

# **OZ439-Piperaquine as Single Dose Treatment for Malaria: A Phase IIb Study**

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# Disclaimer:



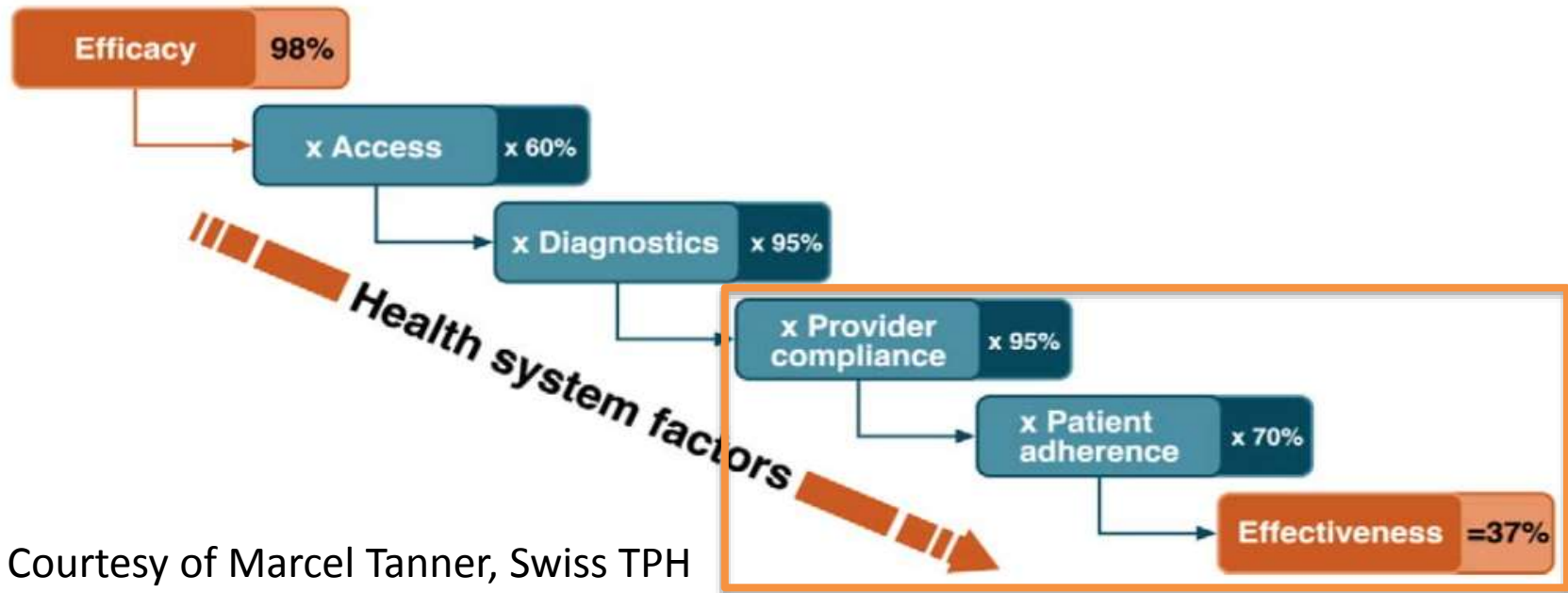
## External adviser for clinical development of pyronaridine-artesunate therapy

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# Single Dose Treatment



## Single dose antimalarial treatment

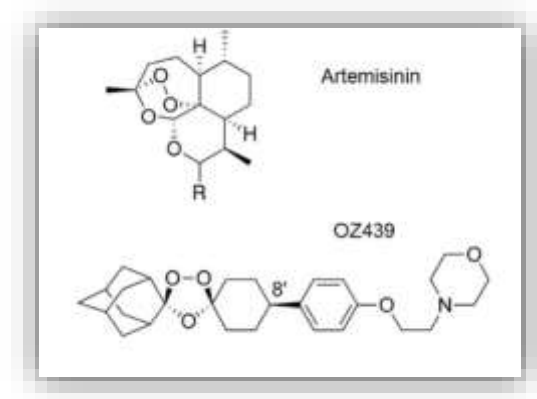
- Reducing the effectiveness gap
- Major breakthrough in malaria control



