



DiaMedica
THERAPEUTICS

Corporate Presentation

April 2024

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, uncertainties relating to 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; the possibility of additional future adverse events associated with or unfavorable results from the ReMEDy2 trial; 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 cardio-renal disease and its expectations regarding the benefits of DM199; 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; uncertainties relating to regulatory applications and related filing and approval timelines; 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 cardio-renal disease, and the risks identified under the heading "Risk Factors" in DiaMedica's annual report on Form 10-K for the fiscal year ended December 31, 2023.

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.

Company Overview

Cash: ~\$53 million
(Runway to 2026)

>\$10 Billion US Market Opportunity for Acute Ischemic Stroke (AIS)

- ~80% of patients have no treatment option today
- No new therapeutics since tPA over 25 years in US and Europe

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

- Recombinant KLK1 (rKLK1) protein with FDA Fast-Track Designation
- Increases collateral circulation in the ischemic penumbra
- 24-hour treatment window, beyond tPA's 4.5 hours

Extensive Supporting KLK1 Clinical Data for AIS Patients

- Encouraging DM199 phase 2 results
- >1 million est. treated yearly with human urinary KLK1 (HUK) in China
- >200 clinical studies demonstrated efficacy with HUK

AIS Phase 2/3 Study: Potential Single Study for FDA Approval

- Fast path to data: ~340 participant study with 90-day endpoint
- Interim analysis after 144 participants enrolled
- *Now recruiting participants*

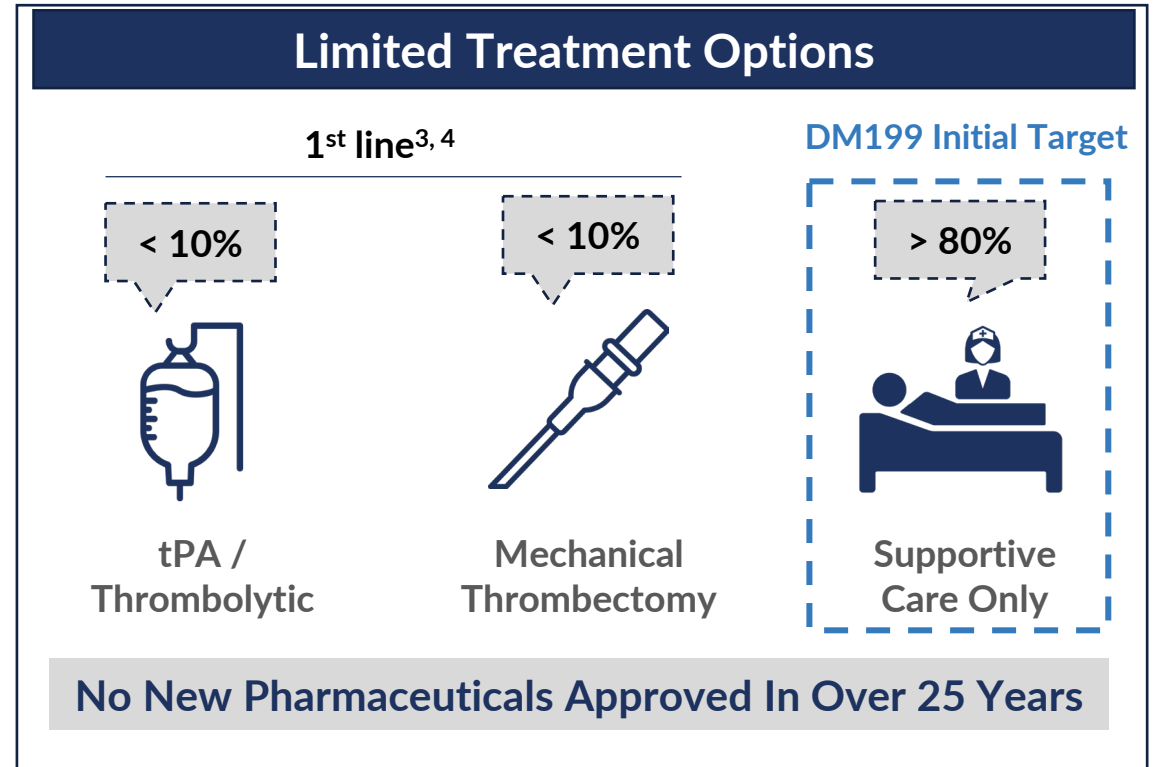
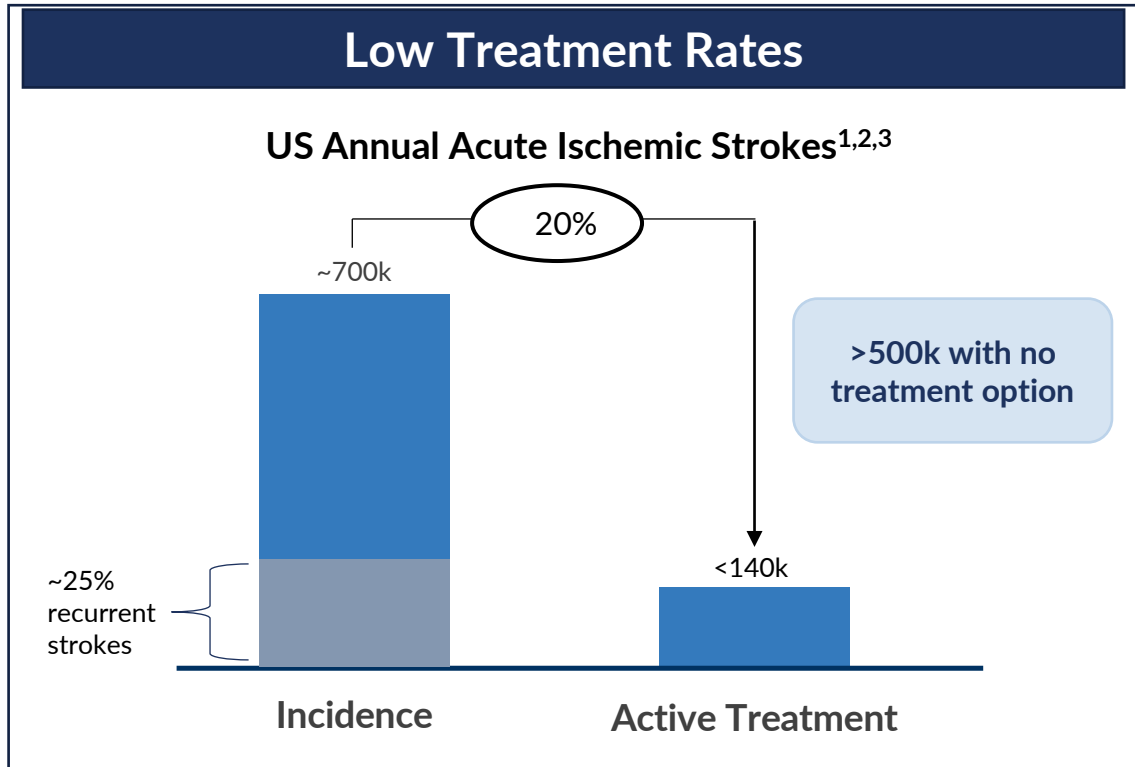
DiaMedica Pipeline

