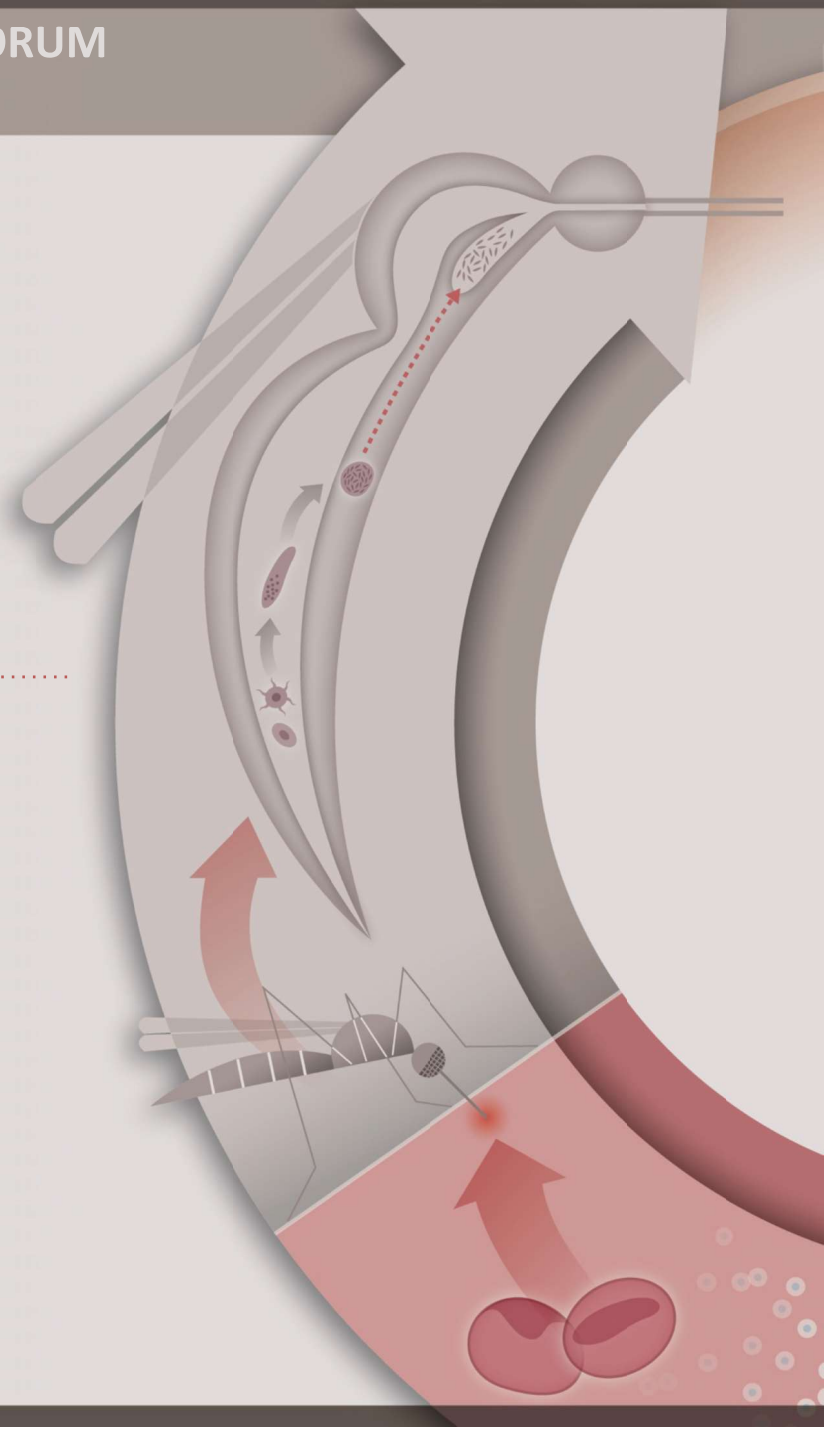
GLOBAL VACCINE AND IMMUNIZATION RESEARCH FORUM
BETHESDA MD / MARCH 4-6, 2014

Progress towards the development of a malaria vaccine

A summary of key findings



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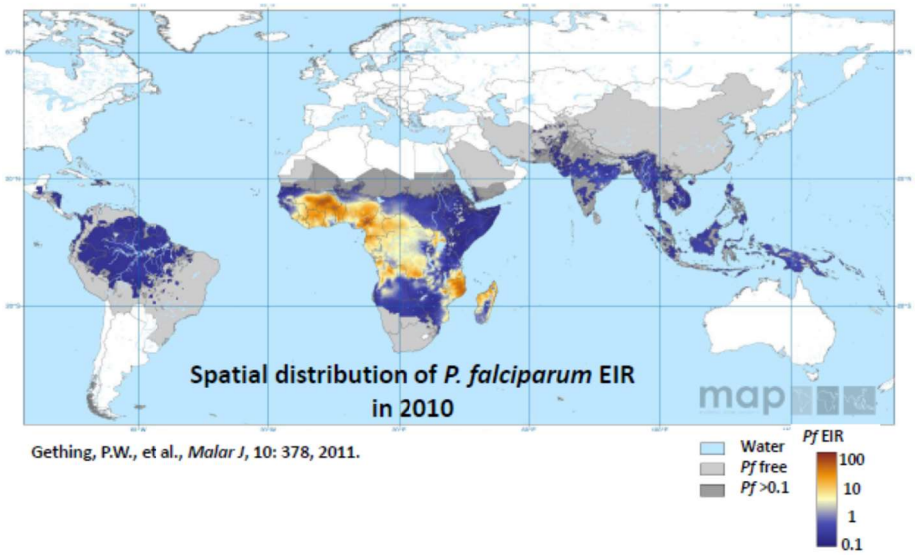