# Single-Dose Combination OZ-439 + Piperaquine

- OZ 439: Artefenomel

- Synthetic trioxolane endoperoxide
- Pharmacophore similar to artemisinins
- Considerably longer half-life
- Well tolerated in phase I, II studies



- Piperaquine

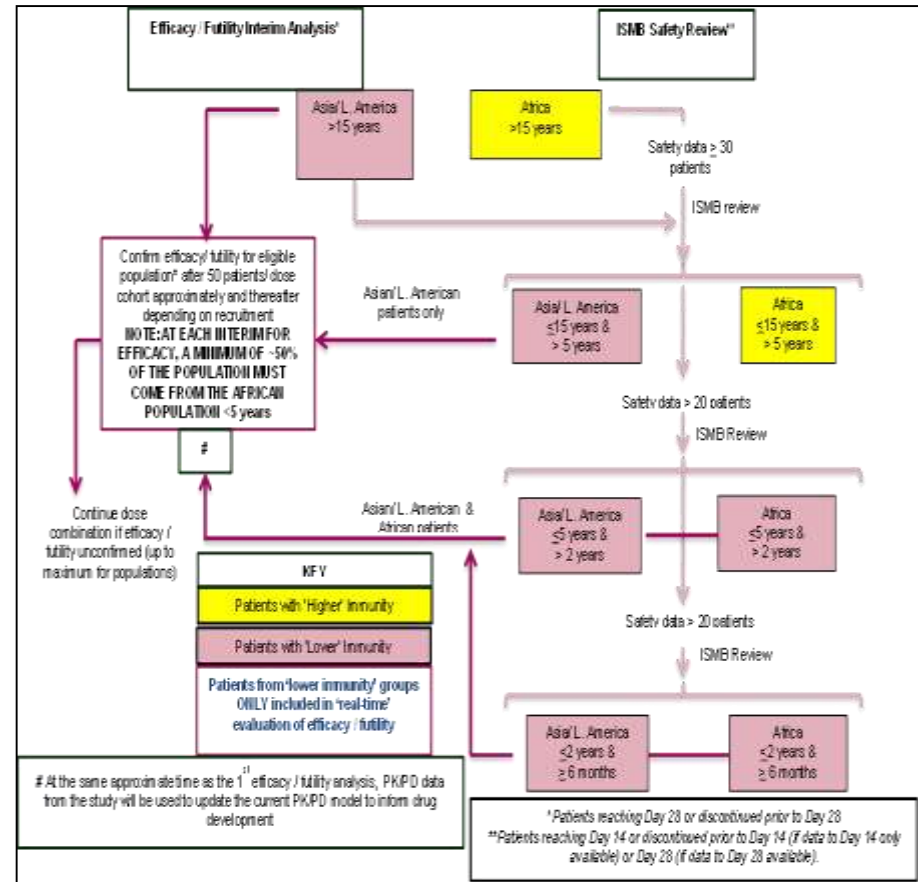
- Long acting drug (half-life: 18 days)
- Extensively used in combination with DHA
- Good efficacy, potential for QT prolongation

