# ReMEDy2 Update

November 14, 2024

DiaMedica THERAPEUTICS

Transforming Care for Stroke and Preeclampsia

# Executive Summary

## Primary updates to ReMEDy2 AIS program:

1. Inclusion of patients who did not 'respond' to tPA/TNK (thrombolytic)
   - Anticipate strong treatment responses (strong DM199 response, low placebo response) and up to 50%+ increase in eligible patient pool
2. Increase interim analysis sample size from 144 to 200
   - Additional data points enhance the precision of the algorithm used to determine the final sample size, potentially reducing the total number of participants required for the study

## These updates are intended to achieve the following outcomes:

***Increase*** probability of success for the ReMEDy2 trial (achieve statistical significance)

***Expedite*** overall completion of the study, with potential for a reduced sample size and cost savings

***Expand*** the initial label and global commercial market opportunity

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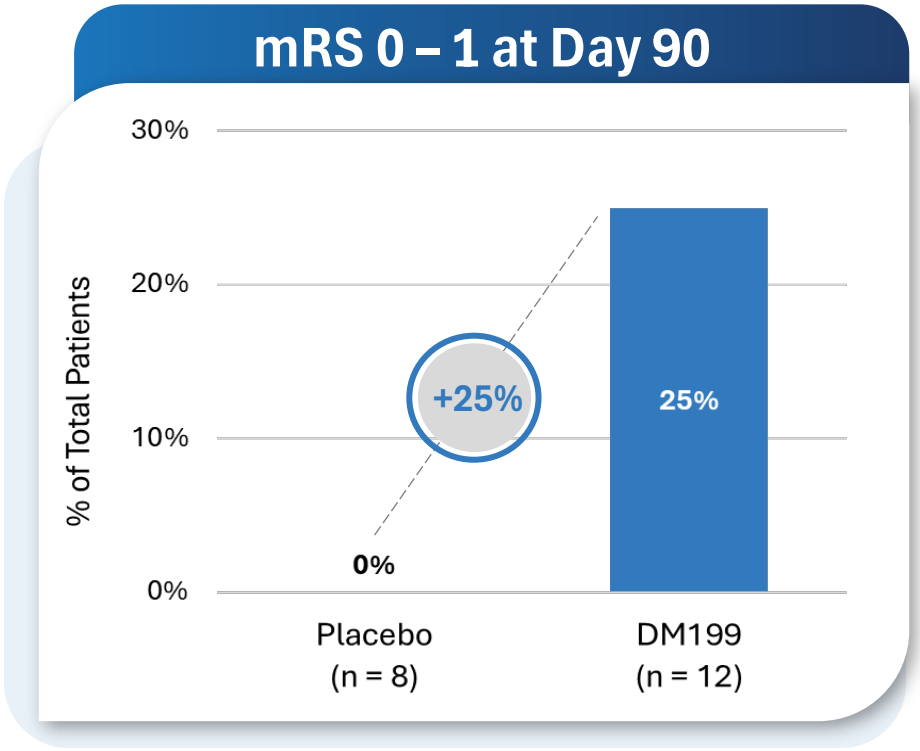
# Why Including tPA/TNK Non-responders is Beneficial

- **Potential Benefits:**
  - tPA/TNK non-responders exhibited high treatment effect (low placebo response rate) in our Phase 2 ReMEDy1 trial
    - Potentially benefits interim analysis calculation and lowers final sample size
  - Larger eligible patient pool has the potential to significantly increase ReMEDy2 enrollment rates
    - Potential to complete study more quickly
  - Broadens initial commercial label and global market opportunity

## ReMEDy1 Phase AIS – Subgroup of tPA Pre-treated Participants

- Low placebo response rates suggestive of participants' "non-response"
- Patients were enrolled on average **13.5 hours after receiving tPA/TNK**

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# Updated Protocol Inclusion Criteria

- If the participant has received tPA/TNK (thrombolytic) treatment for AIS within 4.5 hours of last known normal/AIS stroke onset, and at least 6 hours after completing thrombolytic treatment, the participant meets all the following criteria:
  - Participant’s initial NIHSS score prior to thrombolytic was ≤15; and
  - At least six hours after thrombolytic, the participant has an NIHSS score of ≥5 and ≤15 with a persistent or worsening deficit; and
  - The participant’s NIHSS score showed less than a 4-point improvement, or worsened, after receiving thrombolytic; and
  - Participant meets all other inclusion and exclusion criteria, including repeat brain imaging to rule out hemorrhagic transformation.

**Waiting 6 Hours:**
- Reduces likelihood of “delayed” responders
- Risk of developing a bleed from tPA cut by ~50%

- Same stroke severity as non-tPA/TNK patients

- 4-point improvement suggests patient is on a trajectory to recover

- Rule out worsening because of a bleed
- Must still be treated within 24 hours

**Anticipate Strong Treatment Responses and Accelerated Enrollment**

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# Potential Benefits of Increasing Sample Size

2. Interim Analysis at 200

## Increases precision of final sample size determination – potential for significant cost/time savings

- The following **actual simulation** demonstrates the potential benefit of improving precision in determining the final sample size
  - Treatment effect (improvement driven by DM199) and placebo response rates are identical under both cases, but to maintain the integrity of the algorithm they cannot be shown; only difference in simulation parameters is sample size of 144 versus 200 participants
  - Final sample size variance of 146 participants equals potential cost and time savings

| | 144 Patients | | 200 Patients |
|---|---|---|---|
| Treatment Effect | X% | Same | X% |
| Placebo Response | Y% | Same | Y% |
| Final Sample Size | 485 | | 339 |

**146 Participant Difference =**
**Estimated $10m+ cost savings and ~6 month reduction in study timeline***

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# ReMEDy2 Trial Summary of Updates

- We believe adding non-responsive tPA/TNK may:
  - Accelerate enrollment → increased per-site enrollment rates
  - Anticipate favorable treatment response → increases probability of clinical success and lower sample size
  - Expand the commercial potential of DM199 increasing value
- We also believe that increasing the sample size from 144 to 200 is prudent to enhance the precision of the simulation, potentially reducing the final sample size which has significant implications on both costs and time to complete the trial

**We believe these updates may increase the probability of success and accelerate the timeline to completion**

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