mvi PATH
MALARIA VACCINE INITIATIVE

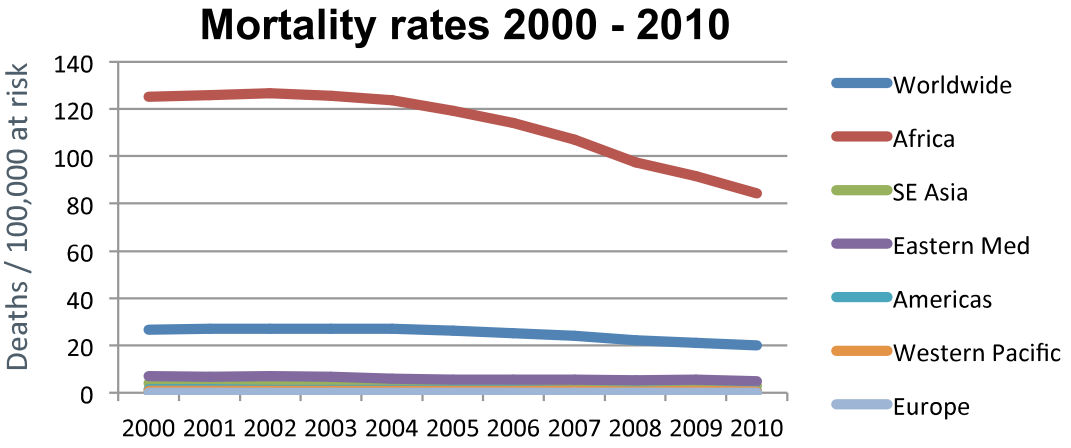
Malaria: The burden and unmet need

- **Malaria epidemiology**
  - ~207 million cases/year, 80% in sub-Saharan Africa
  - ~627,000 deaths/year, mostly African children under five years

(WHO World Malaria Report 2013)