# Phase IIb study

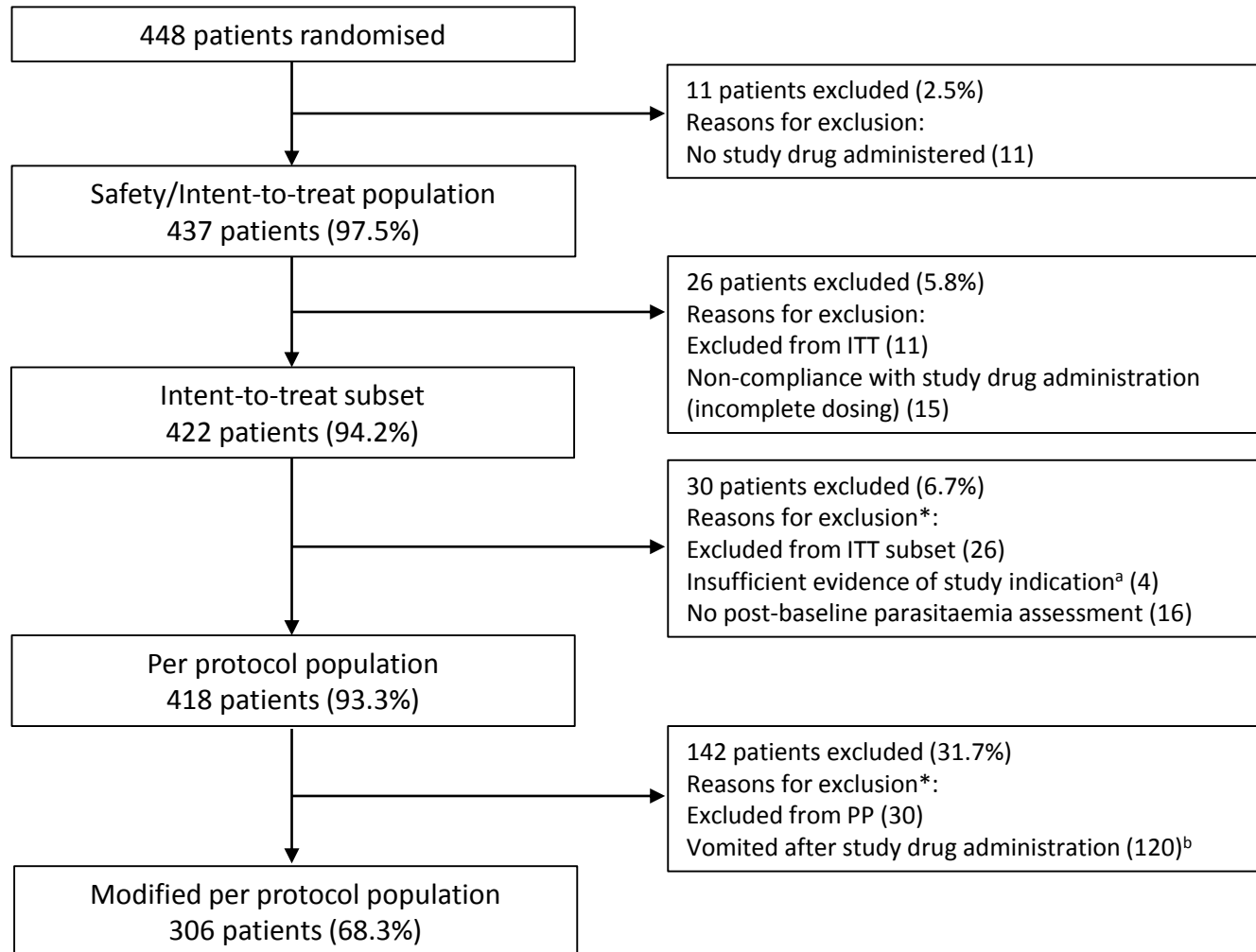
## Single Dose OZ439+Piperaquine for uncomplicated malaria

