Translating **science** into **global** health impact

IAVI VSV Lassa Fever Vaccine Candidate Development Overview

25 October 2022

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Emerging Infectious Diseases and Epidemiology
IAVI
WHO-CEPI Lassa Workshop, Abuja, Nigeria

IAVI gratefully acknowledges the generous support provided by the following major funders

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THE WORLD BANK

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CEPI | New vaccines for a safer world

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SERUM INSTITUTE OF INDIA
Cyrus Poonawalla Group

The Research Council of Norway

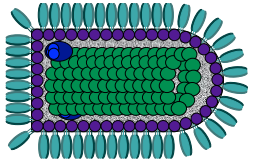
Biomedical Advanced Research and Development Authority (BARDA) | Foundation for the National Institutes of Health | National Institute of Allergy and Infectious Diseases | amfAR, The Foundation for AIDS Research | Broadway Cares/Equity Fights AIDS | Cancer Research UK | The City of New York, Economic Development Corporation | Congressionally Directed Medical Research Program (DoD) | GSK | The Hearst Foundations | Keith Haring Foundation | Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the USA and Canada)

And many other generous individuals and partners around the world

As of April 2022

IAVI and an extensive network of partners are advancing multiple VSV-Vectored vaccines

VSVΔG-SUDV*

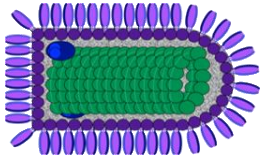


Funded by *Biomedical Advanced Research and Development Authority (BARDA)*

Pre-clinical studies underway

VSVΔG-MARV*

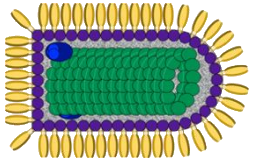
Funded by *US Defense Threat Reduction Agency (DTRA)*



Pre-clinical studies complete

VSVΔG-LASV*

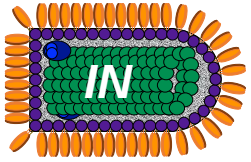
Funded by *Coalition for Epidemic Preparedness Innovation (CEPI) and European & Developing Countries Clinical Trials Partnership (EDCTP)*



Ph1 in U.S. and W. Africa

Preclinical Research → Early Development → Manufacturing Dev. → GMP Manufacturing / Regulatory / Nonclinical safety → Clinical Development

VSVΔG-SARS-CoV-2

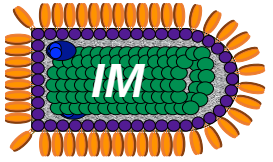


Funded by *DTRA, Japan MOF/World Bank*

財務省 Ministry of Finance, JAPAN

Pre-clinical studies underway

VSVΔG-SARS-CoV-2



Funded by *Merck, BARDA, DTRA, Japan MOF*

財務省 Ministry of Finance, JAPAN

Ph1 Trial Complete –

* Licensed through the Public Health Agency of Canada

Key attributes of our rVSVΔG-LASV-GPC (lineage IV) vaccine

- A single IM injection is **100% efficacious** in cynomolgus macaques – protection is **durable out to 1-year** post vaccination
  - The original research vaccine (2x10e7 PFUs) protected when LASV challenge (IM challenge; Lineage IV) was conducted 1 month after vaccination (Geisbert et al, 2005, PMID: 15971954)
  - Vaccine prepared from the IAVI-CEPI preMVS (2x10e7 or 2x10e5 PFU doses) protected at 1 month and 12 months after vaccination
- Murine biodistribution study **supports an acceptable tolerability and safety profile**
  - No viable virus distribution to the brain after mice were injected (IM) with a human dose
  - From the large number of samples evaluated only a single injection site sample from Day 3 had a viable viral titer above the LLOQ
- Vaccination of macaques induces **detectable serum nAbs** active against Lineage IV GPC
  - Detectable cross-neutralization against geographically diverse Lineages I-III, V and VII
- Capable of inducing **fast-acting immunity** that will be important in outbreak situations
  - High dose (2x10e7 PFUs) of IAVI-CEPI vaccine induced detectable binding antibodies by d10 in macaques
  - Protection against a Lineage II challenge virus as soon as 3 or 7 days following vaccination (Cross et al, 2022, PMID: 35858566)
- Builds on the **VSV technology used for licensed ERVEBO® vaccine**
  - High probability of success moving through product development
  - VSVΔG-LASV-GPC US Phase 1 trial safety data is encouraging (currently blinded[1])
- **Promising immunogenicity** in Phase 1 clinical study

