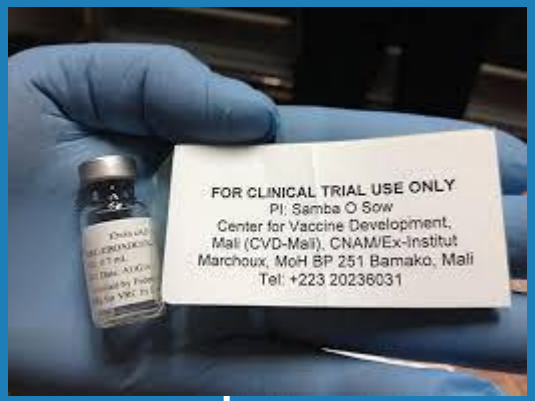
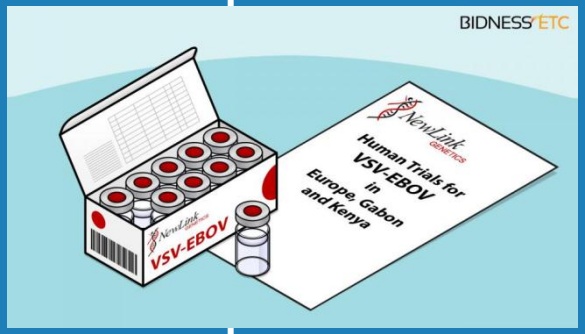


15 April 2015

Vasee Moorthy MRCP PhD

Accelerated Ebola Vaccine Development: Phase 1-2



World Health Organization

WHO calls for accelerated ebola vaccine development

We call on the international vaccine community to accelerate development of high quality, safe and effective ebola vaccines