Randomization OZ439: 800mg; Piperaquine: 640mg, 960mg, 1440mg

### Africa & Asia



# Study flow



# Results: Adverse events

System Organ Class	Artefenomel mg : PQP mg			
	800:640	800:960	800:1440	Total
At least 1 TEAE (n (%) E)	115 (80.4) 266	127 (85.8) 324	122 (83.6) 308	364 (83.3) 898
Infections and infestations (n (%) E)	74 (51.7) 102	76 (51.4) 106	63 (43.2) 82	213 (48.7) 290
Malaria	43 (30.1) 44	45 (30.4) 48	34 (23.3) 34	122 (27.9) 126
Bronchitis	13 (9.1) 16	13 (8.8) 19	10 (6.8) 11	36 (8.2) 46
Rhinitis	11 (7.7) 11	9 (6.1) 10	10 (6.8) 10	30 (6.9) 31
<i>Plasmodium falciparum</i> infection	9 (6.3) 9	10 (6.8) 10	7 (4.8) 7	26 (5.9) 26
Investigations (n (%) E)	58 (40.6) 75	68 (45.9) 100	70 (47.9) 95	196 (44.9) 270
Electrocardiogram QT prolonged	27 (18.9) 29	41 (27.7) 48	44 (30.1) 56	112 (25.6) 133
Neutrophil count decreased	18 (12.6) 18	11 (7.4) 11	12 (8.2) 13	41 (9.4) 42
Haemoglobin decreased	9 (6.3) 9	20 (13.5) 22	11 (7.5) 11	40 (9.2) 42
Gastrointestinal disorders (n (%) E)	31 (21.7) 39	47 (31.8) 60	44 (30.1) 54	122 (27.9) 153
Diarrhoea	11 (7.7) 12	21 (14.2) 21	20 (13.7) 20	52 (11.9) 53
Vomiting	14 (9.8) 14	20 (13.5) 20	16 (11.0) 16	50 (11.4) 50
Abdominal pain	5 (3.5) 5	8 (5.4) 9	12 (8.2) 13	25 (5.7) 27
General disorders and administration site conditions (n (%) E)	11 (7.7) 11	14 (9.5) 16	17 (11.6) 21	42 (9.6) 48
Pyrexia	5 (3.5) 5	12 (8.1) 13	9 (6.2) 11	26 (5.9) 29



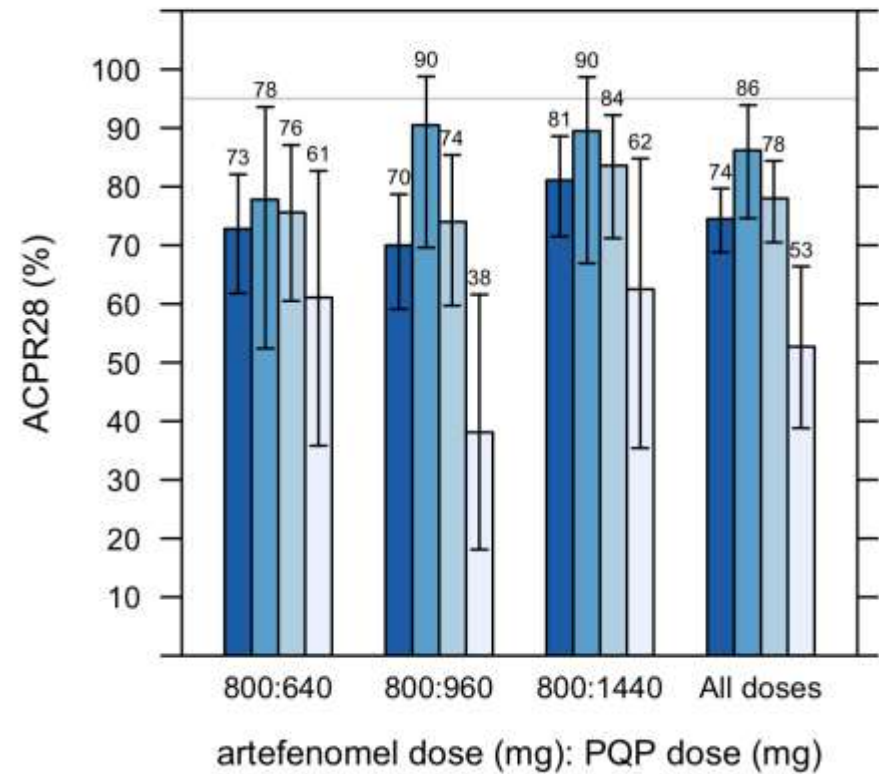
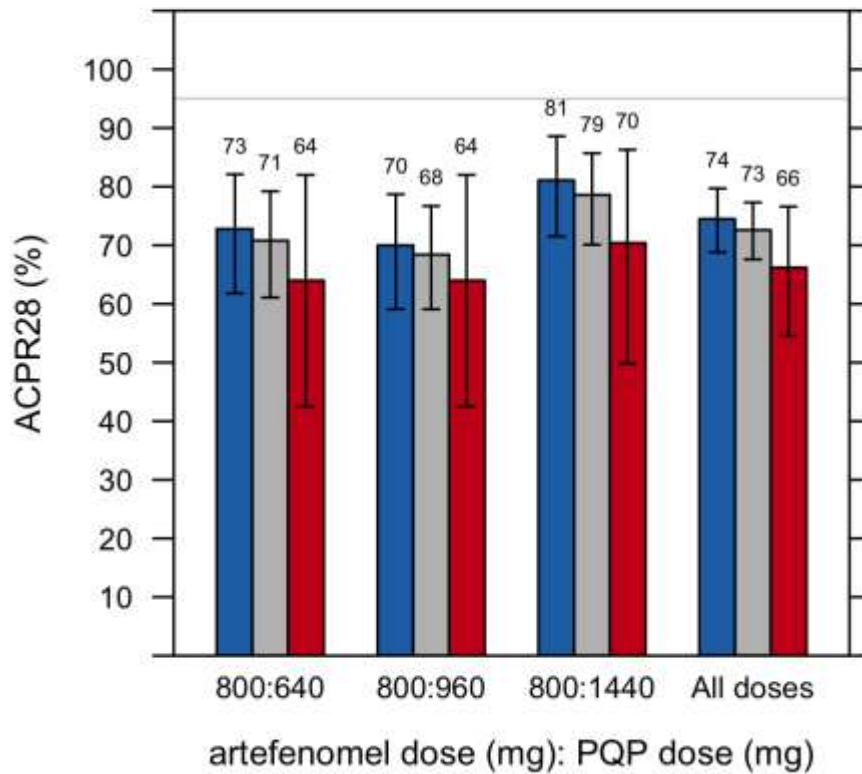
# Results: Efficacy

