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MALARIA IN MOTHERS AND BABIES
AN MMV INITIATIVE

Accelerating the development of appropriate antimalarial options for pregnant and lactating women

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RBM MIP Annual Meeting
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Medicines for Malaria Venture

Significant gaps remain to serve the needs of women of reproductive age in malaria-endemic countries

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MiMBa strategy aims to address the gaps to better serve the needs of women

MMV will accelerate discovery, development and delivery of appropriate antimalarial options for women who are/could become pregnant and for women who are breastfeeding

1	2	3
Broaden access to currently used antimalarial medicines	**Invest in appropriate new molecules for the future**	**Accelerate population appropriate compounds in the current pipeline**
…by collecting evidence on the safety and efficacy of existing antimalarials in pregnancy and lactation and ensuring quality-assured supply of medicines	……by exploring new modalities and enriching the future pipeline with appropriate New Chemical Entities for medicines that serve all malaria populations from the start	…by intentionally addressing the needs of women who are - or could become – pregnant and breastfeeding women

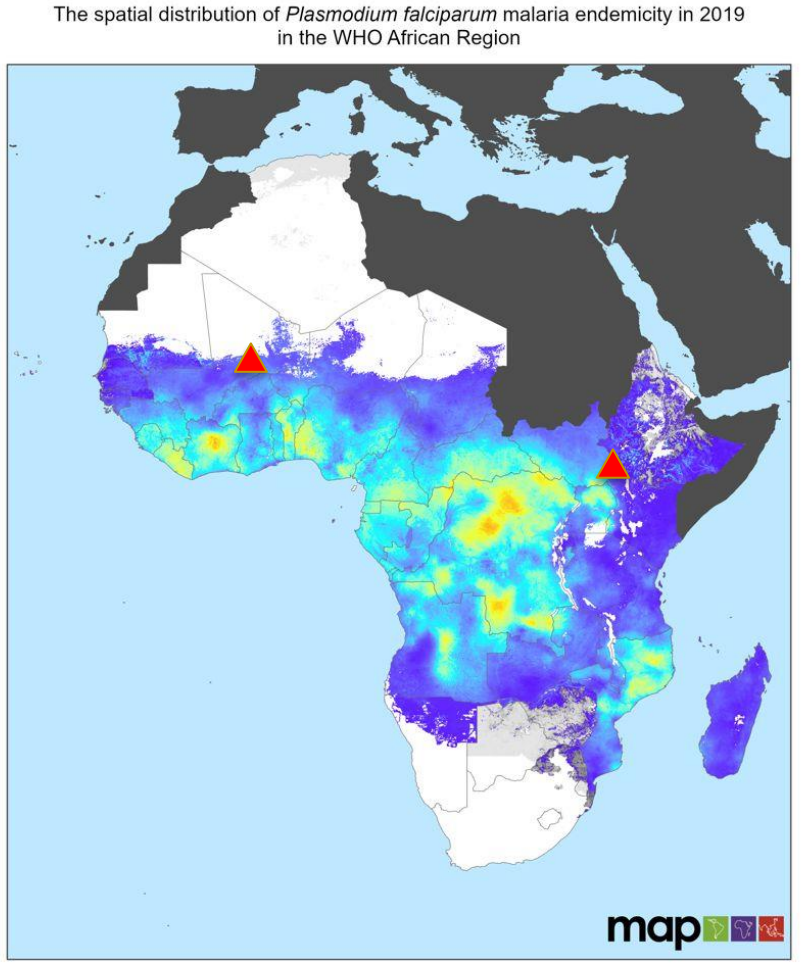
4

Advocate for greater inclusion of women who are – or could become – pregnant and lactating across antimalarial R&D and access

…by leveraging MMV's position at the interface of academic, pharmaceutical industry, regulatory, and global health communities

Broaden access to existing drugs - MiMBa Pregnancy Registry

- Co-led by LSTM and MMV - In collaboration with WWARN (Oxford), KEMRI (Kenya), IRSS (Burkina Faso)
- **Aim**: to generate robust data on the safety of a range of antimalarials in pregnancy and particularly **in the first trimester to inform regulators and policymakers**
- **Design**: Multi-centre prospective observational cohort
- **Timelines**: 2020-2024
- **Setting**: sites in 2-3 malaria-endemic countries in Africa
- **Population**: Women 15-49 years and pregnant women
- **Data collection**
  - Standardised data elements, procedures, definitions and determination of pregnancy outcomes
  - Using both primary and secondary data