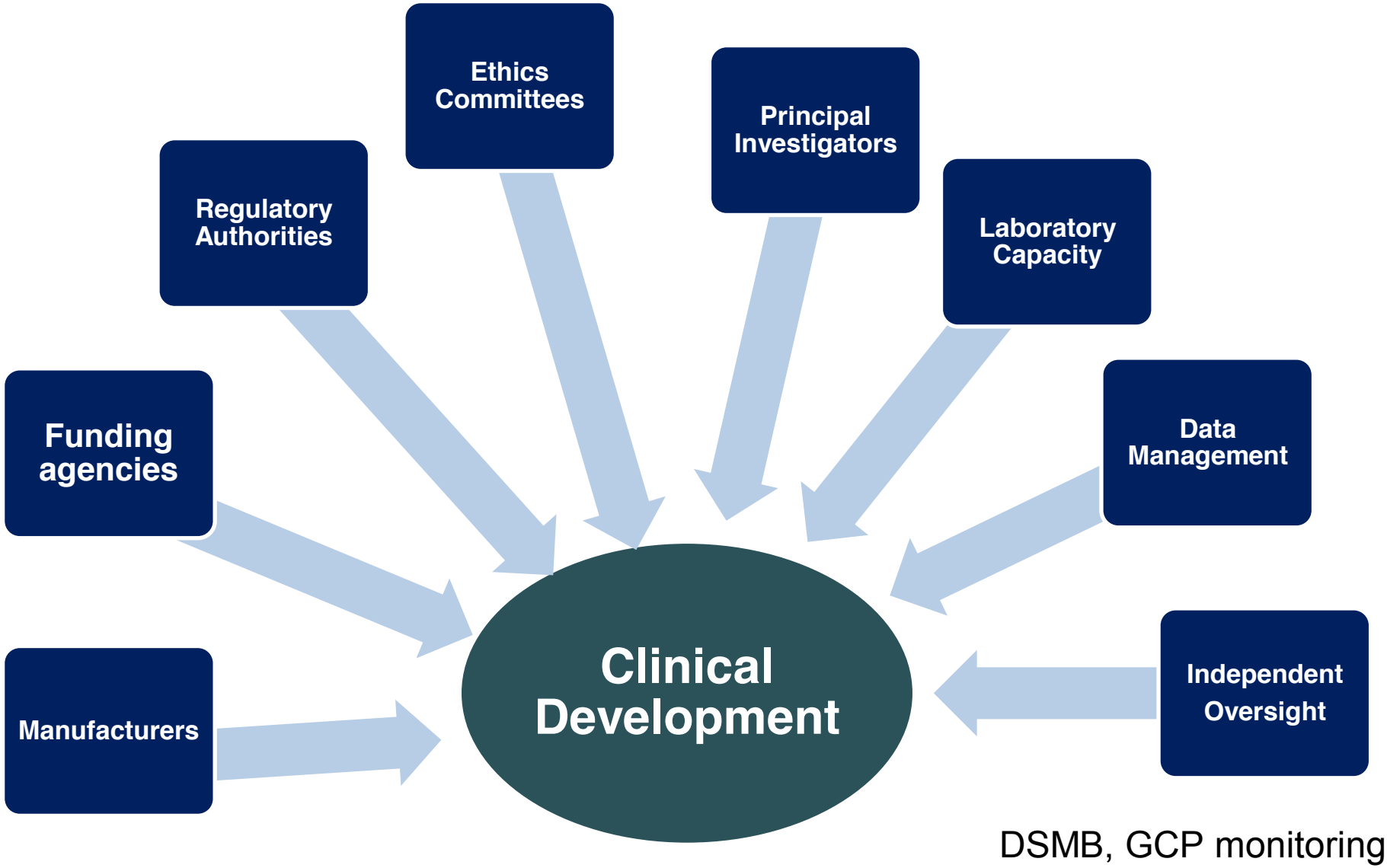
GMP-grade material available

100% efficacy in non-human primates

We will accelerate by bringing all resources to bear on an emergency basis.
Quality and safety will be a paramount concern throughout

WHO's role in Phase 1 for Ebola vaccines

- **Once Public Health Emergency declared WHO called for an international partnership to bring forward availability of high quality safety and immunogenicity data**


Ethics Committees
Principal Investigators
Regulatory Authorities
Laboratory Capacity
Funding agencies
Data Management
Clinical Development
Manufacturers
Independent Oversight
DSMB, GCP monitoring

Pipeline

PRE-CLINICAL DEVT.

CLINICAL TRIALS

Protein Sciences Corporation

VLP

Profectus BioSciences, Inc.

rVSV

Jefferson Thomas Jefferson University

Rec. rabies

Research Institute of Influenza, Ministry of Healthcare of the Russian Federation

Rec. influenza

VAXART

Ad5

5 Jan 2015

J&J

Ad26/MVA

NOVAVAX Creating Tomorrow's Vaccines

VLP

12 Feb 2015

gsk

2 Sep 2014

ChAd3

NewLink Genetics

MERCK Be well

17 Oct 2014

rVSV-ΔG

Chinese Ad5 candidate – no NHP efficacy data

World Health Organization

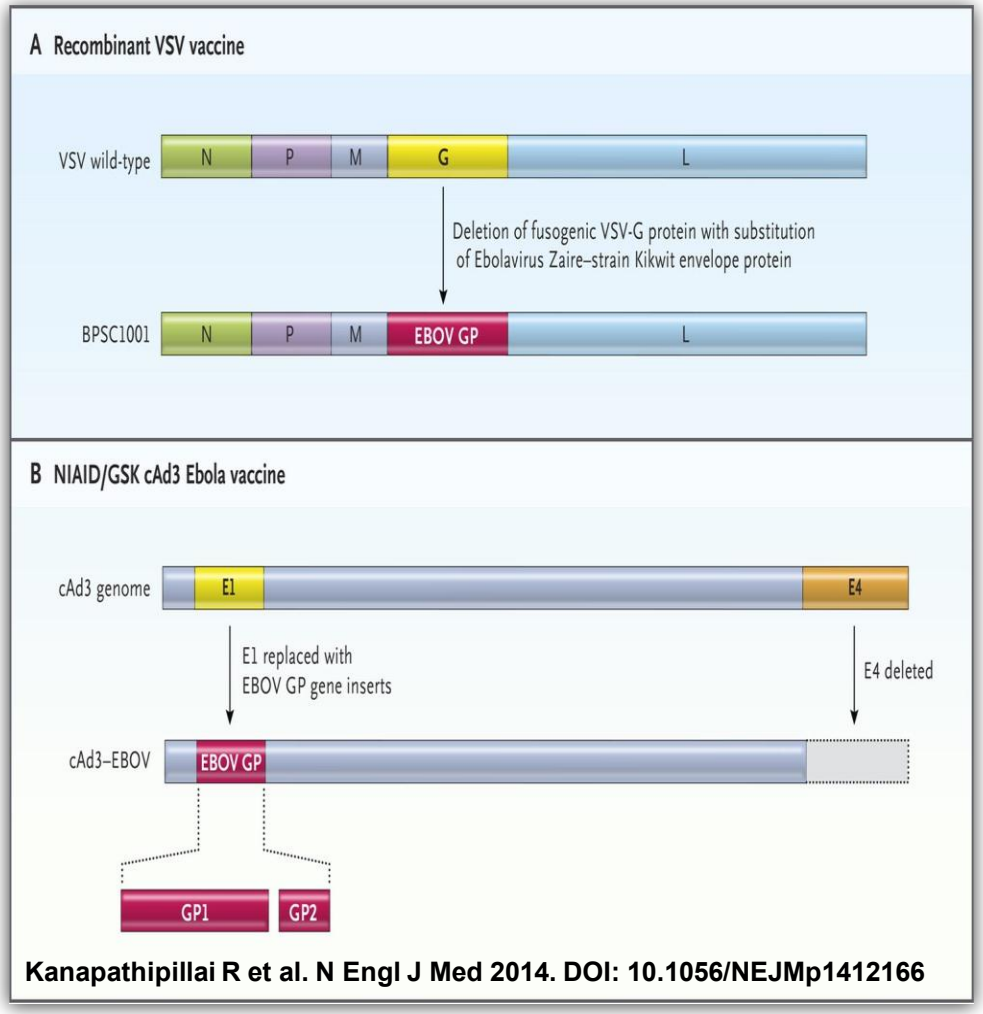
Two candidate vaccines started clinical evaluation in Sep-Oct 2014

