterine radial artery: transient receptor potential vanilloid type 4 channels, caveolae and myoendothelial gap junctions. *J Anat*. 2013 Dec;223(6):677-86. doi: 10.1111/joa.12127.
2. Goulopoulou, S. Maternal Vascular Physiology in Preeclampsia. American heart Association (AHA). *Hypertension*. 2017

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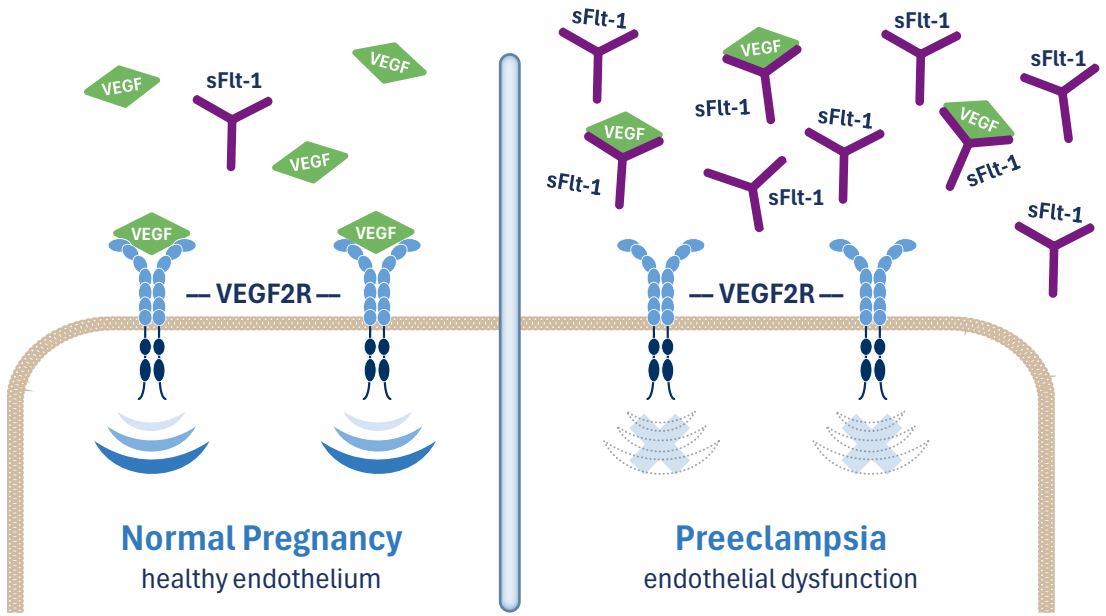
DM199 Potential to Augment VEGF Signaling in Endothelial Cells

02 DOWN STREAM

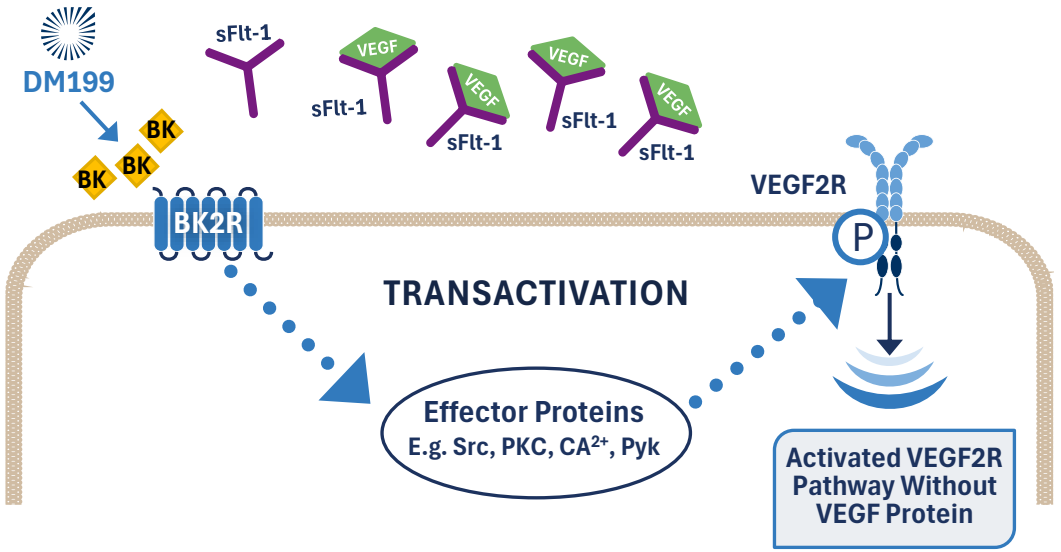
Potential to bypass sFlt-1 antagonism to improve endothelial health & blood flow

Circulating sFlt-1 Increases Significantly in Preeclampsia



sFlt-1 binds to VEGF protein, reducing VEGF2R signaling, which contributes to endothelial dysfunction and vasoconstriction.