Current Focus is on AIS Phase 2/3 Pivotal Study – Now Recruiting

COMPOUND	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 2/3
DM199 (Rinvecalinase alfa) Recombinant KLK1	Acute Ischemic Stroke	ReMEDy2 Study			
	Cardio-Renal (Undisclosed)	Phase 2 ready			
DM300 Recombinant serine protease inhibitor	Severe Inflammatory				

High Unmet Need in Acute Ischemic Stroke

>7.5 Million Acute Ischemic Strokes Globally⁵, ~80% of Patients Have No Treatment Options



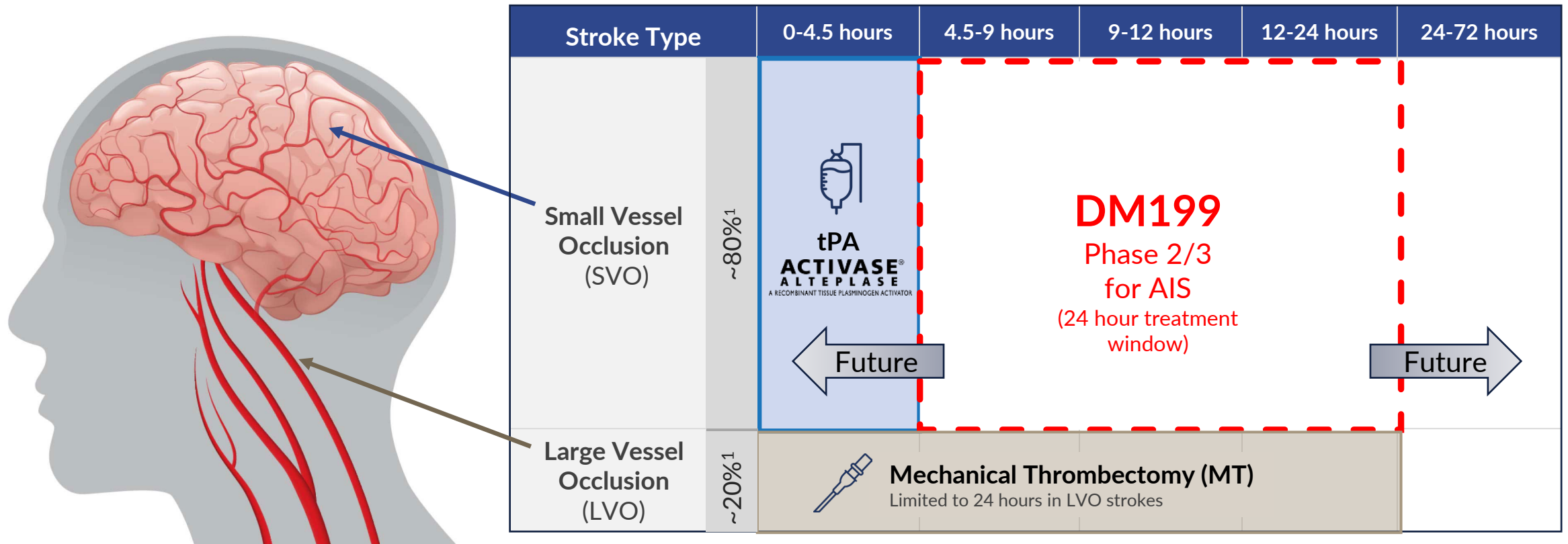
DM199 US Estimated Market Opportunity = \$10+ Billion

Sources: 1. Ej 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: 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

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



Low KLK1 Levels Independently Associated With AIS Incidence & Poor Outcomes

DM199 (rKLK1) Therapeutic Approach is to Increase KLK1 Levels to Treat and Prevent Strokes

Low KLK1 Levels Independently Associated with First Stroke and Predictor of Recurrent Stroke (N=2,478, P<0.001)

ANNALS of Neurology

Plasma Tissue Kallikrein Level Is Negatively Associated with Incident and Recurrent Stroke: A Multicenter Case–Control Study in China

Qin Zhang, PhD,^{1,2} Hu Ding, PhD,¹ Jiangtao Yan, PhD,¹ Wei Wang, PhD,³
Aiqun Ma, PhD,⁴ Zhiming Zhu, PhD,⁵ Katherine Cianflone, PhD,⁶ Frank B. Hu, MD, PhD,⁷
Rutai Hui, PhD,⁸ and Dao Wen Wang, MD, PhD¹

Objective: Tissue kallikrein (TK) cleaves kininogen to produce the potent bioactive compounds kinin and bradykinin, which lower blood pressure and protect the heart, kidneys, and blood vessels. Reduction in TK levels is associated with cardiovascular disease and diabetes in animal models. In this study, we investigated the association of TK levels with event-free survival over 5 years in Chinese first-ever stroke patients.

Methods: We conducted a case–control study with 1,268 stroke patients (941 cerebral infarction, 327 cerebral hemorrhage) and 1,210 controls. Plasma TK levels were measured with an enzyme-linked immunosorbent assay. We used logistic regression and Cox proportional hazards models to assess the relationship between TK levels and risk of first-time or recurrent stroke.

Results: Plasma TK levels were significantly lower in stroke patients (0.163 ± 0.064 mg/l vs 0.252 ± 0.093 mg/l, $p < 0.001$), especially those with ischemic stroke. After adjustment for traditional risk factors, plasma TK levels were negatively associated with the risk of first-ever stroke (odds ratio [OR], 0.344; 95% confidence interval [CI], 0.30–0.389; $p < 0.001$) and stroke recurrence and positively associated with event-free survival during 5 years of follow-up (relative risk, 0.82; 95% CI, 0.74–0.90; $p < 0.001$). Compared with the first quartile of plasma TK levels, the ORs for first-ever stroke patients were as follows: second quartile, 0.77 (95% CI, 0.56–1.07); third quartile, 0.23 (95% CI, 0.17–0.32); fourth quartile, 0.04 (95% CI, 0.03–0.06).

Interpretation: Lower plasma TK levels are independently associated with first-ever stroke and are an independent predictor of recurrence after an initial stroke.

