Expediting Ebola Vaccine Development Via Multistakeholder Partnerships: Progress, Needs and Future Implications

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Merck Vaccines

IOM Workshop on Enabling Rapid Response with Medical Countermeasures to Mitigate Risks of Emerging Infectious Diseases

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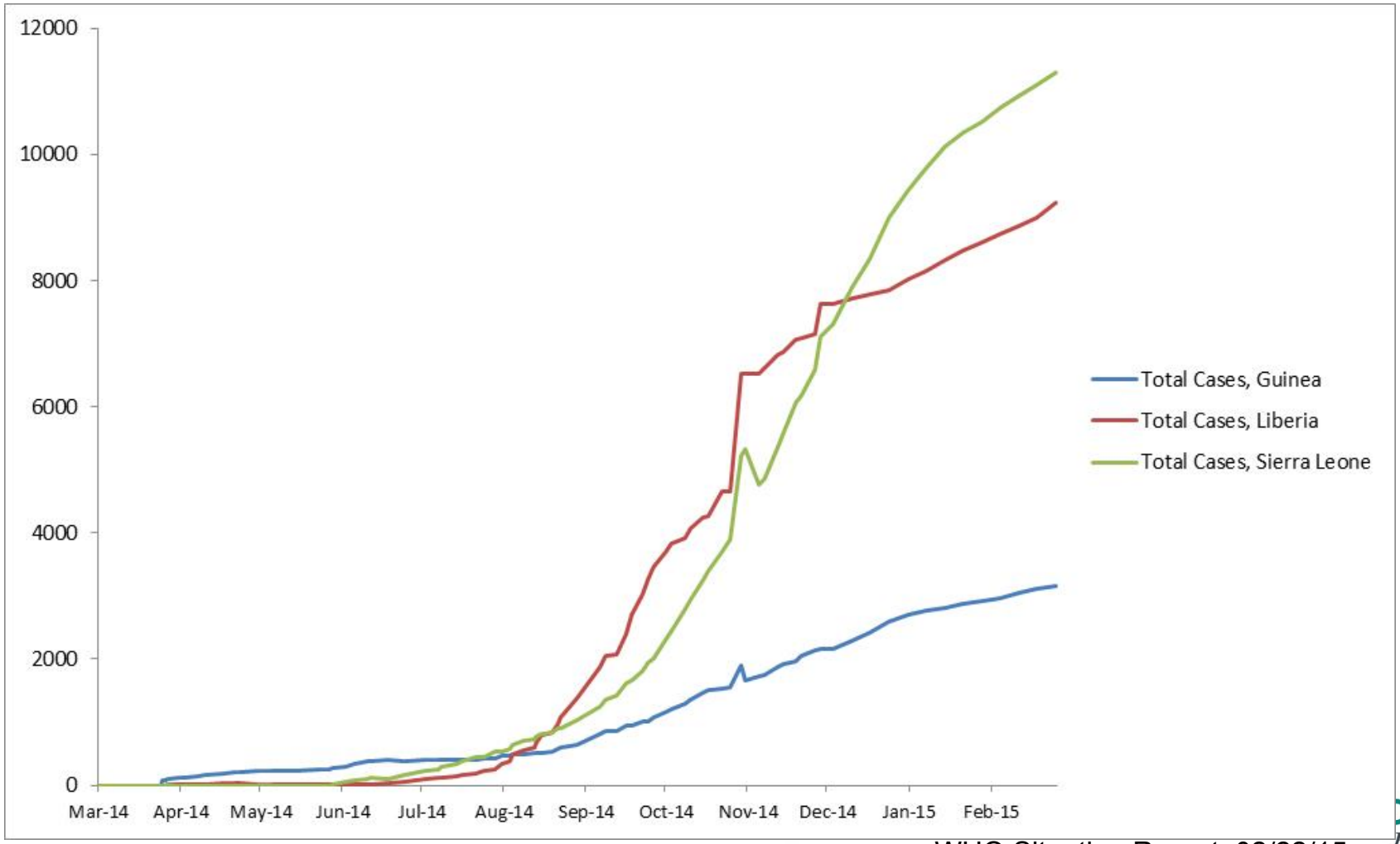
Ebola virus epidemic progression

Total suspected, probable and confirmed cases of Ebola virus disease in Guinea, Liberia and Sierra Leone, March 25, 2014- February 22, 2015



