Objectives

1. Programme Status
2. Timeline for data review for potential policy decision and streamlined policy pathway (seeking agreement)
3. Update on RTS,S/AS01 supply and access
Programme status
COVID-19 cases in MVIP countries: incidence per 1M population
As of 30 Nov 2020

Ghana
51,379 cases
323 deaths

Kenya
82,605 cases
1,445 deaths

Malawi
6,025 cases
185 deaths

Source: https://covid19.who.int/

Data taken from COVID Intel database on 2020-11-30. The lines and associated text show the trend in incidence of COVID-19 cases.
Current situation and trends

- Vaccine uptake ~ 70%, dose 4 administration beginning
- Evaluation components functioning in all countries with data accumulation ongoing

>1.3 million doses administered

~500,000 children received dose 1

Immunization coverage in MVIP areas

**Coverage Jan. – Oct. 2020**

- **Malawi**
  - Penta-3: 95%
  - RTS,S-1: 86%
  - RTS,S-3: 70%

- **Ghana**
  - Penta-3: 90%
  - RTS,S-1: 68%
  - RTS,S-3: 64%

- **Kenya**
  - Penta-3: 76%
  - RTS,S-1: 71%
  - RTS,S-3: 64%

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1 Administrative data
Data Safety & Monitoring Board (DSMB), 1,2 December 2020

- Safety data reassuring; DSMB recommend continuation of pilots
- Noted that GSK biannual report to EMA was received, and EMA maintains the positive scientific opinion; no change in favourable risk-benefit profile
- **DSMB stated that the safety data event rates support analysis for WHO consideration of a policy recommendation in 2021**

Programme Advisory Group (PAG), 3,4 December 2020

- PAG recommends overall event rates for meningitis, severe malaria, cerebral malaria, and mortality at current levels indicate there will be sufficient power to conduct planned safety and impact analyses at 24 months after first vaccination
  - Target timelines for policy review: **Q4 2021**
Timeline for data review and potential policy decision

Credit: WHO/Neil Thomas.

<table>
<thead>
<tr>
<th>Year</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Evidence generation</strong></td>
<td><strong>Pilot DATA</strong></td>
<td>Vaccination start</td>
<td></td>
<td>Evaluation complete</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**WHO policy recommendation**

*Timing dependent on rate of events detected by surveillance systems (among other factors)*

1. **If & when**
   - Concerns regarding *safety signals satisfactorily* resolved; and
   - Severe malaria or mortality data trends assessed as *consistent with a beneficial impact* of the vaccine

2. **End of pilot**
   - Value of 4th dose
   - Impact on mortality

Policy recommendation on broader use

If needed: Adjustments to recommendation

**Global funding decisions**

**Country-level introduction decisions**

MVIP presentation to PWC, 26 November 2020
### Policy and financing pathway

#### Inputs

**Data & info available for analysis (target: Q2 2021)**
- MVPE hospital surveillance
- MVPE mortality surveillance
- MVPE midline household survey (G + M)
- Phase IV progress reports + data request
- EMA positive opinion
- HUS initial findings
- Economic evaluations/updates
- AEFI/AESI (routine system)
- Immunization coverage – administrative data
- New vaccine post introduction evaluation
- Phase 3 (MAL055) & long-term follow-up (MAL076)
- Phase 3b: RTS,S & SMC

#### Outputs

**Evidence package (target: July/August 2021)**
- MVIP statistical analysis on safety and impact
- RTS,S/AS01 full benefit-risk report

**Evidence review (target: Q3 2021)**
- MVIP DSMB formal review of safety analysis
- MVIP PAG review of RTS,S/AS01 benefit-risk
- SAGE/MPAC joint review of PAG recommendations

#### Outcomes

**WHO policy recommendation on broader use (target: October 2021)**

**Financing decision (target: December 2021)**
- Gavi Board investment decision on support for vaccine roll-out

**Regulatory (target: TBC)**
- Prequalification & in-country authorizations

**Country-level decisions (target: begin in 2022)**
- MVIP countries may wish to expand + non-MVIP countries

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**Stakeholder alignment and engagement**
Proposed WHO policy pathway for MPAC endorsement