ANN NEUROL 2011;70:265–273

AIS Patients with Unfavorable Outcomes & Death Had 80% Lower KLK1 on Average (N=75; P<0.05)

Hindawi
Disease Markers
Volume 2019, Article ID 5289715, 6 pages
<https://doi.org/10.1155/2019/5289715>



Research Article

High Level of Serum Tissue Kallikrein Is Associated with Favorable Outcome in Acute Ischemic Stroke Patients

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Background/Objectives. We sought to assess the association between a serum tissue kallikrein (TK) level and a 90-day outcome in acute ischemic stroke (AIS) patients who received acute reperfusion therapy. **Methods.** Consecutive AIS patients within 6 hours after stroke onset between December 2015 and August 2017 were prospectively recruited. Blood samples were collected before acute reperfusion therapy for serum TK measurement. Outcome was modified Rankin scale (mRS) score at 90 days after stroke onset. Binary logistic regression was performed to analyze the association between the baseline TK level and the clinical outcome. **Results.** Between December 2015 and August 2017, 75 patients (age range from 33 to 91 years, 72.0% male) were recruited in this study. Higher baseline TK was independently associated with a favorable functional outcome (mRS 0–2) (odds ratio 1.01, 95% confidence interval (CI) 1.00–1.02, $p = 0.047$) and low mortality rate (odds ratio 0.98, 95% CI 0.96–1.00, $p = 0.049$) at 90 days. Increased TK level was associated with 90 d mRS (0–2) with area under the curve of 0.719 (95% CI 0.596–0.842; $p = 0.002$). **Conclusions.** Serum TK can be a promising predictor of clinical outcome in AIS patients who received acute reperfusion therapy.

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

>1 Million Estimated AIS Patients Treated Per Year

- **HUK for AIS:**
 - Marketed by Shanghai Pharmaceuticals under Kailikang®.
 - Ameliorates neurological symptoms with few adverse events.¹
- **>1 million est. AIS patients treated annually 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



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

Journal of International Medical Research
48(9) 1–10
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DOI: 10.1177/0300060520943452
journals.sagepub.com/home/imr



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.

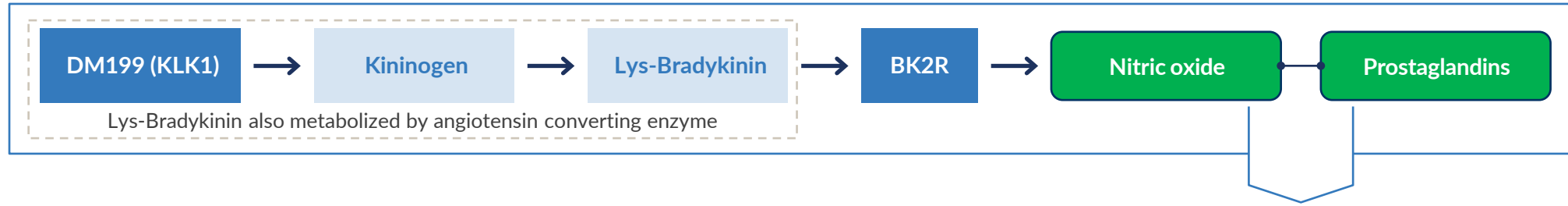
Methods: We searched the online databases PubMed, Embase, Cochrane Library, Google Scholar, and China National Knowledge Infrastructure (CNKI) for papers published between January 2015 and December 2019. The quality of each trial was assessed using the Cochrane Reviewers' Handbook. Randomized controlled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

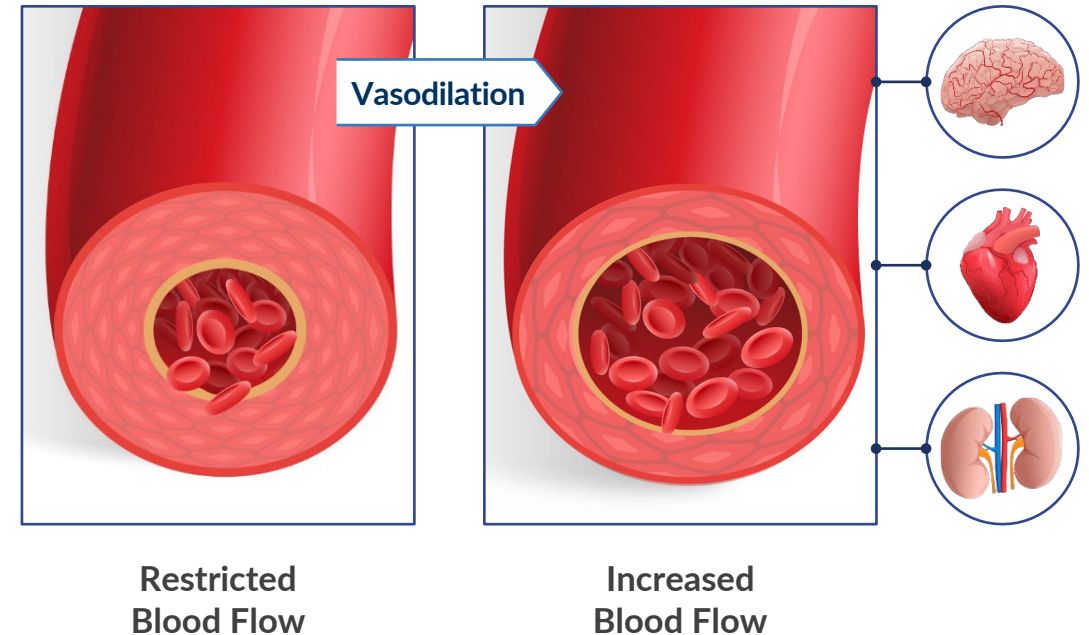
Conclusions: HUK ameliorates neurological symptoms in stroke patients with few adverse effects. Further high-quality, large-scale randomized trials are needed to confirm these results.