WHO Situation Report, 02/22/15

Enablers of Merck's Decision to Engage

- Appreciation of public health imperative and opportunity for Merck to contribute in a valuable, and in some ways unique, manner to the accelerate development of a promising vaccine candidate
- Recognition and ready acceptance of the fact that engagement in Ebola vaccine development is for public health and not commercial reasons
- Expectation that vaccine development efforts will be advanced in collaboration with public sector partners to pool expertise, to share costs and risks, and to manage uncertainties
- Commitment of donor/funding organizations (eg, GAVI, UNICEF) to procure and deliver an Ebola vaccine should it prove efficacious and safe

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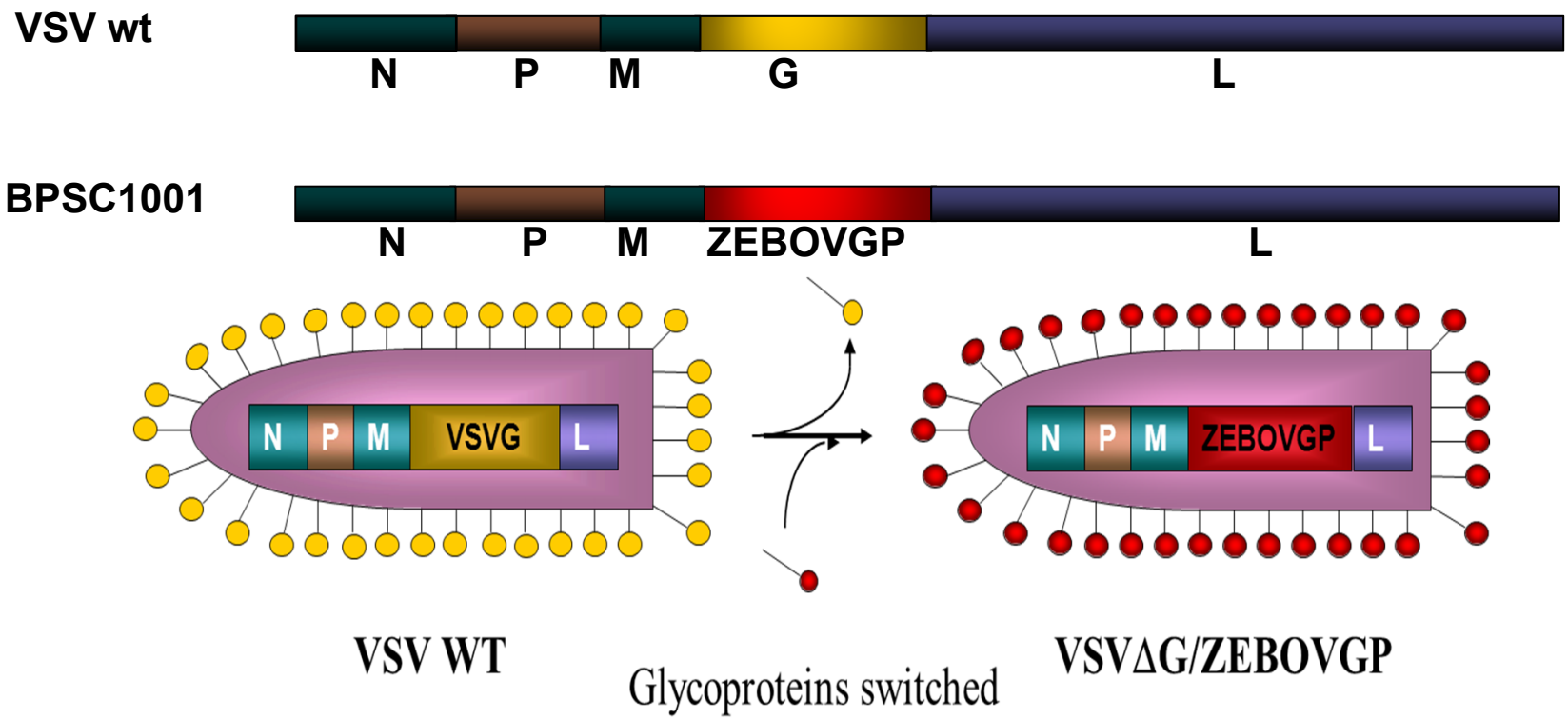
Overview rVSV-ZEBOV-GP