Broaden access to existing drugs – Increasing access to quality medicines

- WHO prequalification update (Sept 2022)

Manufacturer	Submission	Approval
UCL Corporation Ltd, Kenya	Dec 2019	Q3 2022 ★
SWIPHA, Nigeria	Dec 2021	18 -24 months review
EMZOR, Nigeria	May 2022	
Fosum (Guilin), China	N/A	October 2018
S Kant, India	N/A	April 2021
Macleods	N/A	July 2021

MMV supported product through Unitaid funding

Additional ACCESS activities to support MiMBa R&D

Supporting the research and development of new therapeutic alternative by generating evidence on facilitators to pregnant women enrollment in clinical trials

Objective To identify potential strategies for optimising enrolment, and retention of pregnant women in clinical trials.

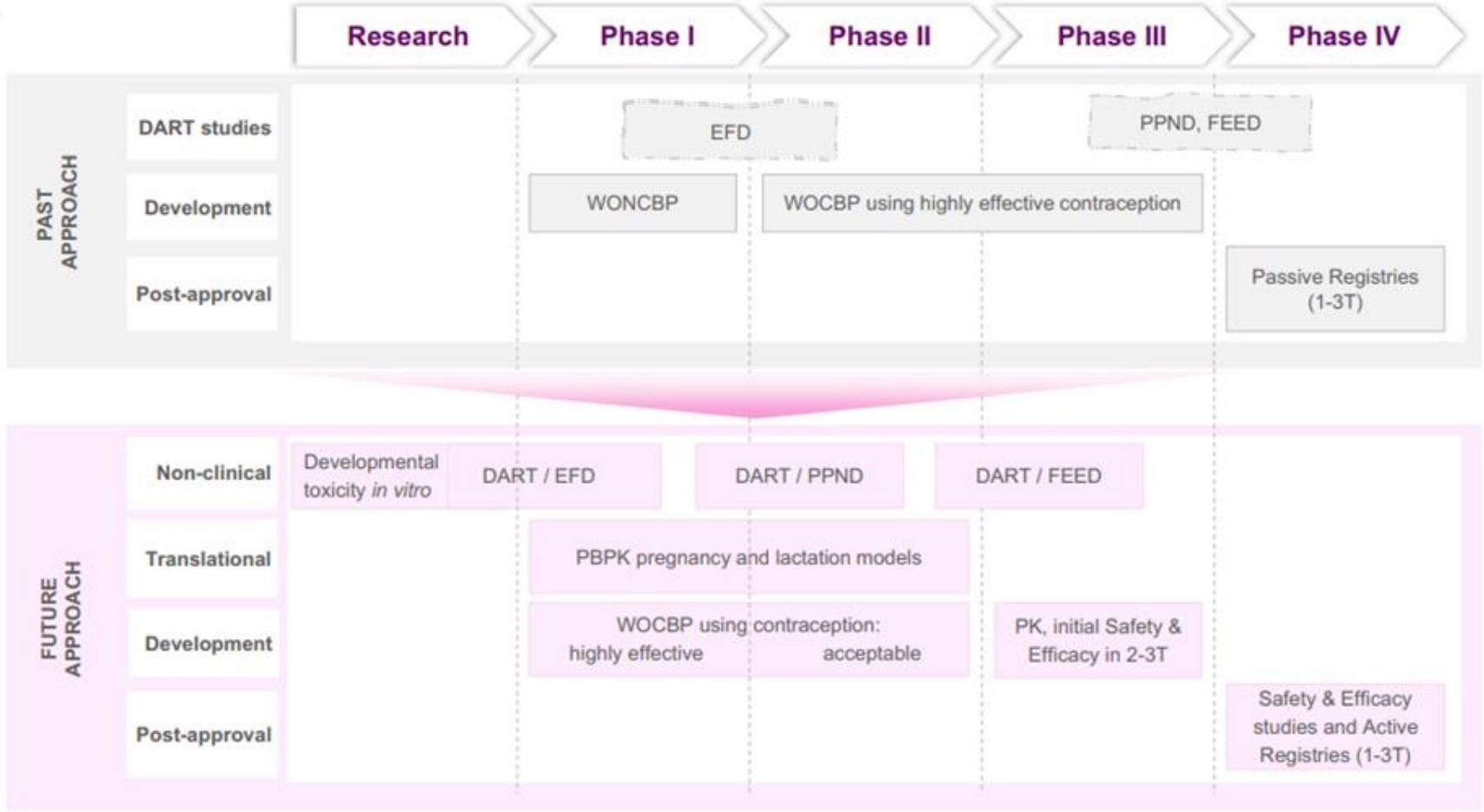
Activities 2022 : Literature research combined with key informant interviews to inform a logic model to recruit PW in clinical trials.