DM199 (rKLK1 – Rivecalinase Alfa) Novel Mechanism of Action

Local Vasodilation in Stroke and Other Vascular Diseases



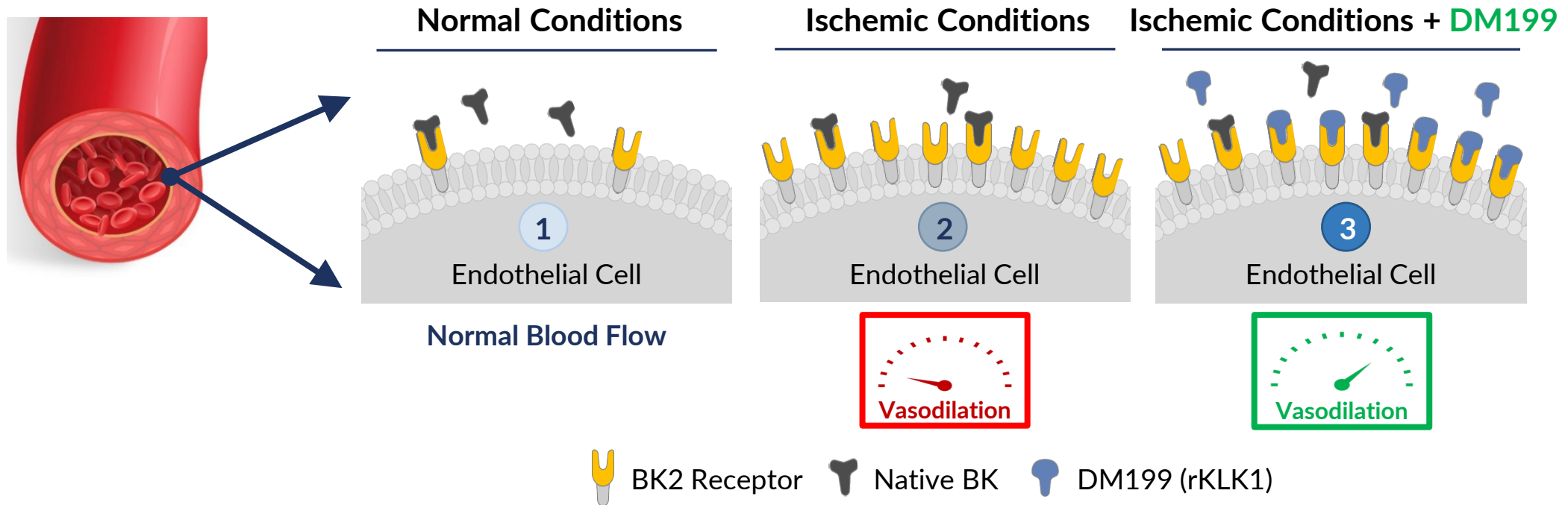
- KLK1 is made predominately in kidneys (present also in the vasculature and brain) and circulates in the blood.
- DM199 (recombinant KLK1) acts on low molecular weight kininogen to produce lys-bradykinin.
- KLK1 is the main lys-bradykinin forming enzyme within organs and blood vessels during resting conditions.¹
 - ACE is the main kinin-inactivating enzyme in the circulation.
- Lys-bradykinin binds to bradykinin receptors (BK2) on arterial endothelium to release nitric oxide (NO) & prostaglandins (PG).
- Increased NO and PG via cGMP and cAMP, respectively, relax arterial smooth muscle cells driving vasodilation.



Ischemia Naturally Induces Upregulation of Bradykinin2 (BK2) Receptors

- 1 The BK2 receptor plays a critical role in regulating vascular tone and blood pressure under normal conditions.
- 2 In response to ischemic conditions, the BK2 receptors are upregulated in affected tissues, including the brain.¹
- 3 DM199 (rKLK1) produces Bradykinin (BK) which activates the upregulated BK2 receptors in the affected arteries (ischemic penumbra), improving collateral circulation to increase blood flow and oxygenation to the ischemic penumbra.

Brain Artery Under Different Conditions



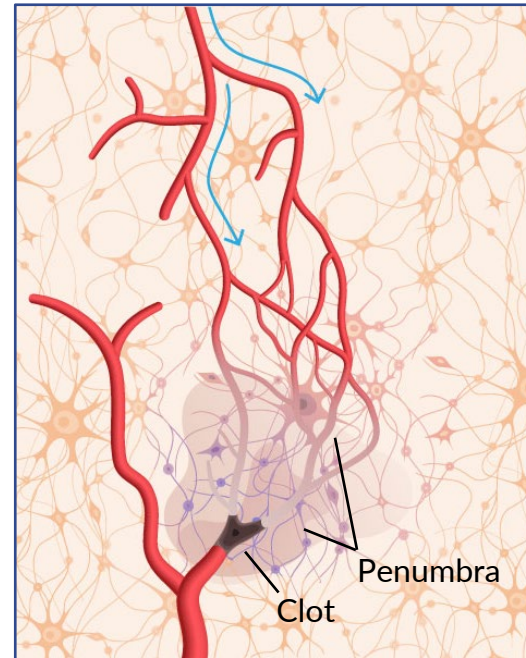
DM199 (rKLK1): Improve Collateral Circulation in Acute Ischemic Stroke

Novel Mechanism With Potential to Improve Stroke Outcomes & Reduce Risk of Stroke Recurrence

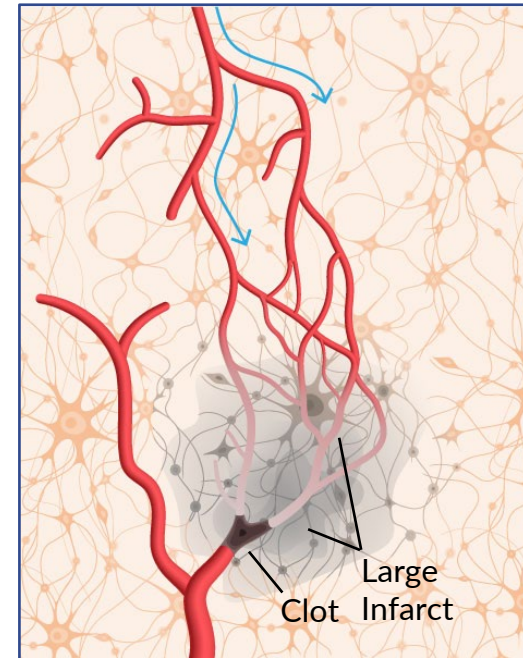
DM199 does **not** need to pass the blood-brain-barrier to deliver therapeutic benefit.