- Two potential indications: *General Use Prophylaxis (GUP)* and Post Exposure Prophylaxis (PEP)
- Recombinant attenuated Vesicular Stomatitis Virus (rVSV) vaccine
  - Nonsegmented, negative-stranded RNA virus (family *Rhabdoviridae*)
  - VSV infects livestock and can rarely be transmitted to humans (with generally mild clinical sequelae)
  - Very low or absent evidence of prior exposure in most geographies
- *Replication competent monovalent,* ***single dose vaccine***
- *Provides 100% protection against high-dose, virulent IM and aerosol Ebola virus challenge in NHPs*
- *Demonstrated ability for multivalent rVSV-Ebola and Marburg virus vaccine to provide broad protection in NHPs*
- *Straightforward and scalable manufacturing process*

rVSV ZEBOV-GP Structure



- Deletion of fusogenic/pathogenic VSV-G protein
- Substitution of Ebolavirus Zaire-strain Kikwit envelope protein
  - Alters target cell tropism, increases degree of vaccine attenuation

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Typical Timeline for Vaccine Development

15 to 20 Years
Standard timeline to develop a vaccine.

- Scientific opportunity
- Translation and feasibility
- Definition of desired target product profile (TPP)
- Clarity on anticipated vaccine demand and economic/public health value
- Definition (and enforcement) of key milestones and “go/no go” criteria
- Process Development
- Dose Selection
- Establishment of proof of concept
- Additional Phase II evaluation
- Manufacturing/supply solution for affordable production
- Phase III demonstration of safety/efficacy
- Licensure (informed by broad and deep evidence base)
- Generation of evidence to guide policies and recommendations
- Demonstration of feasibility and impact of introduction
- Provision of affordable, appropriate, reliable and sustainable supply

2014 **2024+**

The Critical importance of Alignment and Integration (an “end to end” view)

- Successful drug development depends on a highly iterative, integrated system predicated on a bi-directional flow of information (an “end-to-end view”).
- Successful product development and implementation is hard enough when pursued within a single company, and when well-defined accountability, tracking and incentive models in place.
- Successfully defining and reaching the desired “end” is even harder when it involves contributions and hand-offs between different public and private partners (who each have different capacities, resources, constraints, levels of experience in product development, risk profiles and incentives).
- Our collective success will depend upon the extent to which we can develop effective new partnership models and networks to address these challenges.

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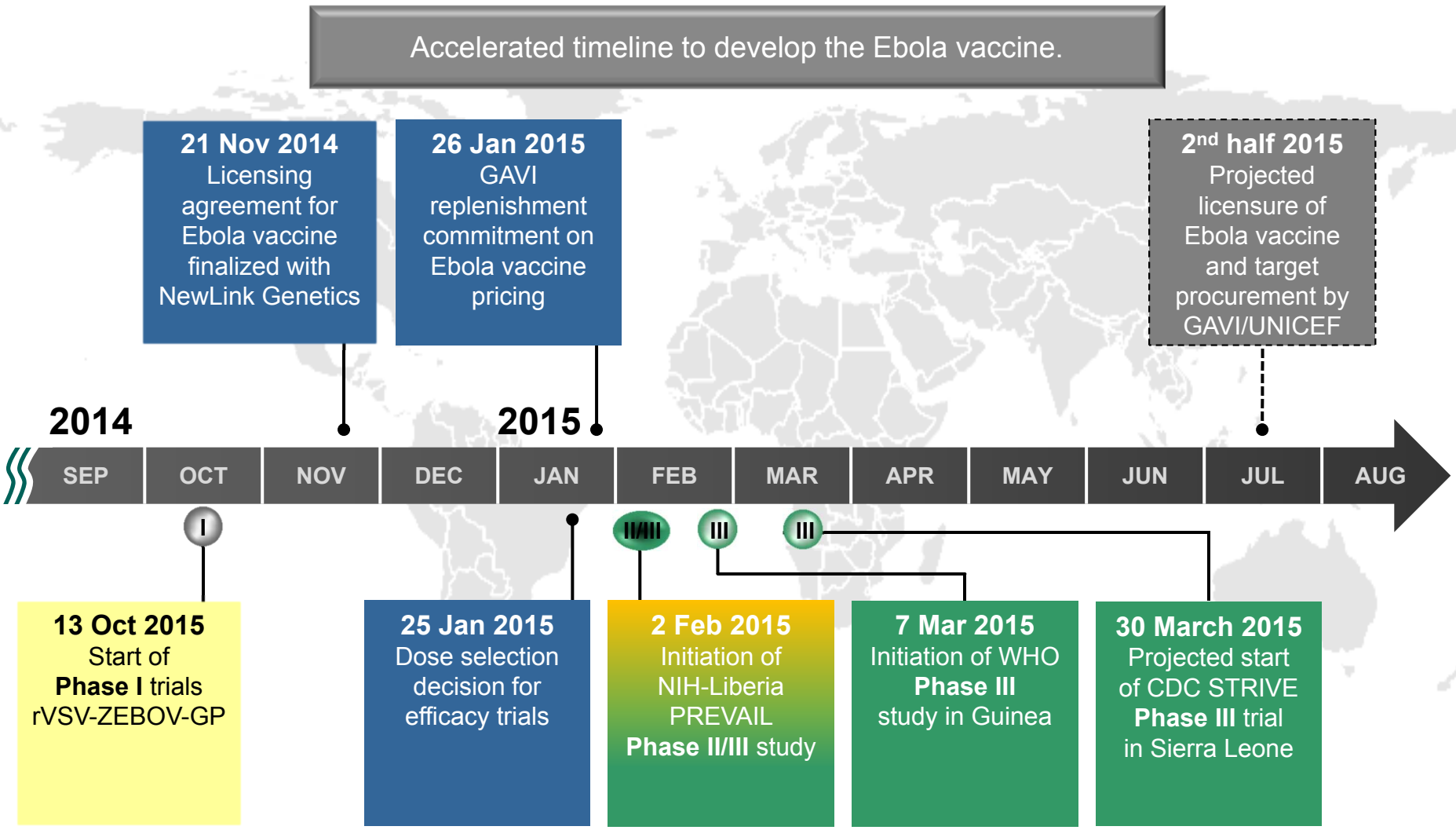
rVSV-ZEBOV-GP Vaccine Milestones, 2014-2015