2023-2024: Qualitive research in MMV study site(s) to test logic model and to get a deeper understanding of local context and barriers and facilitators to pregnant women's enrolment in clinical trials

MiMBa Development Strategy - *Malaria Journal (2022) 21:121*

Re-orienting anti-malarial drug development to better serve pregnant women

Myriam El Gaaloul[1], Belen Tornesi[1], Flynn Lebus[2], David Reddy[1] and Wiweka Kaszubska[1*]



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PBPK modeling to accelerate development and access of new combinations to pregnant and lactating women

Physiologically based pharmacokinetic modeling combines physiology, population, and drug physico-chemical characteristics to **mechanistically describe and predict the PK** of a drug

PBPK Pregnancy Model

- Objective: Predict PK of antimalarials during pregnancy to assess if dose adjustment is needed and evaluate if there is a passage to the fetus

PBPK Lactation Model

- Objective: Predict passage of antimalarials into breastmilk to inform potential need for clinical lactation study

Work Plan

1. **Evaluation of available pregnancy and lactation models ongoing** with antimalarials for which clinical exposures in pregnant and/or lactating women are available:
   - Initial predictions vs clinical observations look very promising with both models (3 antimalarials for pregnancy model; 5 antimalarials for lactation model).
2. **Predict PK, placental and milk passage** of other antimalarials in PRGLAC
3. **Optimize clinical development** and generate data to **adequately inform** on the use of antimalarials in PRGLAC

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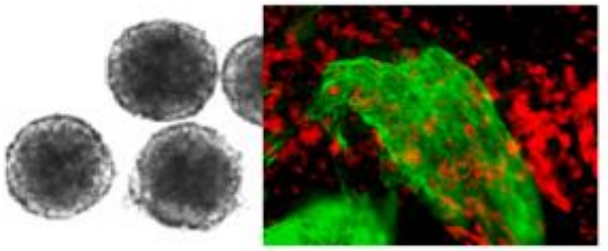
Prioritize antimalarials with non-teratogenic potential in the future pipeline

- Assess developmental toxicity potential before Late Lead selection to prioritize molecules that are inclusive of the needs of women
- Zebrafish and human induced pluripotent stem cell in vitro models predictivity of antimalarials was tested by comparing with the findings from mammals in vivo studies
- Both in vitro tests were generally predictive of mammal study results
- Ideally use the 2 *in vitro* assays for every compound in discovery. ZF will be the first option due to cost

Zebrafish embryo test



Embryonic stem cell test

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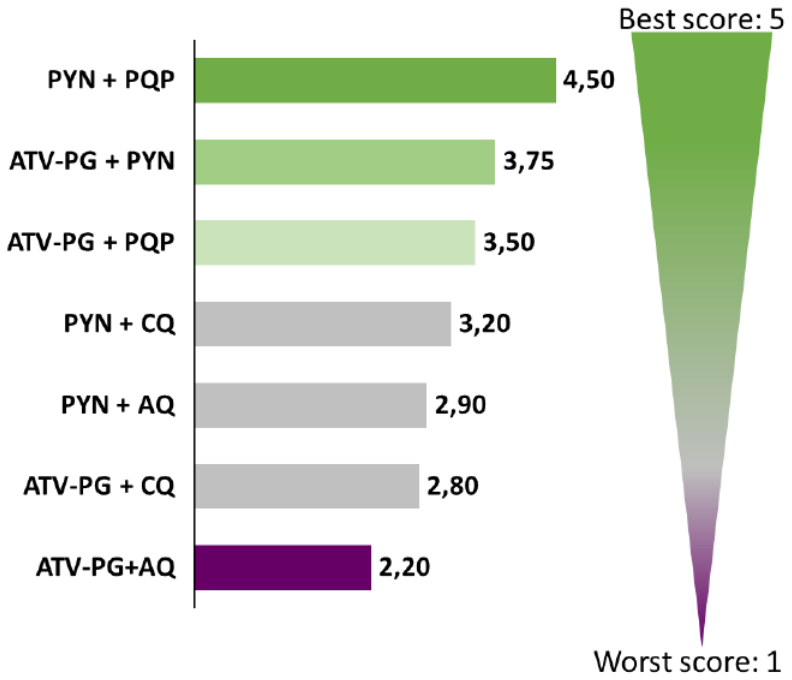
Potential alternative(s) to SP-containing treatments for SMC & IPTp