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

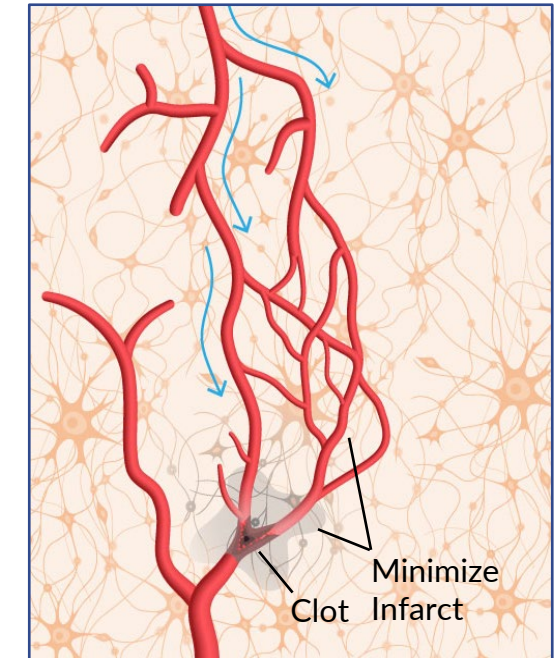
Early stroke



No DM199 treatment



DM199 treatment

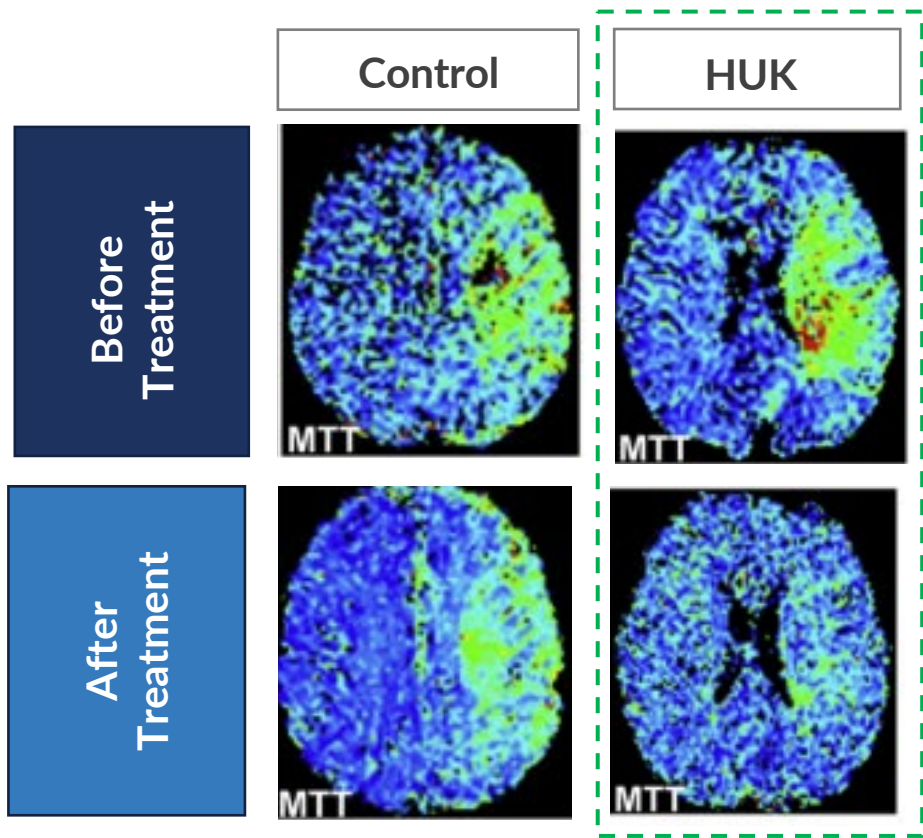


- **Improve stroke outcomes** – save cerebral tissue in the ischemic penumbra reducing the size and impact of the stroke

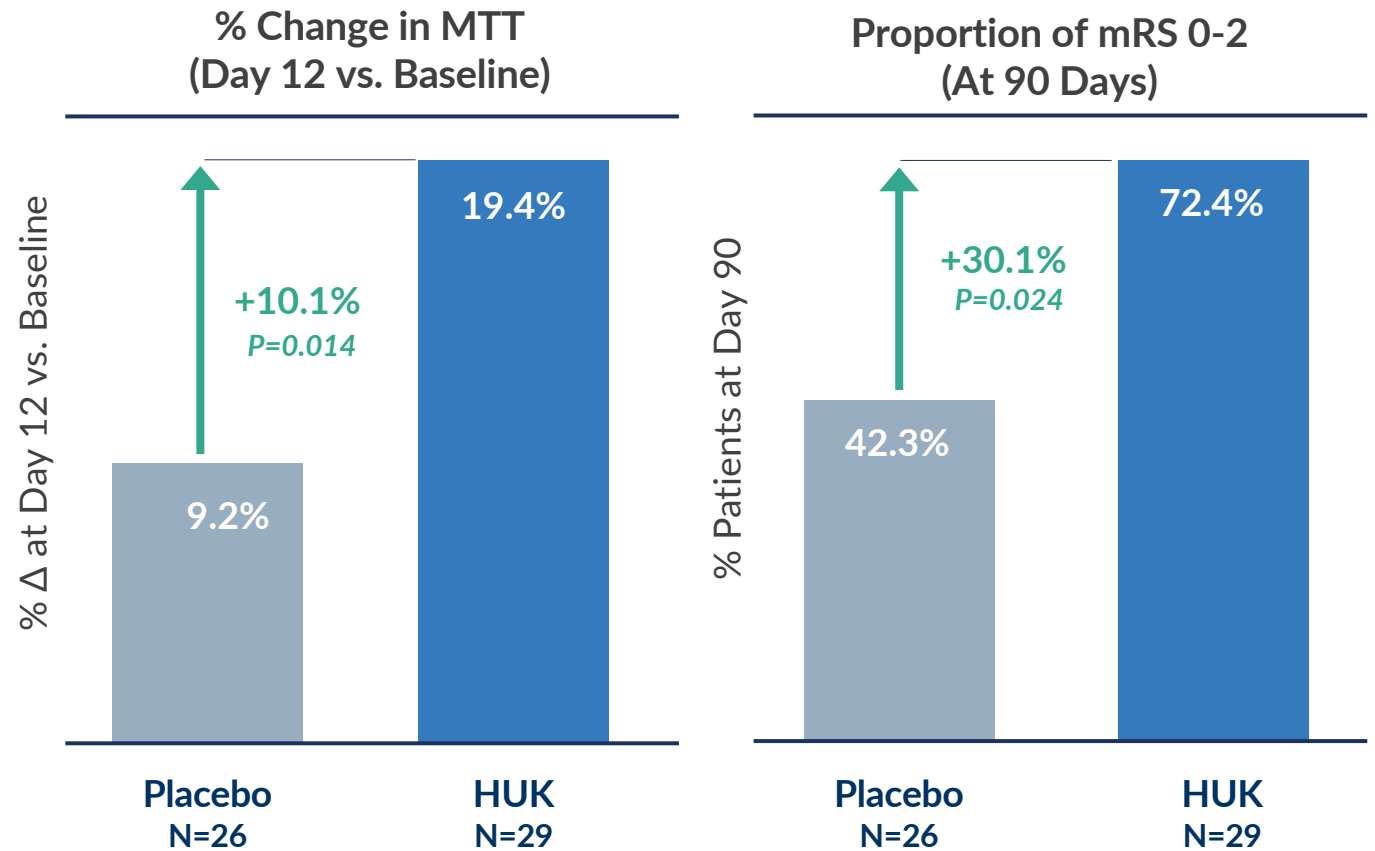
- **Reduce risk of stroke recurrence** – improved collateral blood flow reduces the risk of arterial re-occlusion (stroke)

