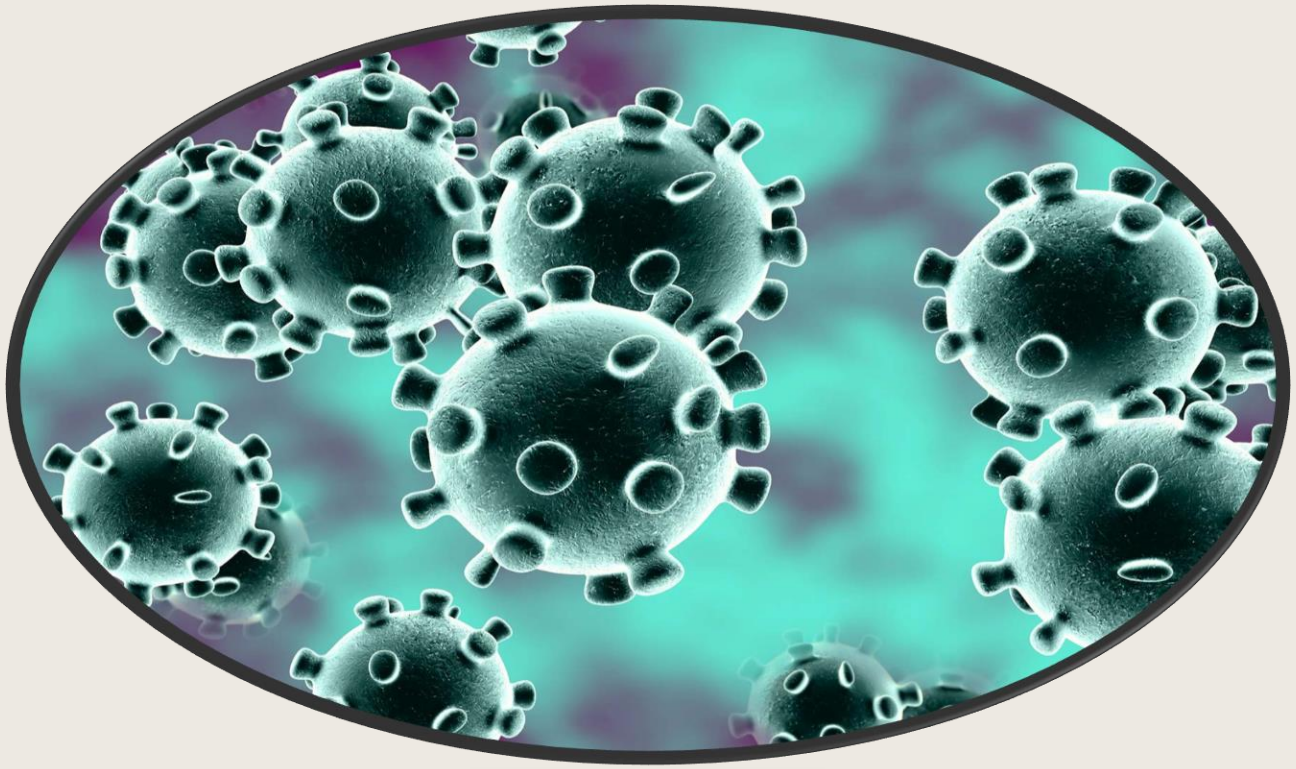

# WHO Emergency meeting R&D Blueprint 14FEB2023 MARVAC - Therapeutics

Dr Simon G P Funnell PhD FRSBiol.
Scientific Leader, UK Health Security Agency
Translational Research Manager, Quadram Institute Norwich, UK

World Health Organization

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# MARVAC 14/JUN/2022 Therapeutics developers

1. mAb therapy (Larry Zeitlin, Mappbio)

2. Marburg virus PEP (Tom Geisbert, UTMB)

3. Small molecules (Elizabeth Lapatovich, JPM CBRN MED)

# MARVAC 14/JUL/2022 Conclusions (Therapeutics)



1. **mAb Mappbio**: mBP091 binds GP near receptor binding site & neutralizes, high efficacy (100%) in GP & NHP when given @ D4 or D5 post challenge (n=6 each group). CHO cell produced. In phase I. Planning for animal rule.

2. **PEP using vaccines or therapeutics:** Angola more aggressive, but NHP studies show protection in PEP with various vaccines or therapeutics. Combination of mAb + remdesivir better than either alone @ d6.

3. **Remdesivir** approval being sought via animal rule. NHP ~80% efficacy. Natural history study completed. Is available for potential off label use.

4. **Human studies are viewed as important.** Timing of diagnosis may limit studies of early treatment. Combinations may be more effective than individual agents, though numbers may be too small to do factorial design studies & Ph I data may be needed.