Accelerated timeline to develop the Ebola vaccine.



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Partnerships and Alliances

Public Health Agency of Canada

Public Health Agency of Canada (PHAC)

NewLink GENETICS

NewLink Genetics (Bio-Protection Systems Corporation)

I

Phase I Studies

WHO Clinical Consortium/ Wellcome Trust

wellcome trust

World Health Organization

- **Switzerland**: University Hospitals of Geneva
- **Germany:** University Medical Center Hamburg/Clinical Trial Center North
- **Gabon:** Centre de Recherches Medicales de Lambarene/University of Tuebingen
- **Kenya:** Kenya Medical Research Institute
- Marburg Laboratory

- CCV – Halifax
- US Department of Defense (WRAIR, JVAP, USAMRIID, DTRA)
- NIAID/NIH
- BARDA

II/III

Phase II/III Studies

- **Liberia:** Liberia – NIH Partnership (NIAID)
- **Sierra Leone:** CDC/ Sierra Leone Medical School
- **Guinea:** WHO/Norwegian Institute of Public Health//MSF/HealthCanada
- With contributions from Department of Defense (JVAP, USAMRIID, DTRA) and BARDA

National Institutes of Health

CDC Centers for Disease Control and Prevention

Department of Defense United States of America

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The International Partnership Facilitating rVSV-ZEBOV Clinical Trial Evaluation