Africa, all ages  
All patients

Asia, all ages

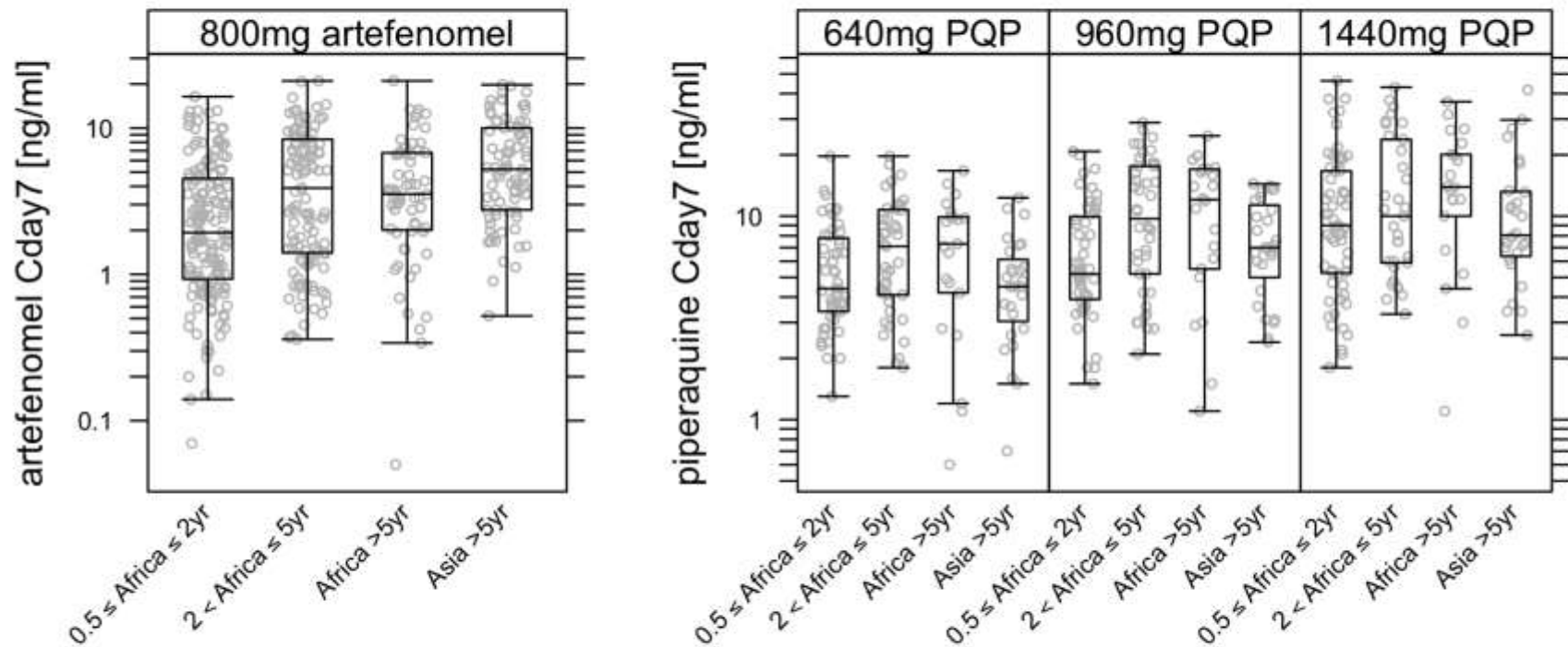
All patients (Africa)  
>5 years (Africa)