A- rVSV-ZEBOV

- **Recombinant vesicular stomatitis virus**
  - NewLink Pharmaceuticals / Merck / Public Health Agency of Canada

B - ChAd3-ZEBOV

- **Replication deficient chimpanzee adenovirus 3**
  - GSK/NIAID



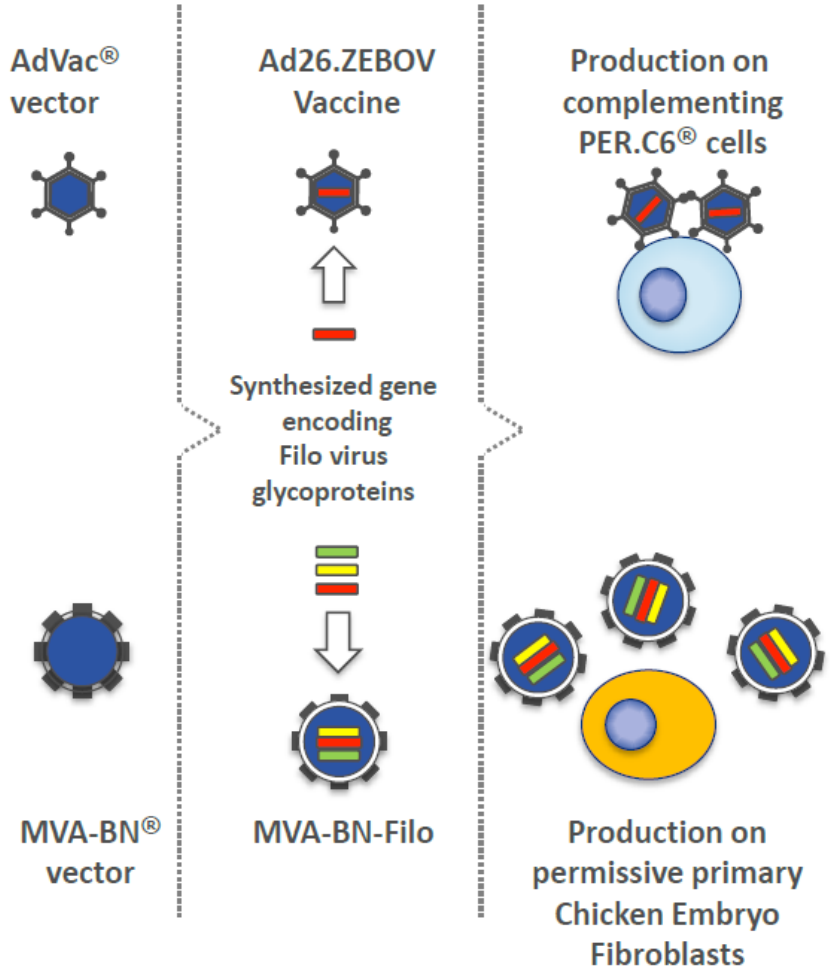
Kanapathipillai R et al. N Engl J Med 2014. DOI: 10.1056/NEJMp1412166