BK2R Activation Can Directly Transactivate VEGF2R



Increased Nitric Oxide Signaling Can Also Increase VEGF Protein Synthesis and Receptor Expression

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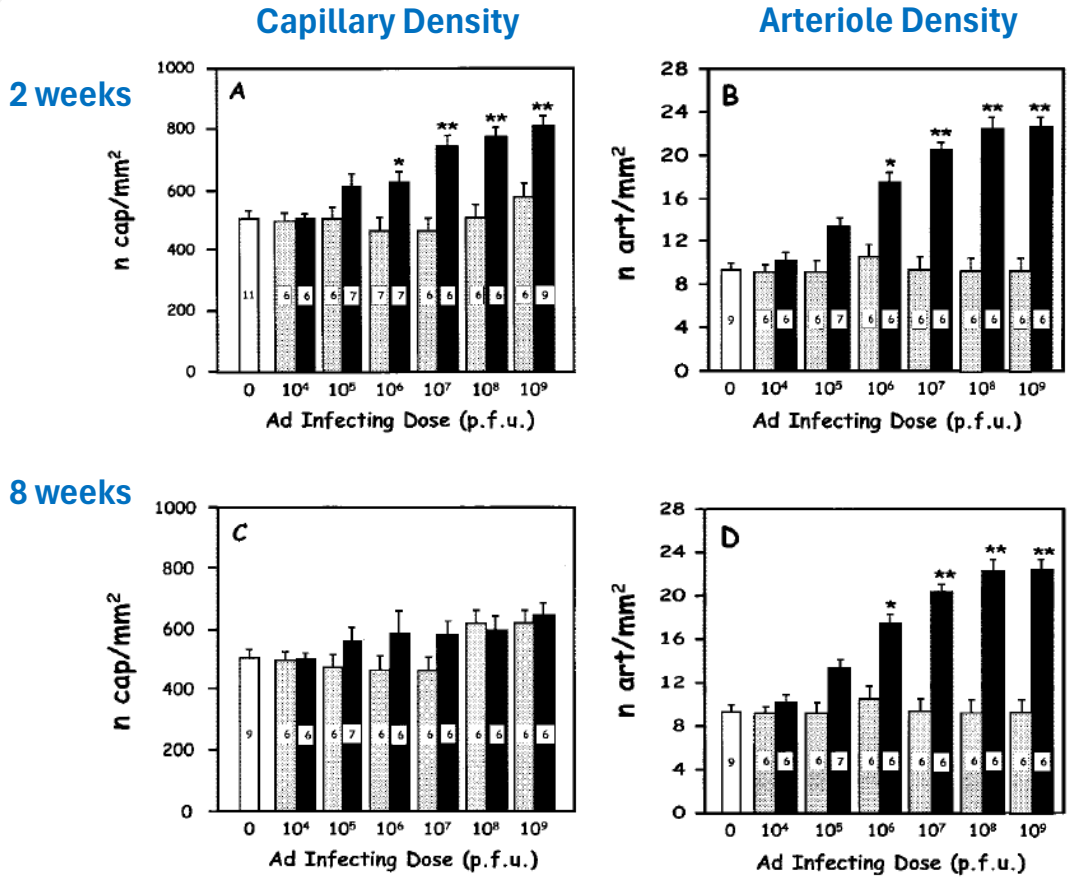
1. Thuringer D, Maulon L, Frelin C. Rapid transactivation of the vascular endothelial growth factor receptor KDR/Flk-1 by the bradykinin B2 receptor contributes to endothelial nitric-oxide synthase activation in cardiac capillary endothelial cells. *J Biol Chem* 2002; 277(3): 2028-32.
2. Yao YYet al. Tissue kallikrein promotes neovascularization and improves cardiac function by the Akt-glycogen synthase kinase-3beta pathway. *Cardiovasc Res* 2008; 80(3): 354-64.
3. Bader M. Kallikrein-kinin system in neovascularization. *Arterioscler Thromb Vasc Biol* 2009; 29(5): 617-9.