>2 to <=5 years (Africa)  
>0.5 to <=2 years (Africa)





# Results: Pharmacokinetics

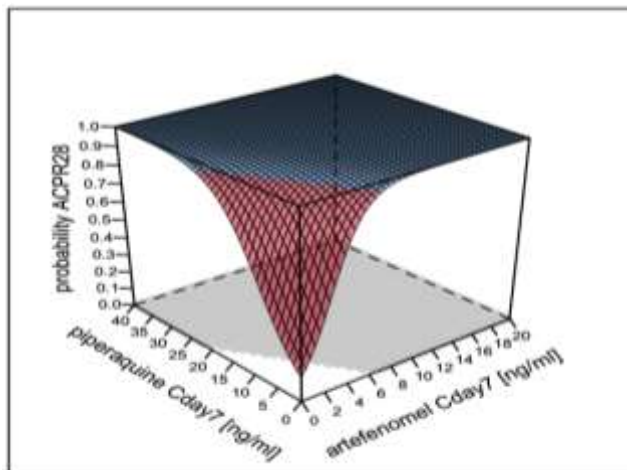


# PK-PD-Modelling

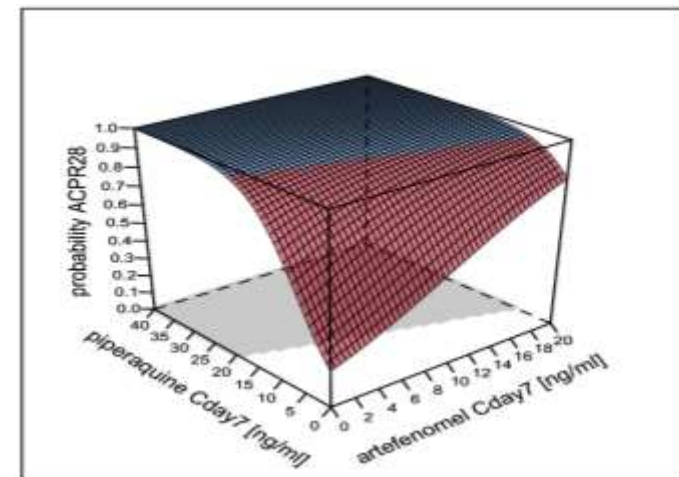
Probability of achieving ACPR28 (pACPR) is a function of:

- artefenomel and piperaquine exposures
- baseline parasitaemia ( $p \leq 0.0001$ )
- region (interaction between region and artefenomel Cday7) ( $p = 0.002$ ):

## Africa



## Asia



# Summary and Outlook

OZ439-piperaquine will not be further developed as single dose antimalarial

Alternative partner drugs for OZ439 are explored

Currently phase IIb study with OZ439-Ferroquine ongoing

# Acknowledgements

Medicines for Malaria Venture

Sanofi - Pharmaceuticals

All Clinical Trial Sites in Africa and Asia