[1] All safety data are blinded; data current as of July 28, 2022

Clinical

Phase 1 trial design and update

- FIH at US sites achieved 15 July 2021
- All volunteers in the U.S. have been enrolled and day 28 immunogenicity data are complete
- Regulatory and ethics approval received in Liberia and participants are being enrolled
- Protocol amended to include a booster dose for half the participants in all 3 dose groups in Liberia

		Study Design	Vaccine Dosage (pfu)	N (Active / Placebo)	Month 0	Week 6
Dose Escalation	US Sites	1	2 X 10^4	8/2	X	
		2	2 X 10^5	8/2	X	
		3	2 X 10^6	8/2	X	
		4A	2 X 10^7	8/2	X	
		4B	2 X 10^7	8/2	X	X
SMC Review						
Dose Group Expansion	Liberia (and US sites if needed)	5A	2 X 10^5	8/2	X	
		5B	2 X 10^5	8/2	X	X
		6A	2 X 10^6	8/2	X	
		6B	2 X 10^6	8/2	X	X
		7A	2 X 10^7	8/2	X	
		7B	2 X 10^7	8/2	X	X
Total = 110 (88/22)						

US	GW	Washington, D.C.
	BWH	Boston
	EWMRI	Honolulu

Liberia	Redemption Hospital	Monrovia

Safety Summary – General Information

Study Status[1]

52 participants enrolled in a US population between July 2021 - June 2022

- Group 1: 2x10^4 pfu (n=10)
- Group 2: 2x10^5 pfu (n=10)
- Group 3: 2x10^6 pfu (n=10)
- Groups 4A: 2x10^7 pfu, single dose (n=11)
- Group 4B: 2x10^7 pfu, prime/boost (n=11)
- All groups were randomized 4:1 active: placebo

Enrollment is complete in the US and participants are being followed

Enrollment in Liberia is open, and participants are being screened

[1] All safety data are blinded; data current as of July 28, 2022

Phase 1A Reactogenicity Summary

	Group 1 (N=10)	Group 2 (N=10)	Group 3 (N=10)	Group 4A/4B Dose 1 (N=22)	Group 4B Dose 2 (N=11)
Participants ever experiencing an event	8 (80.0%)	8 (80.0%)	9 (90.0%)	22 (100%)	10 (90.9%)
Participants with local site reactions	3 (30.0%)	4 (40.0%)	6 (60.0%)	18 (81.8%)	8 (72.7%)
Participants with systemic reactions	8 (80.0%)	7 (70.0%)	8 (80.0%)	22 (100%)	7(63.6%)
Maximum Reported Severity					
Grade 1	4 (40.0%)	5 (50.0%)	4 (40.0%)	4 (18.2%)	6 (54.5%)
Grade 2	4 (40.0%)	3 (30.0%)	4 (40.0%)	8 (36.4%)	3 (27.3%)
Grade 3 *	0 (0.0%)	0 (0.0%)	1 (10.0%)	10 (45.5%)	1 (9.1%)
Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Average onset of events (days post vaccination)	3.1	3.1	2.1	2.3	2.6
Grade 3+ events			10	2.2	4.0
Average duration of events (days)	1.3	1.6	2.2	2.2	2.3
Grade 3+ events			2.0 **	1.2	2.0

* All systemic events
** Event lasted 12-hours but spanned two days and is therefore counted on each day in the patient diary