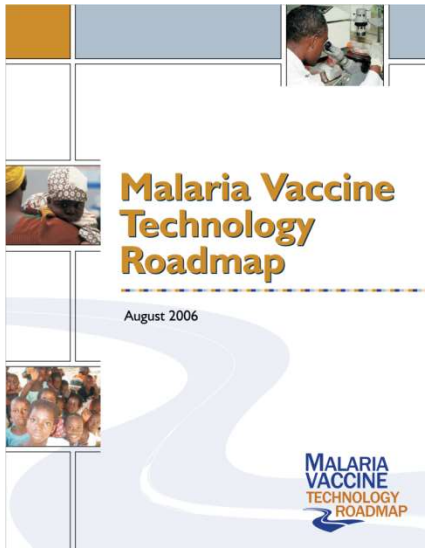


- **Tools available today**
  - Insecticide-treated bed nets
  - Indoor residual spraying
  - Improved case management
  - Rapid diagnosis and treatment



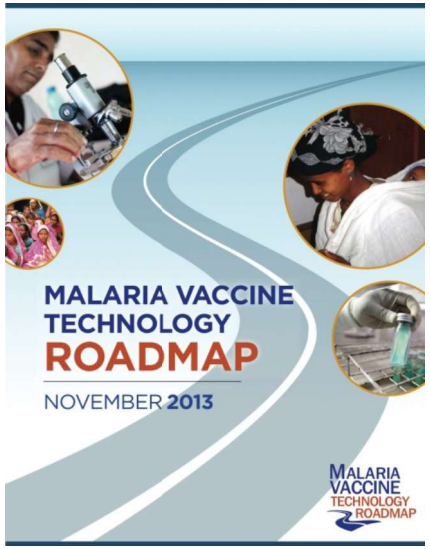
Adapted from: WHO World Malaria Report 2011

Evolution of malaria vaccine goals (2006-2013)



Strategic goal: By 2025, develop and license a malaria vaccine that has a protective efficacy of more than **80% against clinical disease** and lasts longer than four years.

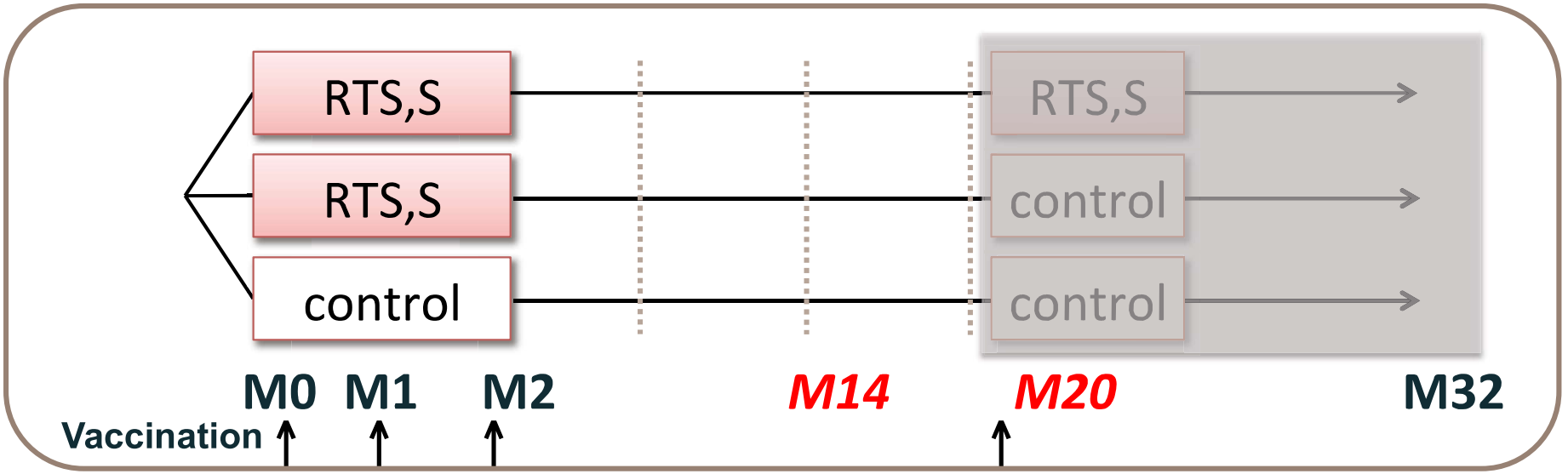
Landmark: By 2015, develop and license a first-generation malaria vaccine that has a protective efficacy of more that **50% against severe disease and death** and lasts longer than one year.