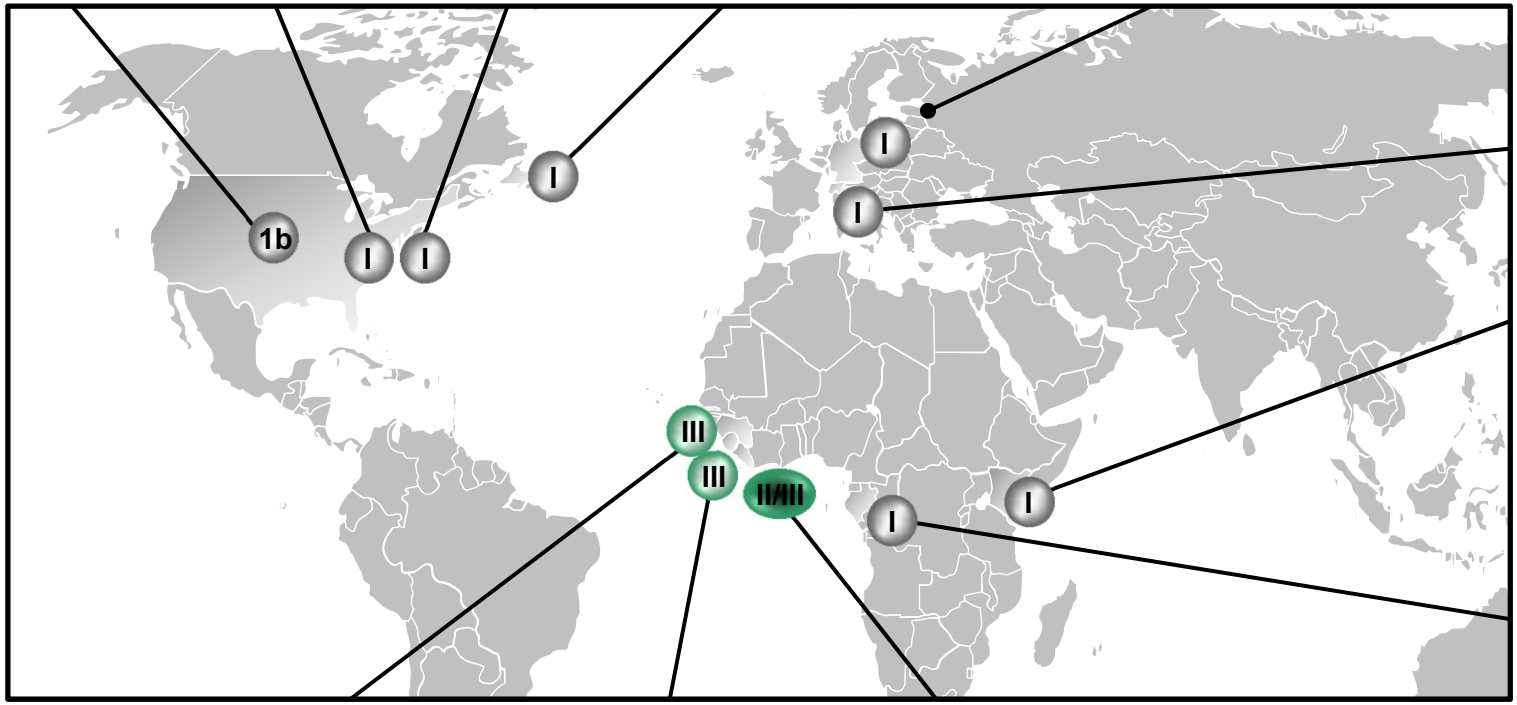
NewLink
8 cities in USA

WRAIR
Silver Springs, MD, USA

NIH
Bethesda, MD, USA

CCV
Halifax, Nova Scotia, Canada

University Medical Center Hamburg + Clinical Trial Center North
Hamburg, Germany



HUG
Geneva, Switzerland

KEMRI
Kilifi, Kenya

CERMEL + University of Tuebingen
Lambarene, Gabon

WHO + Norwegian Institute of Public Health + Health Canada
Guinea

CDC + Sierra Leone Medical School
Sierra Leone

Liberia-NIH Partnership
Liberia

Supported by the WHO, NewLink, Merck, and the Public Health Agency of Canada.
Funding from the US Department of Defense, NIAID, BMGF,
Wellcome Trust, and the European Commission.

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Key considerations awaiting clarification

- Magnitude and timing of vaccine need
- Expediting and integrating regulatory and policy decisions
- Regulatory pathway to licensure should formal demonstration of efficacy not be feasible in context of waning EBOV incidence
- Formulation and implementation of vaccine delivery strategies
- Optimal target product profile (both near term and longer term)
- Clinical and regulatory pathway to optimized “next generation” vaccines (eg, thermostable formulations, multivalent vaccines, etc)
- Will momentum and commitment be sustained if current outbreak is controlled?

Who leads? Who decides what? Who carries risks?
Who is responsible and accountable?

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How and when will it all come together effectively?

- Feasibility and timing of formal demonstration of efficacy
- Timing regulatory approval (eg, FDA, EMA) (whether or not efficacy is formally demonstrated)
- Emergency use authorization (eg, WHO)
- Need for and timing of WHO Prequalification
- Timing of SAGE recommendation
- Definition of magnitude and timing of vaccine demand, and commitment to fund (GAVI) and procure (UNICEF)

Ability to provide vaccine in desired scale at the appropriate time and at the most affordable price will be highly dependent on clarification of these external factors

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Key Considerations Moving Forward

- Optimizing models of effective, trust-predicated multi-stakeholder, multi-sector (public *and* private) partnership and alignment to accelerate EBOV vaccine development and delivery efforts in response to current and future public health needs
- Consideration of how data emerging in coming months will inform, and hopefully enable, future efforts to develop optimized EBOV vaccines (eg, multivalent, thermostable, simplified delivery) to prevent or contain future outbreaks
- Recognizing the precedent set by the nature and ultimate success of the current response will inform and influence the global health community's response to future emerging infectious disease outbreaks