World Health Organization

One candidate vaccine started clinical evaluation in Jan 2015

C. Ad26.ZEBOV / MVA-BN-Filo

- **Replication deficient human adenovirus 26 and modified vaccinia Ankara**
  - Johnson & Johnson / Janssen Pharmaceuticals / Bavarian Nordic



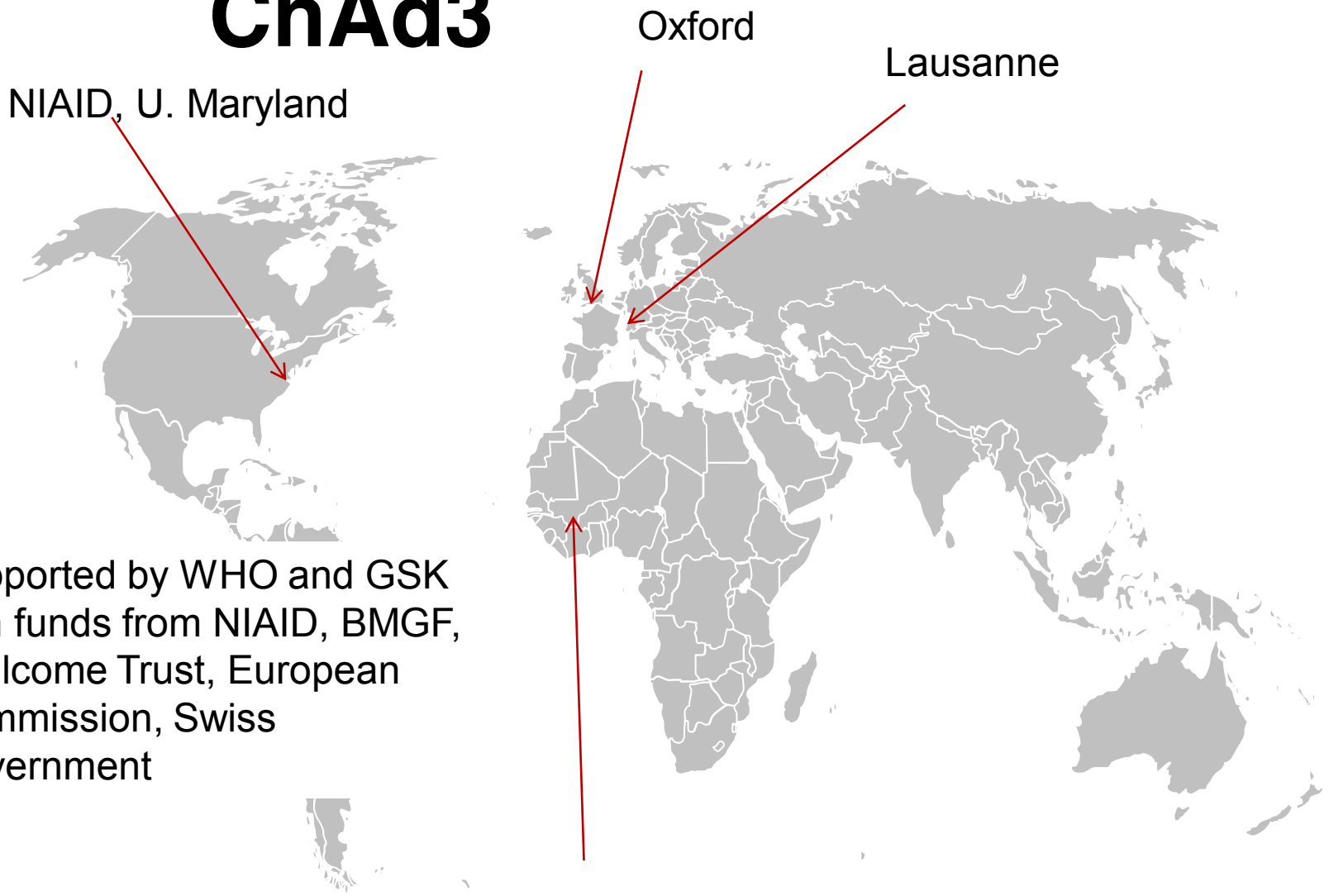
Different regimens

First dose	Second dose at ?D14-28	
rVSV-ΔG		
ChAd3	+/- MVA	
Ad26 or MVA	MVA or Ad26	
Protein	Protein	