KLK1 Promotes Neovascularization Despite sFlt-1 Antagonism

02 DOWN STREAM

KLK1 Gene Transfer Increased Capillary and Arteriole Density[1]



Adenoviral Tissue Kallikrein-1 Injected into adductor muscles

Arteriole density **remained elevated for 8 weeks**, long after transgene infection expired

Inhibition of VEGF-A Action The role of VEGF-A was addressed by 3 approaches: (1) A VEGF-A neutralizing antibody (2.5 µg IP twice a week, R&D Systems)[22] or nonimmune IgG was given in combination with Ad.hTK or Ad.Luc (10^9 PFU IM). (2) The VEGF-R2 antagonist PTK 787 (kindly provided by Dr J. Wood, Novartis Pharma AG, Basel, Switzerland), that was previously shown to block VEGF-A–induced angiogenesis,[23] was given in drinking water (25 mg/kg body weight per day for 15 days) starting 1 day before Ad.hTK or Ad.Luc (10^9 PFU IM). Control mice drank regular water. (3) An Ad carrying soluble VEGF-R1 gene (Ad.s-flt-1, 10^9 PFU, kindly provided by Drs S.A. Karumanchi, Beth Israel Deaconess Hospital and Harvard Medical School, Boston, Mass, and R. Mulligan, Harvard Medical School and Children's Hospital, Boston, Mass) was cotransfected with Ad.hTK or Ad.Luc (each at 10^8 PFU). Soluble VEGF-R1 is able to entrap several VEGFs, including VEGF-A. Therefore, it inhibits the biological effects of VEGF-A.

The capacity of VEGF-A antibody, PTK 787, or Ad.s-flt-1 to block VEGF-A–induced neovascularization was confirmed by using them or their respective controls (nonimmune IgG, normal drinking water, or Ad.Luc) in mice whose muscles were infected with Ad.VEGF-A (10^7 PFU). Mice (n=6 per group) were humanely killed at 14 days from gene transfer for evaluation of neovascularization.

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1. Emanueli et al. "Akt/Protein Kinase B and Endothelial Nitric Oxide Synthase Mediate Muscular Neovascularization Induced by Tissue Kallikrein Gene Transfer". American Heart Association (AHA). *Circulation*. 2004;110:1638-1644.

DM199 Has Been Shown To Lower Blood Pressure

IV Dose

- Has been show to rapidly (within minutes) lower blood pressure at higher dosages

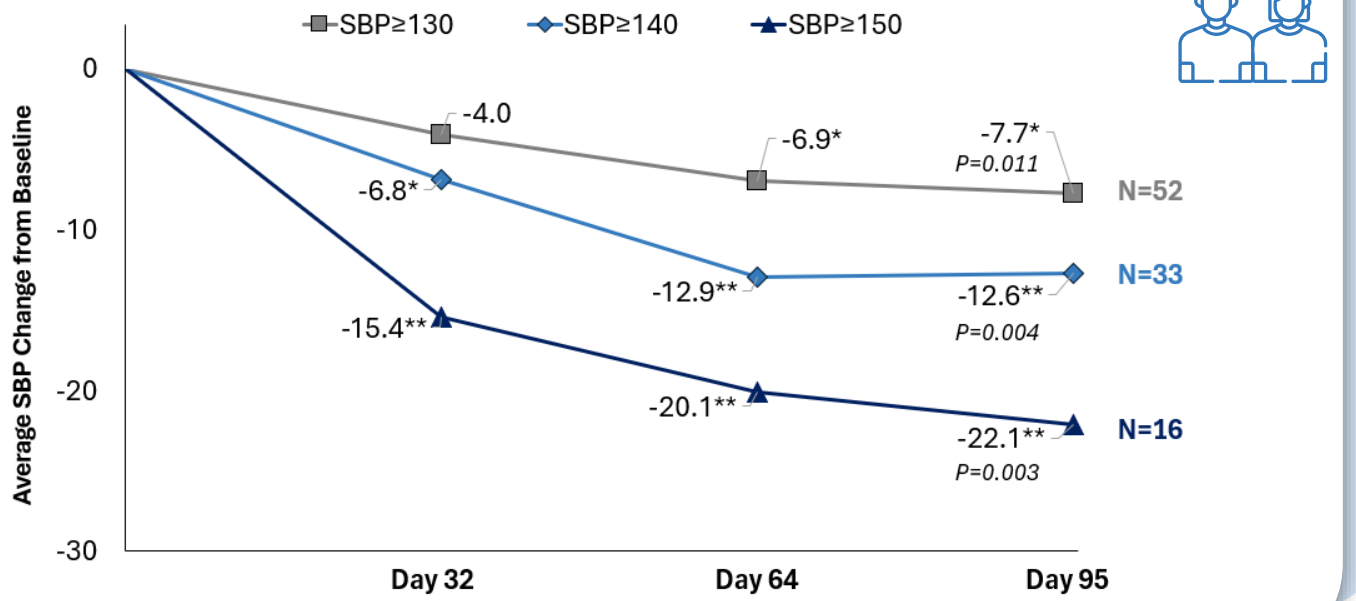
Subcutaneous Dose (SC)