**Acronyms:**
- SAGE: Strategic Advisory Group of Experts on Immunization
- MPAC: Malaria Policy Advisory Committee
- RITAG: Regional Immunization Technical Advisory Group for AFRO
- GACVS: Global Advisory Committee on Vaccine Safety
- AACVS: African Advisory Committee on Vaccine Safety

**MVIP specific:**
- DSMB, PAG

**Global advisory bodies:**
- MPAC, SAGE, IVIR-AC

**Regional advisory bodies:**
- RITAG, AACVS**
  - **Meeting dates TBC

**Q1 2021**
- DSMB
- PAG
- SAGE Update

**Q2 2021**
- 24 months MVIP data
- PAG
- MPAC Update
- AACVS** Update
- RITAG Update

**Q3 2021**
- DSMB
  - Formal analysis
- PAG
  - Risk-benefit analysis
- DSMB presents analysis to PAG, in presence of GACVS, AACVS & RITAG members

**Q4 2021**
- SAGE/MPAC
  - Policy review

**Target:** October 2021

Analysis & policy recommendation development

Malaria Vaccine Implementation Programme update, MPAC 4 Dec 2020
Thank you
The four components of the Malaria Vaccine Implementation Programme

1. RTS,S/AS01 Implementation through EPI Programme
   - In selected areas of Ghana, Kenya & Malawi with community engagement

2. Pilot evaluation commissioned by WHO
   - Incl. sentinel hospitals surveillance; community-based mortality surveillance; 3 household surveys

3. Qualitative assessment (HUS) & economic analyses
   - commissioned by PATH

4. GSK Phase IV study
   - Safety, effectiveness and impact
   - Part of GSK’s EMA Risk Management Plan
Future access: Importance of continued RTS,S bulk production

- Sufficient donation doses to complete the MVIP. However:

<table>
<thead>
<tr>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
<th>2024</th>
<th>2025</th>
<th>2026</th>
</tr>
</thead>
</table>

Earliest timepoint for WHO policy decision
Funding decisions on introduction support
Earliest expansion in MVIP countries (1) and earliest non-MVIP country introduction (2)

RTS,S production scenarios:

1. Continued
2. Stop - restart

Bulk financing decision needed
At risk period
3 years to restart
## Future access: funding needs

<table>
<thead>
<tr>
<th>Type of investment</th>
<th>Risks (if no investment)</th>
</tr>
</thead>
</table>
| **1) Immediately needed:** Guarantee to cover costs of continuation of RTS,S bulk production (~$20 M per year) | • Expansion beyond vaccinating areas in MVIP countries likely not possible until 2025.  
  • Introduction in non-MVIP countries at least 2 years delayed.  
  • Risk to RTS,S product transfer & risk of a second RTS,S supply gap in 2029/2030.  
  • Inherent risks and delays caused by stop-and-restart.  
  • Higher average vaccine price. |
| **2) Soon needed:** Funding to enable expansion of vaccine production capacity      | • Supply is limited to 15 million doses per year (estimated 5-7 years needed for expansion)                                                               |
Timing of analyses: number of events required for analyses of safety and impact

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effect in the phase 3 trial</th>
<th>Population effect if average coverage is:</th>
<th>Number of cases required for 90% power</th>
<th>Observed event rate/1000</th>
<th>Events up to July 2020</th>
<th>Projected events by Q2 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safety:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>10-fold increase</td>
<td>6.4</td>
<td>70-100 cases under 5 yrs</td>
<td>0.01-0.06</td>
<td>48</td>
<td>77</td>
</tr>
<tr>
<td>Cerebral malaria</td>
<td>2-fold increase</td>
<td>1.6</td>
<td>300-350 cases under 5 yrs</td>
<td>0.1-0.2</td>
<td>191</td>
<td>355</td>
</tr>
<tr>
<td>Mortality ratio girls:boys</td>
<td>2-fold increase in mortality in girls</td>
<td>1.6</td>
<td>2000-2500 deaths (among vaccine-eligible)</td>
<td>0.8-2.7</td>
<td>1632</td>
<td>3200</td>
</tr>
<tr>
<td><strong>Impact:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe malaria</td>
<td>34% efficacy*</td>
<td>20%</td>
<td>about 4000 cases under 5 yrs</td>
<td>0.9-3.9</td>
<td>2913</td>
<td>5476</td>
</tr>
</tbody>
</table>