Stability profiles

Vaccine	Stability
rVSV-ΔG	< -20, -20 & 2-8 in process
ChAd3	<-20, -20 & 2-8 in process
Ad26 /MVA	2-8 short term, -20 medium term, -60 long term

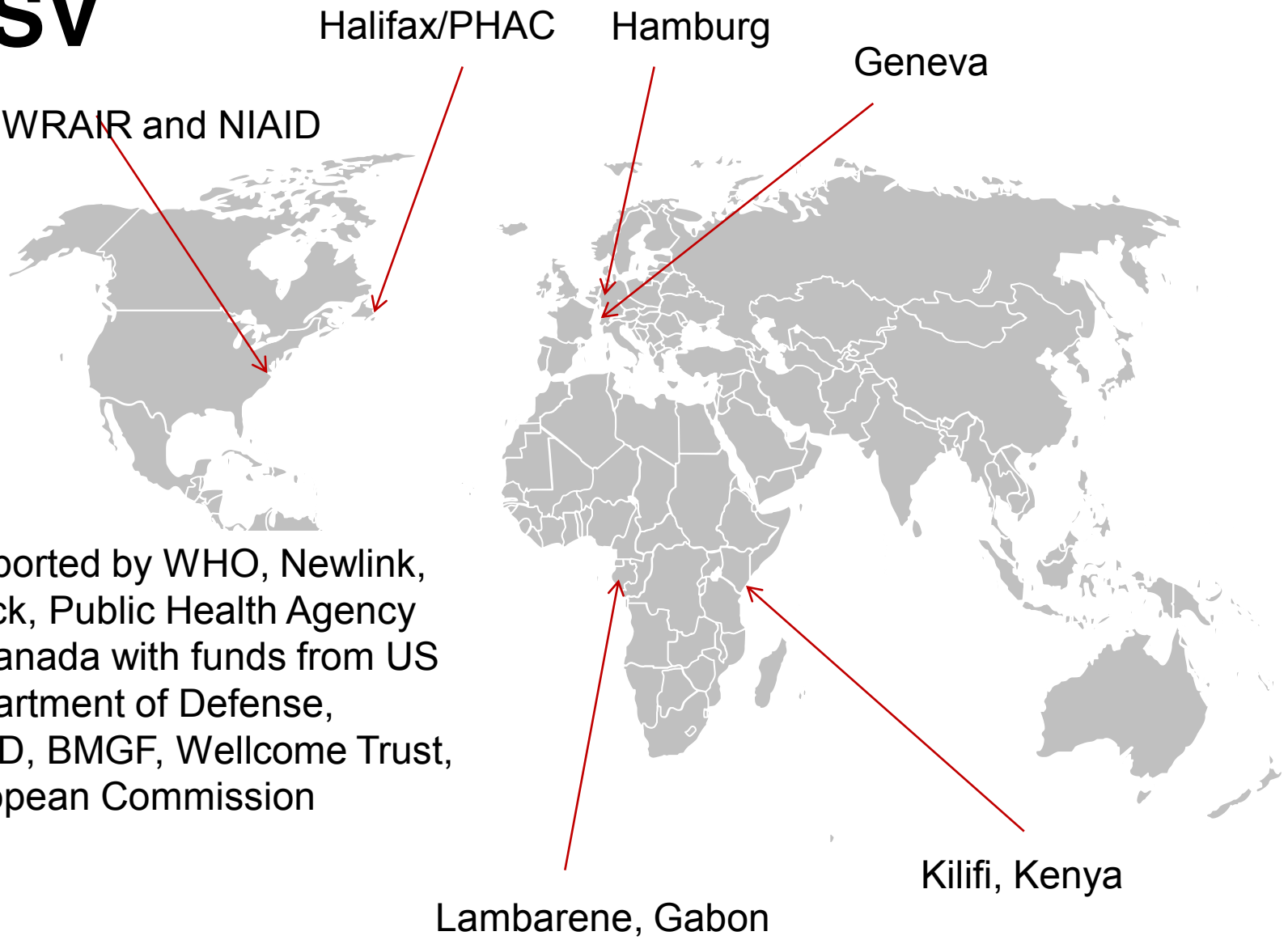
ChAd3



Supported by WHO and GSK with funds from NIAID, BMGF, Wellcome Trust, European Commission, Swiss Government