- Sustained, clinically relevant and statistically significant SBP reduction in CKD patients with elevated SBP at Baseline

Subcutaneous Injection

DM199 REDUX Phase 2 CKD Trial (N=82)

- **Statistically significant systolic blood pressure (SBP) reductions ≥ 130 mmHg baseline**
- Greater reductions ≥ 140 mmHg and ≥ 150 mmHg



Student's T-test vs. baseline: *p<0.05 | **p<0.01

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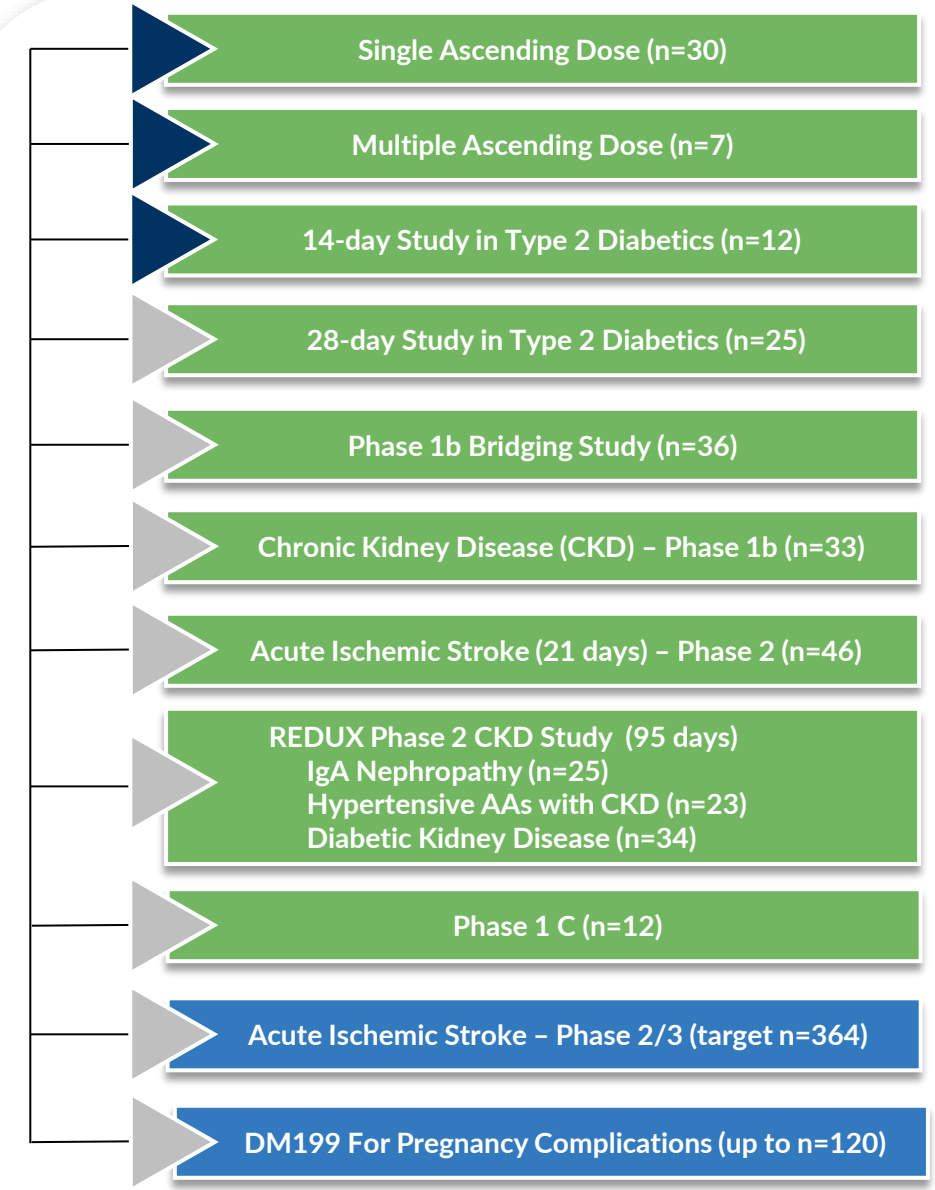
Clinical Summary: >300 patients dosed with DM199 to date

- Generally safe and well tolerated, in both IV and SC formulations
  - Most common related adverse events observed, all of which self-resolved:
    - Constipation
    - Injection site reactions
    - Nausea
    - Headache
- Consistent evidence of target engagement/activity (blood pressure, nitric oxide and prostacyclin)
- AE of interest is hypotension
  - Hypotension can occur if DM199 is dosed at significantly higher levels than targeted, and/or if the patient is on an ACE inhibitor (which prevents the degradation of bradykinin)



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