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



Representative reperfusion MR images of 1 control patient and 1 HUK-treated patient

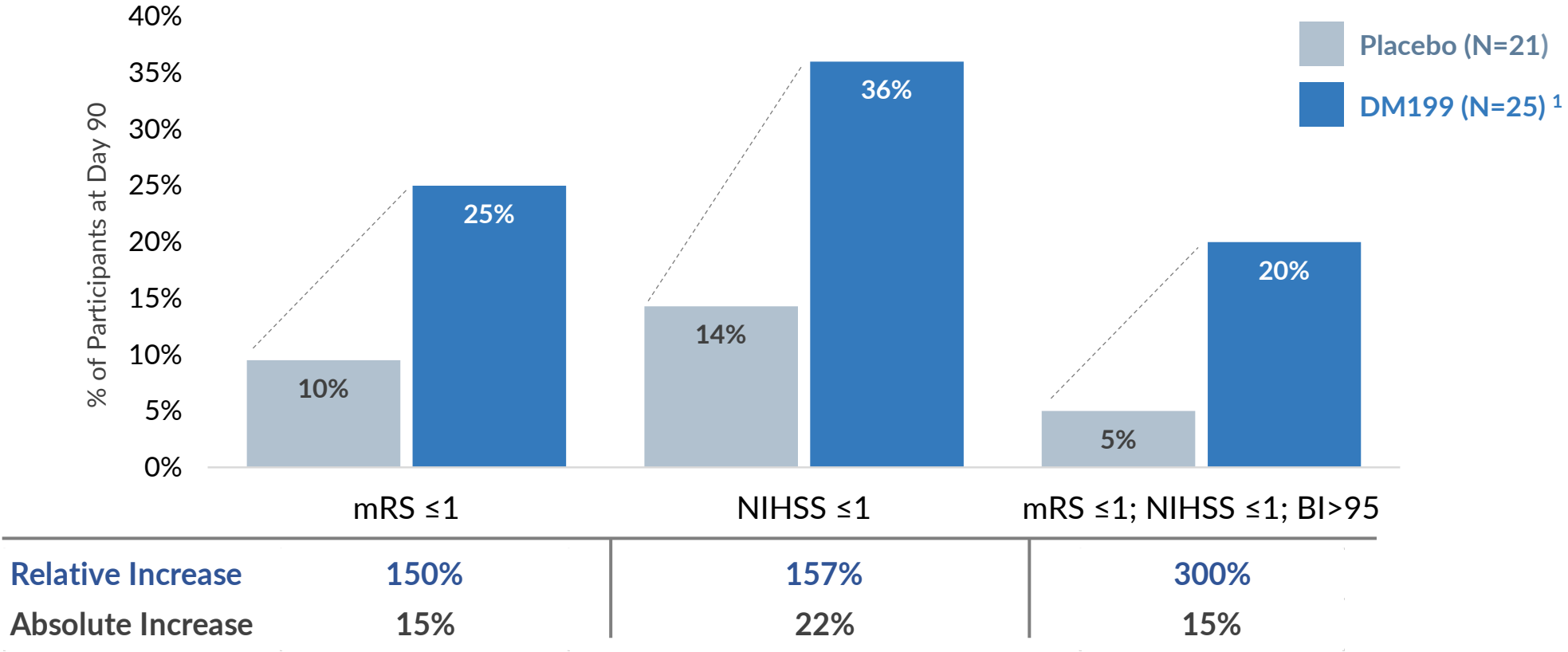


Improved relative MTT associated with favorable functional outcome OR=0.483 95% CI (0.243-0.960) p=0.038¹

DM199 (rKLK1) Phase 2 Results: Improved Excellent Outcomes In Non-MT Subgroup

Patient Population Closely Aligns with ReMEDy2 Phase 2/3 Study and HUK

DM199 (rKLK1) Excellent Outcomes at 90 Days in non-MT Pretreated Patients¹



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

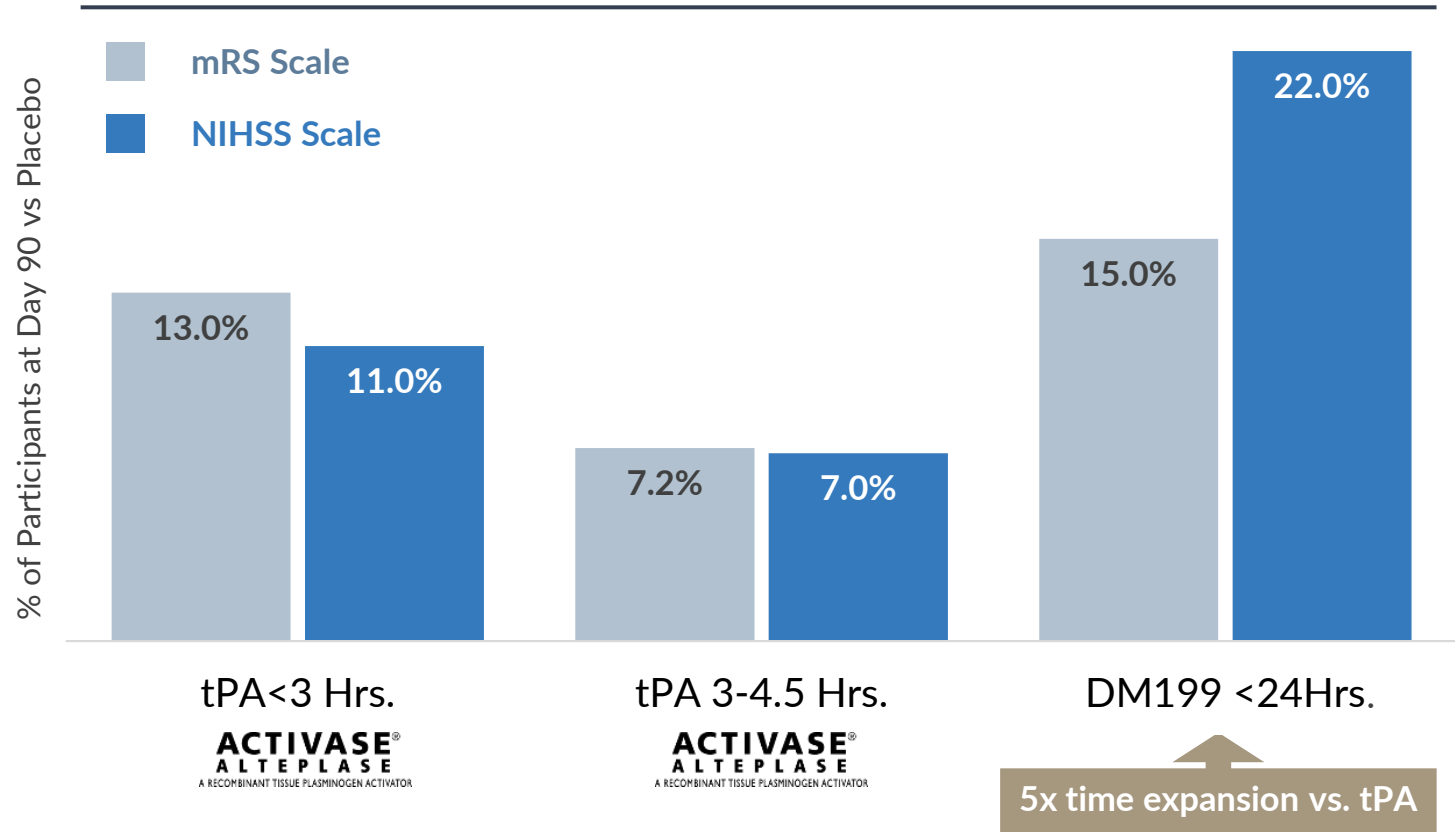
1. N=24 for DM199 mRS data; The excluded participant had an NIHSS score of 1 at day 22, but did not complete day 90 visit