The international partnership facilitating ChAd3-ZEBOV Phase 1 evaluation

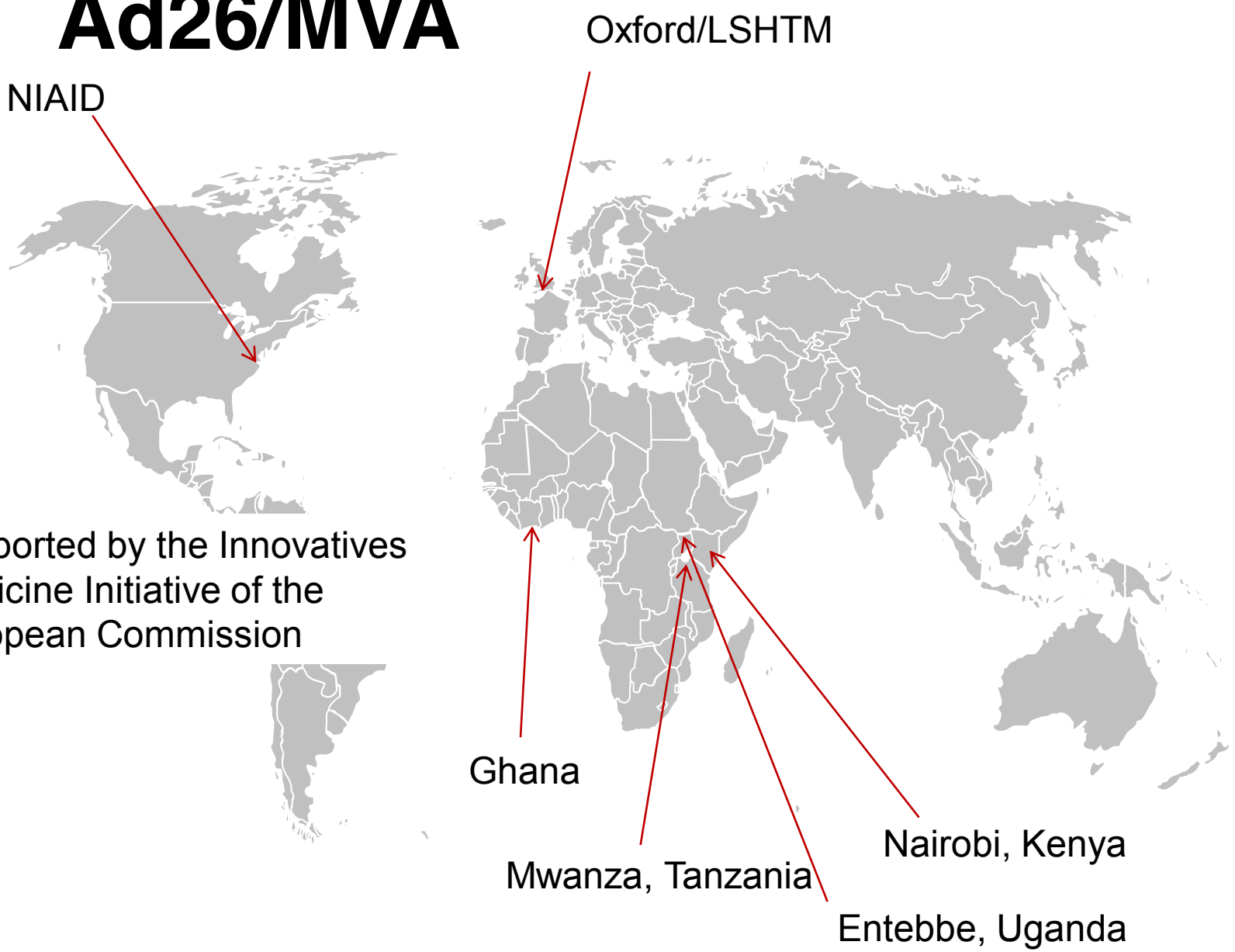
VSV



Supported by WHO, Newlink, Merck, Public Health Agency of Canada with funds from US Department of Defense, NIAID, BMGF, Wellcome Trust, European Commission