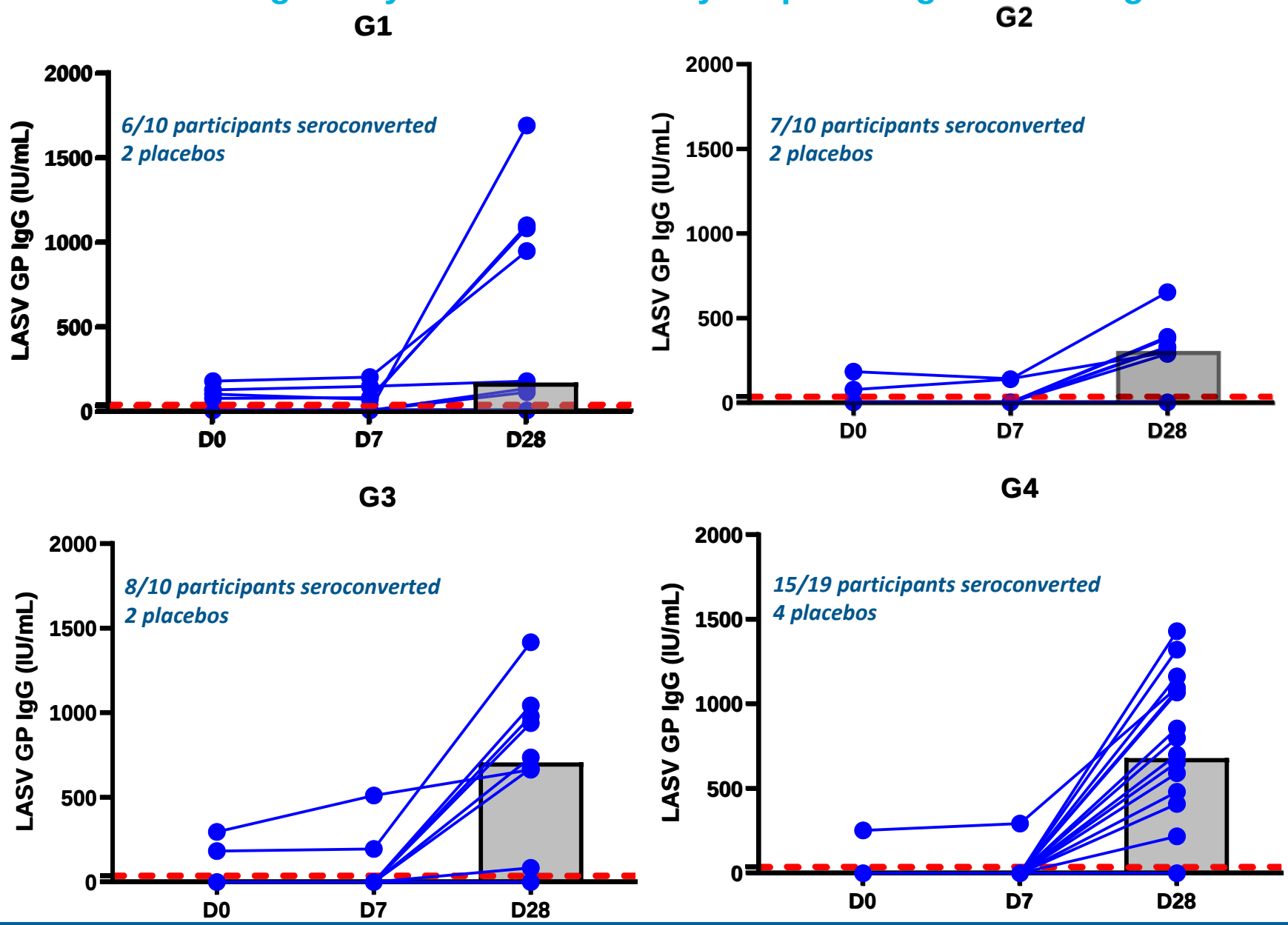
Safety Conclusions

- No related SAEs
- No unsolicited adverse event pattern of concern reported
- No hearing loss
- Average duration of reactogenicity is between 1.3-2.2 days and resolved without sequelae
- Grade 3 reactogenicity are mainly systemic events and the vast majority are in Groups 4A and 4B
- Reactogenicities did not result in any participant discontinuing from study participation and there has been no safety signal warranting a study pause per the Independent Safety Monitoring Committee review

NOTE: In the Phase 2a trial we will evaluate two doses, 2x10^6 pfu and 1x10^7 pfu (half the highest dose in Phase 1) to determine which dose provides the optimal safety and immune response profile