*Efficacy against severe malaria, months 0-20
### Predicted power at month 24

#### Person time in hospital catchments (total 3 countries)

<table>
<thead>
<tr>
<th>Months from start of vaccine introduction (May 2019)</th>
<th>Vaccine eligible (dose 1)</th>
<th>Vaccine eligible (dose 3)</th>
<th>Not eligible</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Power to exclude rate ratio of:

<table>
<thead>
<tr>
<th>No. of events</th>
<th>Coverage</th>
<th>Cerebral malaria</th>
<th>Meningitis</th>
<th>Population level effect:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
</tbody>
</table>

#### Coverage:

<table>
<thead>
<tr>
<th>No. of events</th>
<th>2</th>
<th>2.1</th>
<th>2.2</th>
<th>2.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>340-350</td>
<td>76%</td>
<td>81%</td>
<td>85%</td>
<td>89%</td>
</tr>
<tr>
<td>330-340</td>
<td>76%</td>
<td>80%</td>
<td>83%</td>
<td>86%</td>
</tr>
<tr>
<td>320-330</td>
<td>71%</td>
<td>77%</td>
<td>82%</td>
<td>84%</td>
</tr>
<tr>
<td>310-320</td>
<td>71%</td>
<td>76%</td>
<td>81%</td>
<td>84%</td>
</tr>
<tr>
<td>300-310</td>
<td>69%</td>
<td>75%</td>
<td>79%</td>
<td>83%</td>
</tr>
</tbody>
</table>

#### Power to exclude rate ratio (Rate ratio in phase3):

<table>
<thead>
<tr>
<th>No. of events</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>80-90</td>
<td>83%</td>
<td>89%</td>
<td>92%</td>
</tr>
<tr>
<td>70-80</td>
<td>78%</td>
<td>85%</td>
<td>89%</td>
</tr>
<tr>
<td>60-70</td>
<td>73%</td>
<td>80%</td>
<td>85%</td>
</tr>
</tbody>
</table>
Predicted range of point estimates (rate ratios for cerebral malaria, meningitis), assuming no effect
### Mortality

<table>
<thead>
<tr>
<th>month</th>
<th>Effect % reduction</th>
<th>Events (Total)</th>
<th>Events (Eligible)</th>
<th>power</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>15%</td>
<td>9014</td>
<td>4308</td>
<td>95%</td>
</tr>
<tr>
<td>24</td>
<td>10%</td>
<td>9100</td>
<td>4396</td>
<td>64%</td>
</tr>
<tr>
<td>46</td>
<td>10%</td>
<td>17671</td>
<td>8443</td>
<td>92%</td>
</tr>
<tr>
<td>46</td>
<td>9%</td>
<td>17727</td>
<td>8499</td>
<td>87%</td>
</tr>
<tr>
<td>46</td>
<td>8%</td>
<td>17784</td>
<td>8554</td>
<td>78%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coverage</th>
<th>70%</th>
<th>70%</th>
<th>70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>40%</td>
<td>40%</td>
<td>30%</td>
</tr>
<tr>
<td>% deaths due to malaria</td>
<td>20%</td>
<td>30%</td>
<td>30%</td>
</tr>
<tr>
<td>% impact</td>
<td>5.6%</td>
<td>8.4%</td>
<td>6.3%</td>
</tr>
</tbody>
</table>