DM199 (rKLK1) Phase 2 AIS Results Compared with Published tPA Data

>2x Increase in Excellent Outcomes (NIHSS ≤ 1 and mRS ≤ 1) with Longer Treatment Window

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

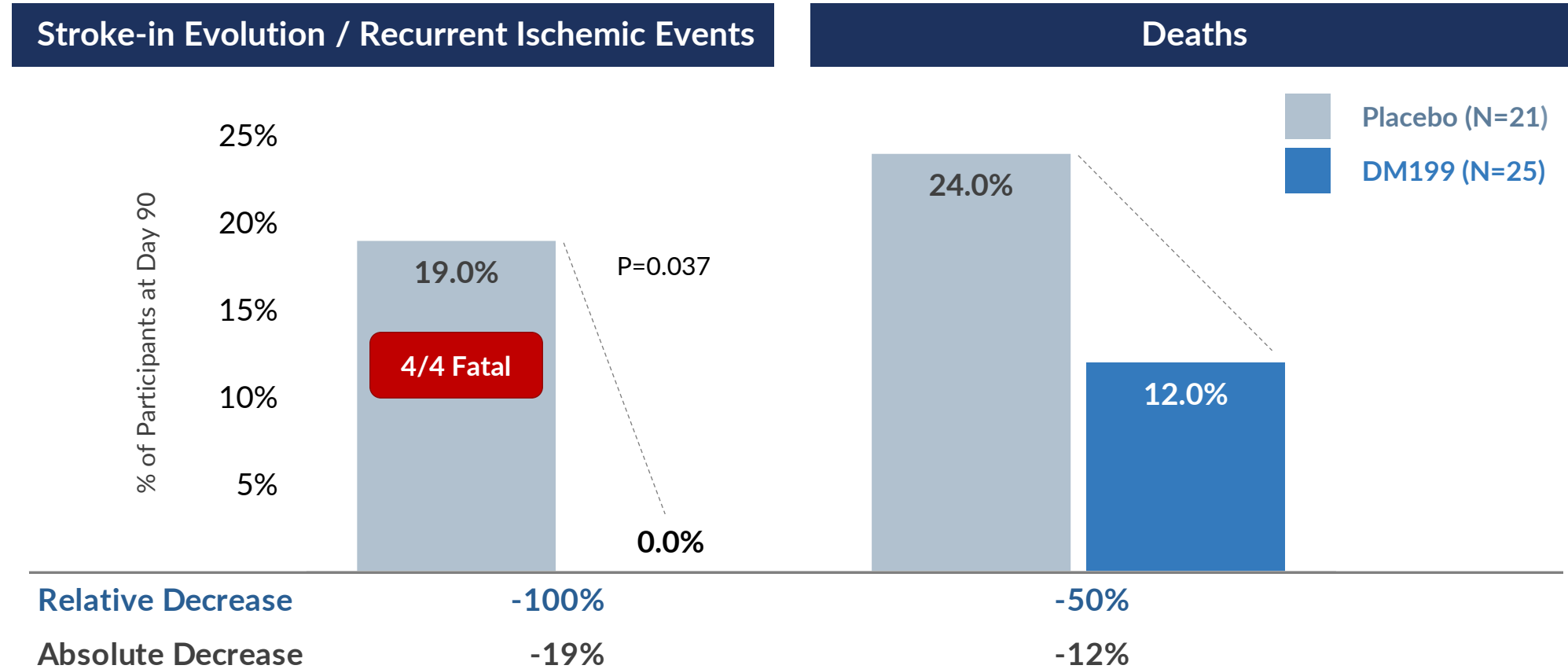
Comparison of Improvements in % of Participants with Excellent Outcomes (NIHSS ≤ 1 and mRS ≤ 1) vs Placebo (DM199 and tPA analysis excludes MT treated participants)



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 (rKLK1) Phase 2 AIS Results: Reduced Stroke Recurrence & Deaths