Goal 1: Development of malaria vaccines with **protective efficacy of at least 75 percent against clinical malaria** suitable for administration to appropriate at-risk groups in malaria- endemic areas.

Goal 2: Development of malaria vaccines that **reduce transmission of the parasite** and thereby substantially reduce the incidence of human malaria infection. This will **enable elimination in multiple settings**. Vaccines to reduce transmission should be suitable for administration in mass campaigns.

Study design pivotal RTS,S efficacy trial



- **Control vaccines:** Rabies vaccine in 5-17 month old children
  MenC-conjugate vaccine in 6-12 week old infants
- **Co-primary endpoints:** Efficacy against malaria through Study Month 14, over first 12 months of follow-up post dose 3, comparing pooled RTS,S groups to control group

Vaccine efficacy (VE) and safety over 18 months

	VE in children [95%CI]	VE in infants [95%CI]
Clinical malaria	**46%** [42 to 50]	**27%** [20 to 32]
Severe malaria	**36%** [15 to 51]	**15%** [-20 to 39]
Malaria hospitalization	**42%** [29 to 52]	**17%** [-7 to 36]
All-cause hospitalization	**19%** [9 to 28]	**6%** [-7 to 17]

- For every 1,000 children/infants, vaccination averted:
  - In children (ITT)**: 37 to 2365** [average: 829] **cases** of **clinical malaria; -1 to 49** [average:18] **cases of severe malaria**
  - In infants (ITT): **-10 to 1402** [average: 449] **cases** of **clinical malaria; -13 to 37** [average: 6] **cases of severe malaria**
- Case fatality rate for malaria and all-cause mortality was low and VE was not demonstrated against malaria mortality, hospitalized pneumonia, or septicemia.
- Apart from the meningitis signal previously reported, no other safety signal was identified.

Next steps for the RTS,S malaria vaccine candidate

Near-term:

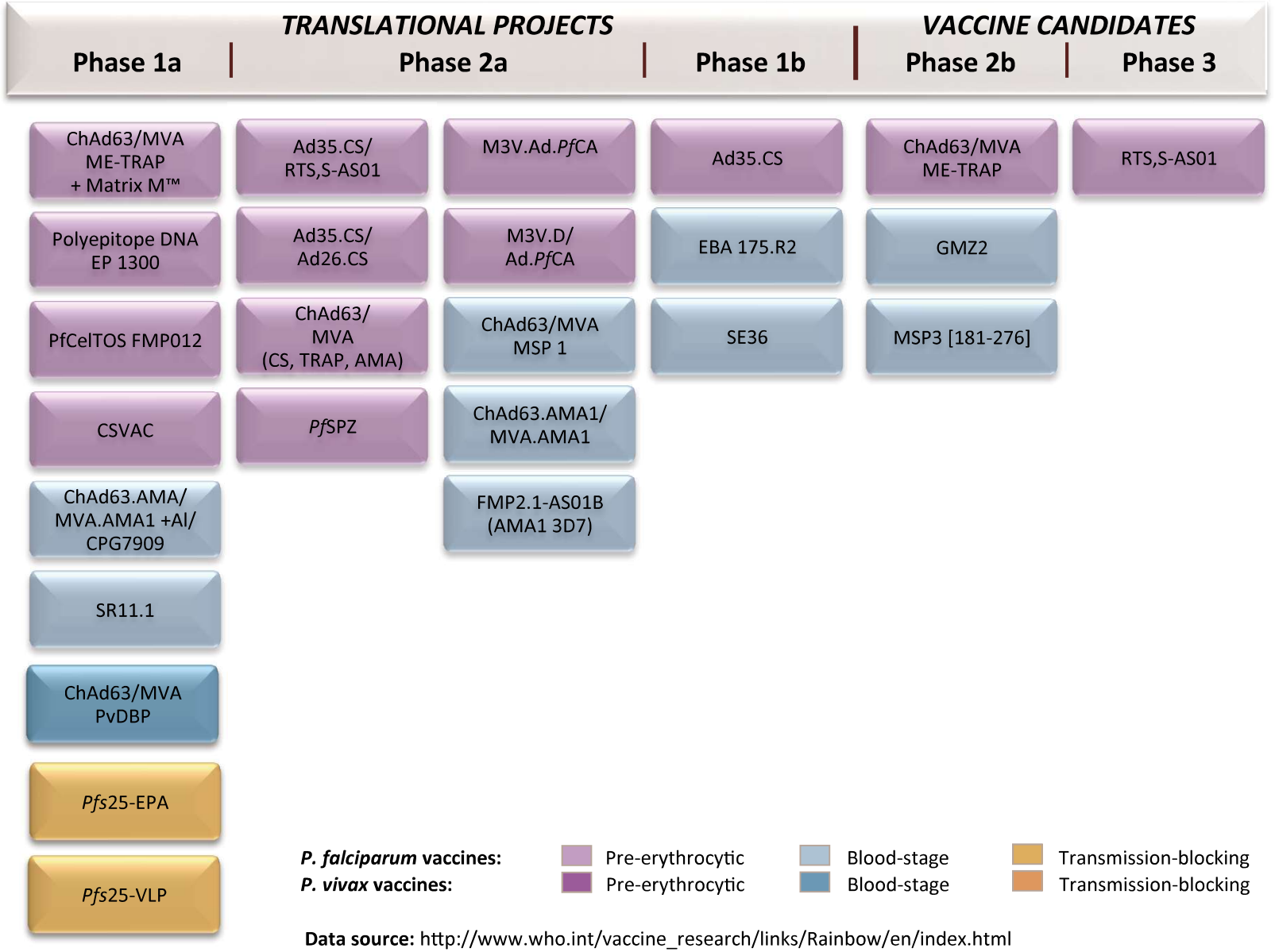
- Evaluations for **GAVI VIS 2014-2018** (initial Board decision Nov 2013)
- Completion of **Phase III clinical trials** in 2014
- Prepare and file submission to **EMA under Article 58** in 2015