Clinical

Phase 1 Immunogenicity – Serum Antibody response against Lineage IV LASV GP at Day 28



Key

Study Group	Dose (pfu)	Active/ Placebo
1	2×10^4	8/2
2	2×10^5	8/2
3	2×10^6	8/2
4A/B	2×10^7	16/4

Lower Limit of quantification

IgG binds GPC from multiple Lassa virus lineages

Research assay (ELISA, day 28)

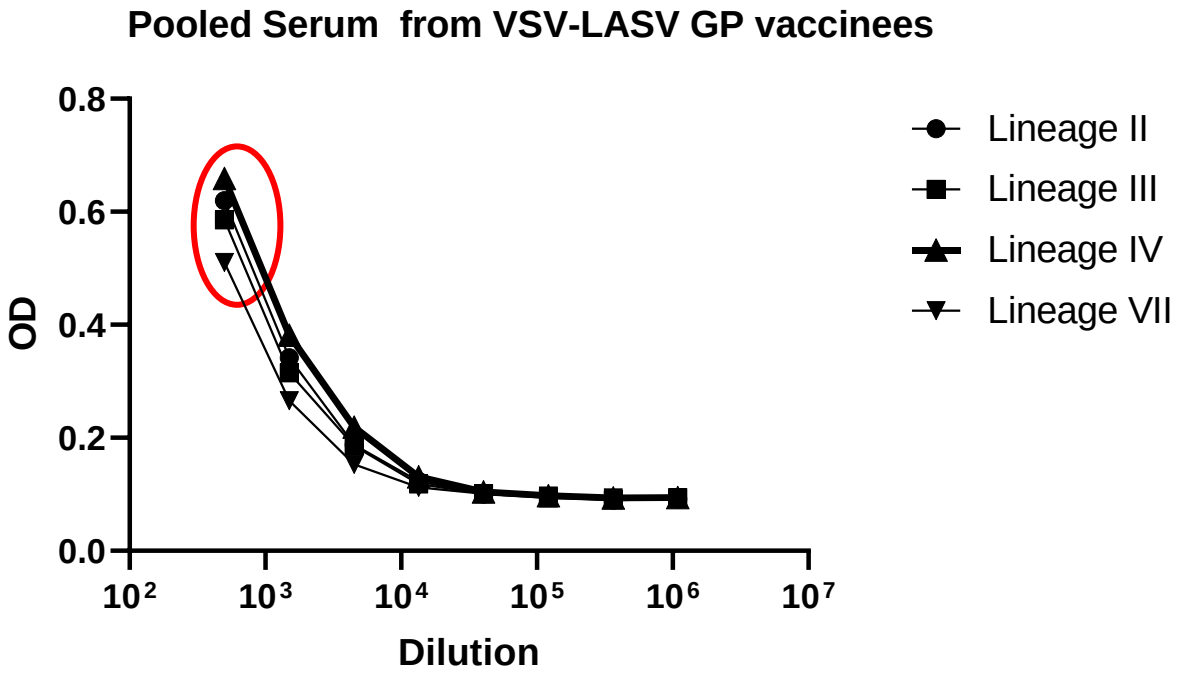


Figure 1. *Titration curves of a pool of high responding vaccinee samples (**from G1, G3 & G4**) to LASV GP from Lineages II, III, IV and VII.*