The international partnership facilitating rVSV-ZEBOV Phase 1 evaluation

Ad26/MVA



The international partnership facilitating Ad26.ZEBOV / MV-BN-Filo Phase 1 evaluation

ChAd 3 Phase 1-2 summary

ChAd3 : Overview of Phase 1 trials for safety and immunogenicity in healthy adults

Site	*Number*	*Start of enrolment*	*End of enrolment*	*Prelim. results*
VRC – USA (Bivalent)	20	2 September 2014	October	Published NEJM Nov 2014
Oxford – UK	60	17 September 2014	November	Published NEJM Jan 2015
CVD – Mali	91	8 October 2014	December	Q1 2015
Lausanne, Switzerland	120	31 October 2014	December	Q1 2015
Univ. of Maryland, USA	20	10 November 2014	December	Q1 2015

Initiated planning for Oxford, Mali, Maryland and Swiss trials in late August to September

Completed enrolment of all 311 volunteers by December 2014!!!

World Health Organization

Planned Phase 2 trials of ChAd3-ZEBOV

Location	Sponsor	Number to be enrolled	Design	Durat-ion	Populat-ion	Est. start date
Senegal, Mali, Ghana, Nigeria, Cameroon	GSK	600 in 3 age strata	RCT	12 months	Healthy children aged 1-17 years	July 2015
Senegal, Mali, Ghana, Nigeria, Cameroon	GSK	3,000	RCT	12 months	Healthy adults aged 18 years and older	May 2015

VSV Phase 1-2 summary

rVSV : Overview of Phase 1 trials for safety and immunogenicity in healthy adults

Site	Number	Trial start	End of enrolment	Prelim. Results (D28 from partial enrolment)
WRAIR – USA	30	17 October 2014	Dec 2014	Dec 2014
NIAID – USA	30	24 October 2014	Dec 2014	Dec 2014
Geneva, Switzerland	100	10 Nov 2014	Jan 2015	Jan 2015
Germany	30	17 Nov 2014	Jan 2015	Jan 2015
Gabon	60	21 Nov 2014	Jan 2015	Jan 2015
Kenya	40	Dec 2014	Jan 2015	?Feb 2015
Canada	30	Dec 2014	Dec 2014	

Total vaccinated Phase I = 320

Phase 1b trial rVSV-ZEBOV
initiated December 2014

Group	*N*	*Dose*	*Route*	Schedule
1	*64*	*3×10^6 pfu*	*IM*	Day 0
2	*64*	*3×10^5 pfu*	*IM*	Day 0
3	*64*	*3×10^4 pfu*	*IM*	Day 0
4	*64*	*3×10^3 pfu*	*IM*	Day 0
5	*74*	*Placebo (0.9% NS)*	*IM*	Day 0

Healthy subjects, 8 sites in US

Safety Summary of rVSV-ZEBOV-GP

- Over 500 volunteers have received vaccine in Phase I studies; range: 3x10^3 - 1x10^8 pfu
- No vaccine-related SAEs to date in all ongoing trials (only SAEs are cases of malaria being reported at African sites)
- Most AEs are consistent with acute “flu-like” symptoms
- Arthralgia / arthritis cases reported in 2nd week post-vaccination frequency varying by site and study
  - Transient and low-moderate severity events, not dose-dependent, and appear to be virally mediated
  - Highest frequency reported at Geneva site (~20%)
  - 0-10 % at other sites

Ad 26/MVA
Phase 1-2 summary

Planned Phase 2 trials of Ad26/MVA-ZEBOV

Possible Location	Sponsor	Number to be enrolled	Design	Duration	Population	Est. start date
Cote D'Ivoire, Burkina Faso, Ghana, Kenya, Uganda	Janssen	1188	RCT	----	Healthy adults aged 18 years and older, children	June 2015
France and UK	Janssen	612	RCT		1-17 years, HIV + adults, Western HCWs	June 2015

Summary

- Safety and Immunogenicity data are available for ChAd3 and rVSV, and emerging for Ad26/MVA
- Phase 1 data expected soon for Novavax protein
- Accelerated, high quality, state-of-the-art Phase 1 trials can be conducted in the context of a PHEIC
- Phase 2-3 protocols were amended to take into account emerging results
- Chances of success have been increased by clinical data to support dose selection

Acknowledgements

All PIs, trial teams, laboratories, data management

Study participants

DSMBs

Funding agencies

Regulators

Ethics Committees

Manufacturers

Participants in WHO Consultations