Mid-term:

- Initiate **Post-Approval Program** (pharmacovigilance, effectiveness, …)
- **WHO policy decision** anticipated in 2015
- WHO **pre-qualification** and file submission to NRAs in sub-Saharan Africa
- Perform **demand forecasting** and secure manufacturing capacity
- Determine **health economical value** of malaria vaccination
- Support **evidence-base decision making**, at the country level, on the malaria vaccine in the context of other interventions.

VIS: Vaccine Investment Strategy
NRA: National Regulatory Authority

Global malaria vaccine pipeline



Data source: http://www.who.int/vaccine_research/links/Rainbow/en/index.html

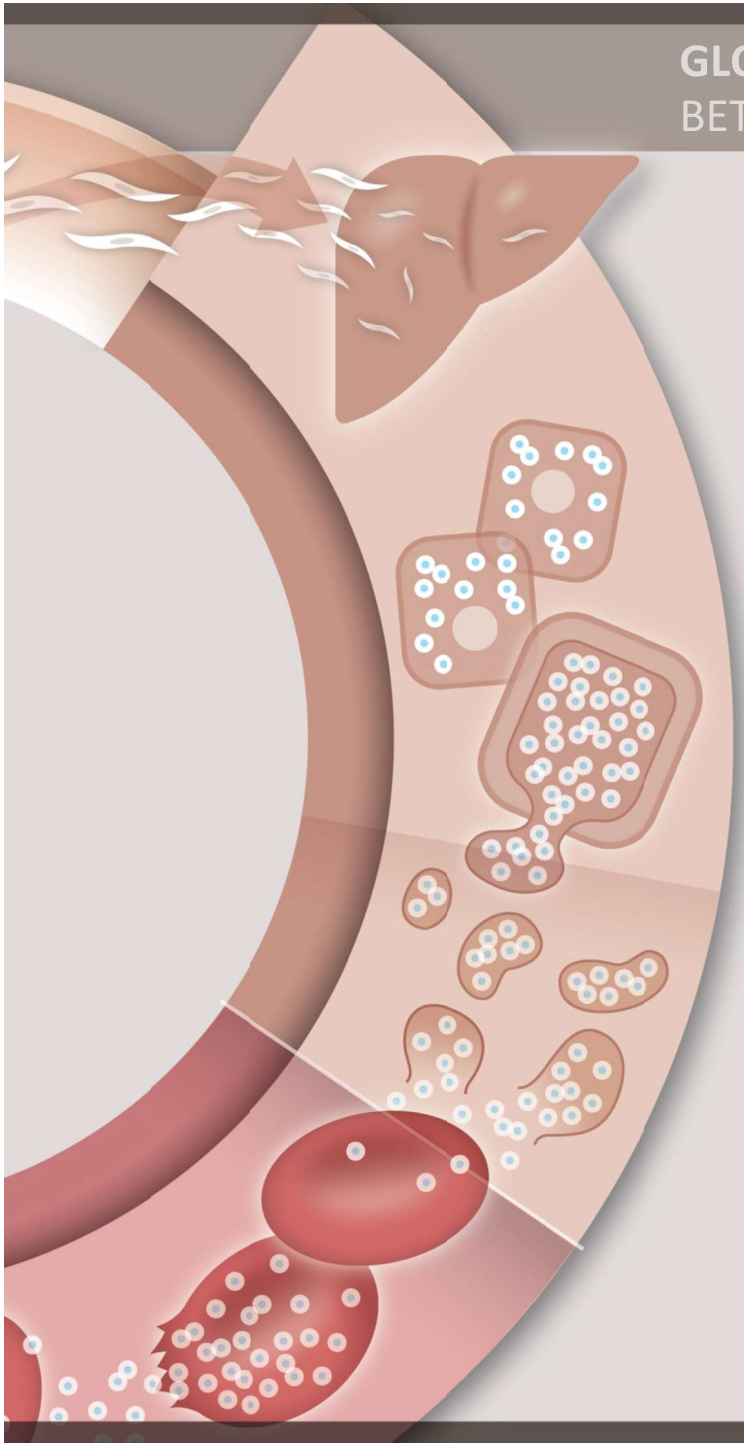
Challenges and opportunities

- **Human vaccinology***
  - Effective delivery systems to induce strong and durable antibody, Th1 CD4+ and CD8+ T-cell responses in humans, particularly very young children
- **Malaria****
  - Alignment on product specifications to achieve Roadmap goals
    - Develop Preferred Product Characteristics (PPC)
  - Absence of dual market opportunity for malaria vaccines
    - Strengthening of developing world pharmacovigilance systems
  - Regulatory approval strategies
    - Determine approval strategy for vaccines conferring delayed benefit
  - Absence of defined biomarkers of protection