- Ranking exercise of potential combinations of existing molecules for malaria prevention

Possible combinations were ranked according to 7 criteria

- Tolerability (25% weighting)
- Safety; Duration of protection; Compatibility of restriction on food intake; Low Risk of rapid emergence of resistance (15% weighting, each)
- Affordability (10% weighting)
- Suitable for pregnant women (5% weighting)

Pyronaridine + Piperaquine has the highest score, and ATV-PG + PYN scored 2nd



- Ongoing Phase 1 studies supporting the top 2 combinations

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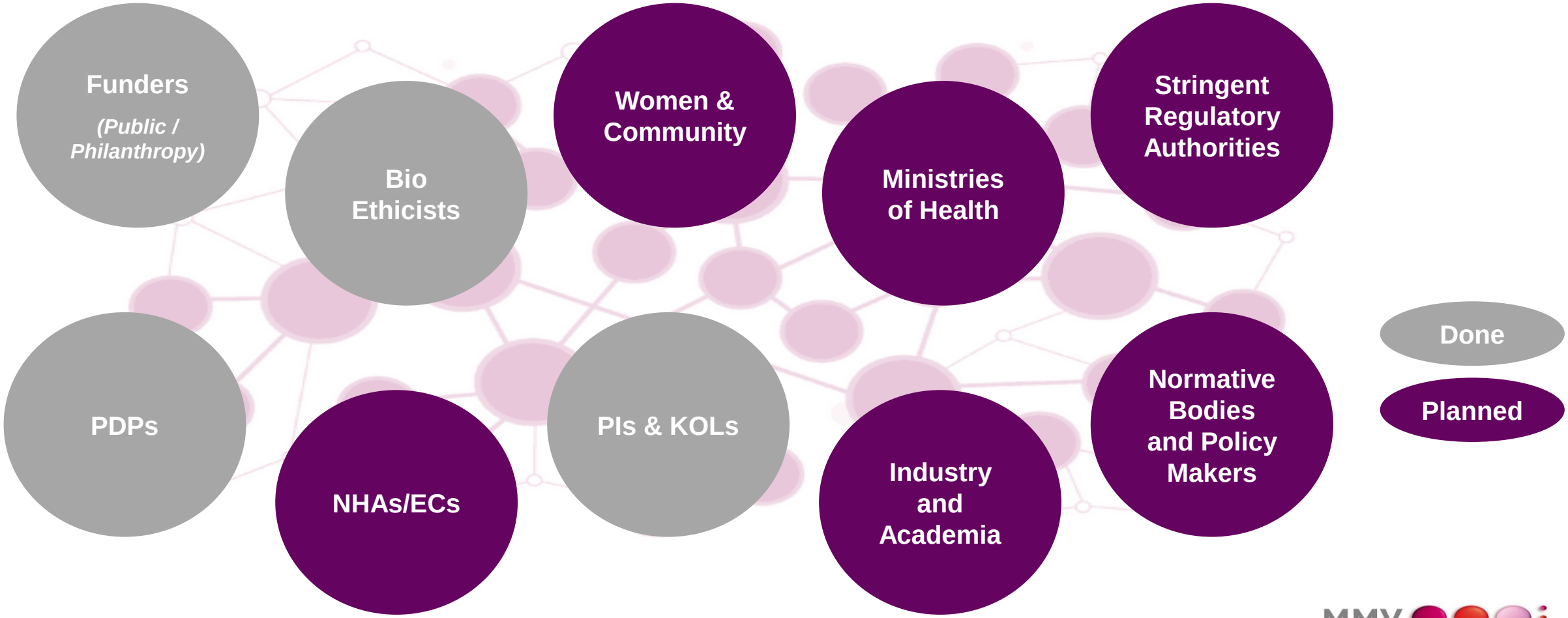
Continue to advocate for greater inclusion into antimalarial R&D of women who are, or could become, pregnant / lactating

- **Emphasis on the vital importance of intentional stakeholder engagement and communications, ie Community, NHAs, ECs, PIs, WHO**



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Q&A

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