Supporting Secondary Endpoints in Non-MT Pretreated Subgroup



DM199 Phase 2/3 AIS Study 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

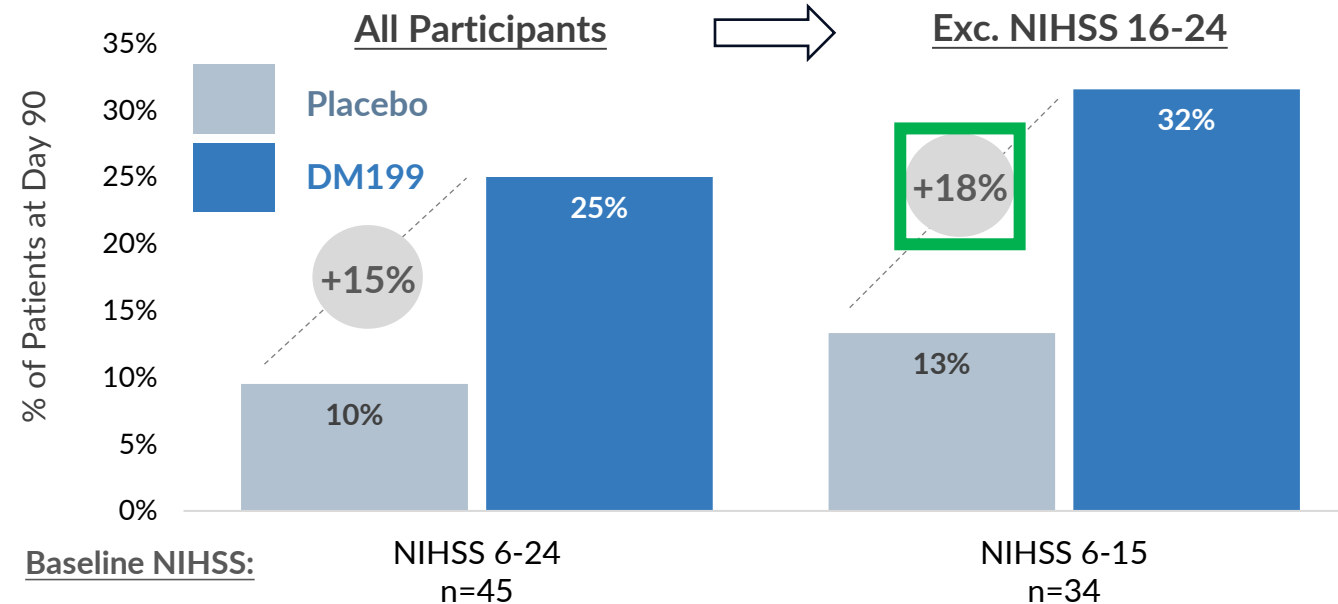
Exclude:
MT

- 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)

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 study

% of ReMEDy1 Participants with mRS 0-1 at 90 Days (Non-MT subgroup)^{1,2}



ReMEDy2 DM199 Phase 2/3 AIS Study Adaptations Based on Phase 2 Results

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

- Believe the greatest clinical benefit will be observed in patients who do not receive mechanical thrombectomy and/or tPA.
- Excluding MT/tPA does not significantly erode the commercial opportunity since less than 20% of patients receive these treatments.

Observations and Rationale

**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)

**Exclude:
tPA**

- Greater DM199 treatment effect observed in supportive care vs. tPA in DM199 phase 2
 - 42% of participants in DM199 supportive care sub-group had NIHSS ≤ 1 despite unfavorable baseline scores
- Future potential DM199 label expansion as an adjunct to tPA

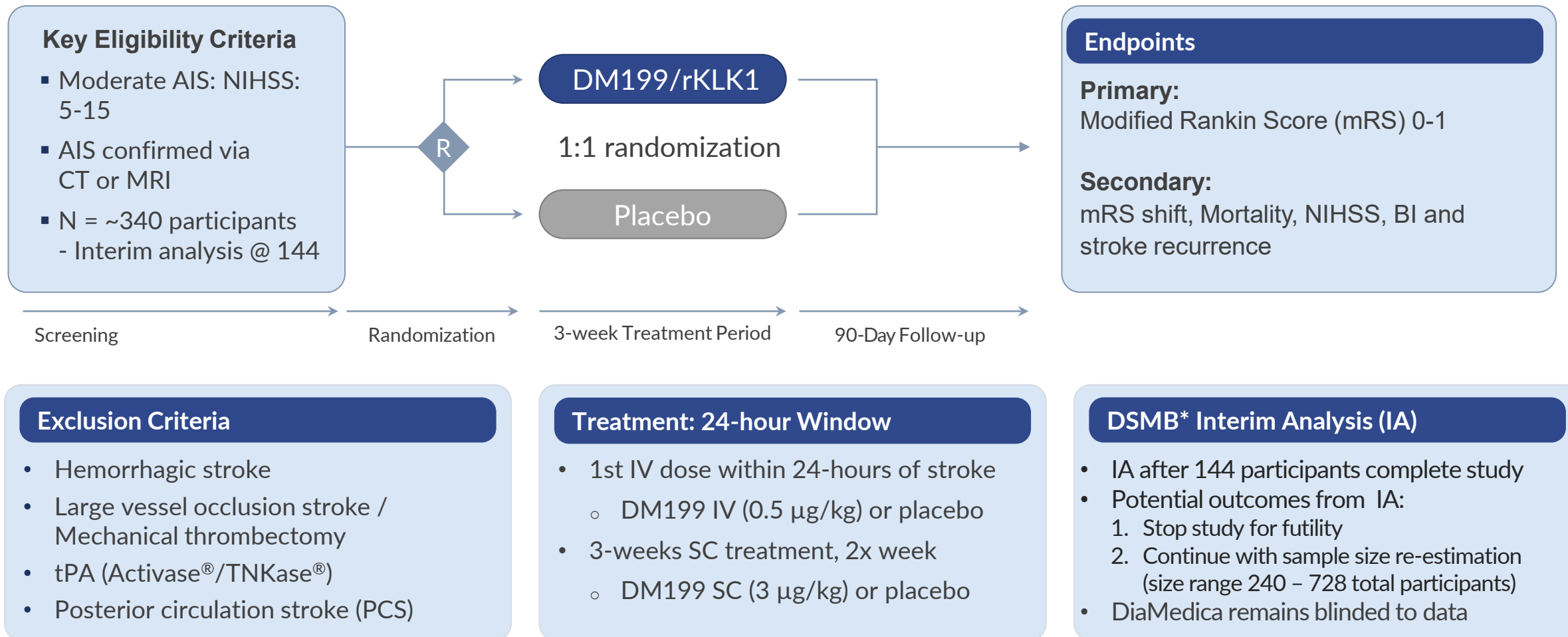
**Reduce Baseline
Stroke Severity:**

- 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 study
- Randomization mechanism to harmonize baseline characteristics between placebo and DM199

DM199 (rKLK1) Pivotal Phase 2/3 Study Design - Now Recruiting



With Interim Analysis to Manage Statistical Powering



Corporate Summary



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

Key Manufacturing Challenges Solved: Protein Activity, Stability and Economical Scale

Protein Development

DM199: (rKLK1) Demonstrates Excellent Potency

- Configuration of high & low molecular weight glycoforms critical for optimal activity
- Reproducible manufacturing process
- 5+ companies unsuccessful in moving recombinant KLK1 proteins to clinic

Patents and Exclusivity

Patents

- **Composition of matter**
 - Issued US/EU (2033)¹
- **Formulation, subcutaneous and improved PK**
 - Issued US (2033)
- **Dosing & route of delivery**
 - Issued US (2038) / pending global

Exclusive license of patented gene expression technology

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

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

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 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 a decade

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.

Summary

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

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AIS Phase 2/3 Study: Potential Single Study for FDA Approval

- Fast path to data: ~340 participant study with 90-day endpoint
- Interim analysis after 144 participants enrolled
- *Now recruiting participants*



NASDAQ: DMAC



www.diamedica.com

Thank you!