    - Define biomarkers of protection for: irradiated sporozoites/mosquito approaches, infection-treatment vaccination (ITV), RTS,S, and naturally acquired immunity
  - Validated targets to support subunit vaccine development
    - Improved target validation strategies
  - Absence of reliable preclinical models
    - Back validation studies (i.e., clinical to preclinical)

***Koff *et al.*, Science. 2013 May 31;340(6136)**
****Birkett *et al.*, Vaccine. 2013 Apr 18;31 Suppl 2:B233-43**

Future directions

- **Short-term goals [2014-2016]**
  - Achievement of the 2015 Landmark Goal
  - Availability of Preferred Product Characteristics (PPC)
  - Define regulatory approval pathway for transmission blocking vaccines
- **Mid-term goals [by 2020]**
  - Evidence that the requisite level of vaccine efficacy can be achieved for both 2013 Roadmap goals
- **Long-term goals [beyond 2020]**
  - *Development of malaria vaccines with **protective efficacy of at least 75 percent against clinical malaria** suitable for administration to appropriate at-risk groups in malaria-endemic areas*
  - *Development of malaria vaccines that **reduce transmission of the parasite** and thereby substantially reduce the incidence of human malaria infection. This will **enable elimination in multiple settings**. Vaccines to reduce transmission should be suitable for administration in mass campaigns.*



THANK YOU

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