5. **Coordination** of studies using a common protocol provides the best hope of collecting useful data, much as has been discussed for vaccines (including similar prioritization scheme). Drugs could be studied under MEURI, randomized study to collect standardized data. A small group will develop plans. Volunteers to help are sought

# Marburg therapeutics Cross *et al*., PLOS Path Oct 2022

**Table 2. MARV therapeutics with protective efficacy in the NHP model.**

| Treatment | Challenge virus | Treatment postchallenge | Treatment dose | Number of doses | Survival [%] | Ref. |
|---|---|---|---|---|---|---|
| **VSV-MARV** | MARV Musoke | 20–30 minutes | $1 \times 10^7$ PFU | 1 | 100 | [40] |
| | MARV Musoke | 1 day | $2 \times 10^7$ PFU | 1 | 83 | [40] |
| | MARV Musoke | 2 days | $2 \times 10^7$ PFU | 1 | 33 | [40] |
| | MARV Angola | 20–30 minutes | $1 \times 10^3$ PFU | 1 | 25 | [41] |
| | MARV Angola | 20–30 minutes | 50 PFU | 1 | 89 | [42] |
| **VSVN2CT1-MARV** | MARV Angola | 20–30 minutes | 50 PFU | 1 | 80 | [42] |
| **VSVN4CT1-MARV** | MARV Angola | 20–30 minutes | 50 PFU | 1 | 60 | [41] |
| **MR191-N** | MARV Angola | 4 days | 50 mg/kg | 2 | 100 | [40] |
| | MARV Angola | 5 days | 50 mg/kg | 2 | 80 | [40] |
| | RAVV | 5 days | 50 mg/kg | 2 | 100 | [40] |
| **MR186-YTE** | MARV Angola | 5 days | 100 mg/kg | 1 | 100 | [43] |
| | | 6 days | 100 mg/kg | 1 | 0 | [43] |
| **MR186-YTE + Remdesivir** | MARV Angola | 6 days | 100 mg/kg | 1 | 80 | [43] |
| | MARV Angola | 6 days | 10 mg/kg load. 5 mg/kg maint. | 12 | 80 | [43] |
| **Remdesivir** | MARV Angola | 5 days | 10 mg/kg load. 5mg/kg maint. | 12 | 80 | [43] |
| | MARV Angola | 6 days | 10 mg/kg load. 5 mg/kg maint. | 12 | 0 | [43] |
| | MARV Angola | 4 or 5 days | 10 mg/kg load. 5 mg/kg maint. | 12 | 85 | [44] |
| | MARV Angola | 5 days | 5 mg/kg load. 5 mg/kg maint. | 12 | 50 | [44] |
| **BCX4430** | MARV Musoke | 1 hour | 15 mg/kg | 30 | 83 | [40] |
| | MARV Musoke | 1 day | 15 mg/kg | 28 | 100 | [40] |
| | MARV Musoke | 2 days | 15 mg/kg | 26 | 100 | [40] |
| **siRNA (NP)** | MARV Angola | 1, 2, 3, or 4 days | 0.5 mg/kg | 7 | 100 | [40] |
| | MARV Angola | 5 days | 0.5 mg/kg | 7 | 50 | [40] |
| | RAVV | 3 or 6 days | 0.5 mg/kg | 7 | 100 | [40] |
| **PMO*plus* (pool)** | MARV Musoke | 30–60 minutes | 40 mg/kg | 14 | 100 | [40] |
| **PMO*plus* (NP)** | MARV Musoke | 1 hour | 15 mg/kg | 14 | 83 | [40] |
| | MARV Musoke | 1 or 4 days | 15 mg/kg | 14 | 83 | [40] |
| | MARV Musoke | 2 days | 15 mg/kg | 14 | 100 | [40] |
| **rNAPc2** | MARV Angola | 10 minutes | 30 μg/kg | 15 | 17 | [40] |
| **IFNβ** | MARV Musoke | 1 hour | 35 μg/kg | 15 | 33 | [40] |
| **Favipiravir** | MARV Angola | at challenge | 250 mg/kg load. 150 mg/kg maint. | 3 | 85 | [45] |

load., loading dose; maint., maintenance dose.

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# MARVAC Therapeutics Summary

1. NHPs have historically served as the benchmark to rate predictive efficacy in humans and justify subsequent clinical trial efforts.

2. Several approaches ranging from pan-filoviral small molecule antivirals to MARV specific McAb approaches or combinations show impressive postexposure efficacy in NHPs at late-stage disease

3. These therapeutic approaches may be ideal for further development for use in humans.

4. Postexposure vaccine approaches have shown promise against MVD.

5. A recent adaptive clinical trial in the DRC has fortified evaluation criteria and allowed for recent approval of immunotherapeutics against EBOV.

6. This approach may serve as an ideal framework for initiation of human trials for MARV exposures in concert with guidance from the MARVAC.

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