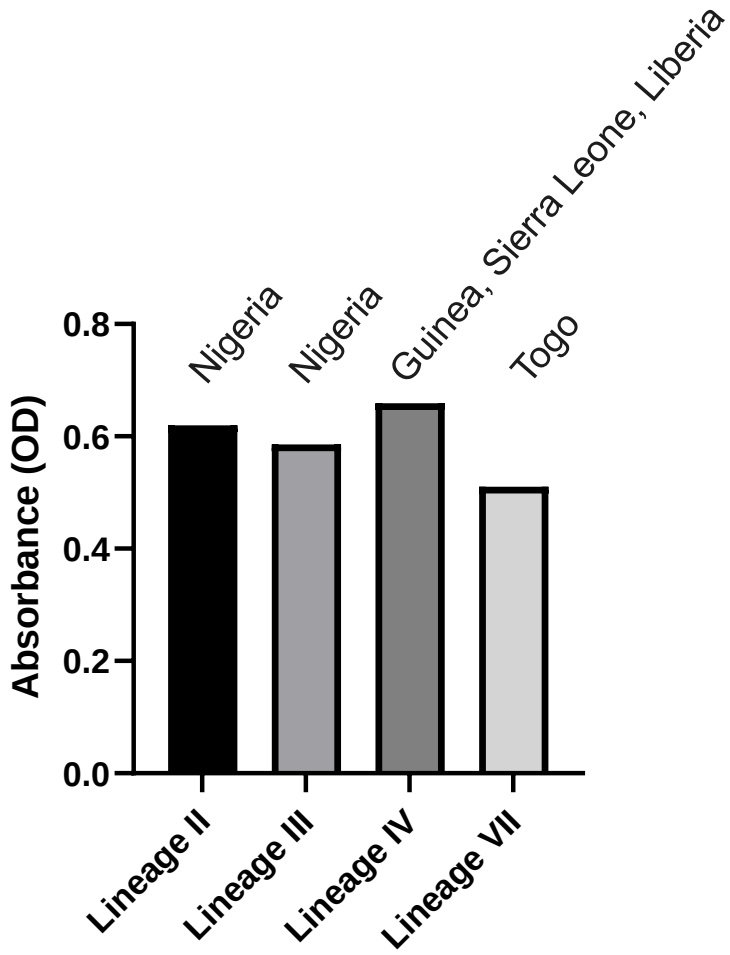


Figure 2. *A pool of high responding vaccinee samples was tested at 1:500 dilution for binding to LASV GP from Lineages II,III, IV and VII*

Clinical

Phase 2a Trial Design

WRP-N (Walter Reed Program - Nigeria)
Abuja, Nigeria

KGH (Kenema Government Hospital)
Kenema, Sierra Leone

PREVAIL, Redemption Hospital
Monrovia, Liberia

Adults
18 – 70 yo
(N=192)

Adolescents
12-17 yo
(N=120)

Children
6-11 yo
(N=120)

Children
18mo - 5yo
(N=120)

HIV-infected adults
18-50 yo
(N=60)

Phase 2a Study Endpoints, Evaluations & Goal

- **Goal:** Select one dose that is safe and immunogenic for the general population (healthy adults and adolescents) and in children and HIV+ and prepare sites for a larger efficacy trial. Phase 2a trial to include 1x10e7 pfu as higher dose and 2x10e6 pfu as lower dose based on tolerability data and immunogenicity in Phase 1 dose escalation trial
- **Primary:** Safety & Tolerability at 2 dose levels (chosen from Phase 1 data)
- **Secondary:**
  - Immunogenicity [percent of volunteers responding and magnitude of neutralizing and binding antibody response to LASV-GPC]
  - Vaccine Viremia
  - Vaccine Viral Shedding
- **Exploratory:** Additional immunogenicity assessments may include Anti-GPC IgG effector functions; Anti-GPC epitope specificity; Anti-GPC T-cell frequencies; Cytokine profiles; Immune responses to VSV; Gene expression profiles (transcriptomics); B cells, plasma and/or serum may also be analysed for epitope specificity and human monoclonal antibodies may be produced

Late-Stage Development Thoughts

- The objective of the late-stage clinical development plan is to demonstrate efficacy through conduct of a field study with a clinical disease endpoint
- Site selection will depend on country-specific surveillance data from ongoing epidemiological studies to identify regions expected to have the highest incidence of Lassa virus infection
- A 2nd Phase 2 study is being considered in high-risk areas to evaluate site readiness, prior to pivotal efficacy trial
- Phase 2B/3 safety/efficacy registration study in adults and children (aged ≥18 months) is planned for Sierra Leone, Liberia and Nigeria
- Safety and immunogenicity trials to support a path toward larger trials designed to support an indication for pregnant and lactating women and children from 6 months of age for prophylaxis and possibly younger for acutely exposed infants.
- Important to determine timing for a lot-to-lot consistency trial

Lassa Epidemiology studies

ENABLE, funded by CEPI

- Benin, Guinea, Liberia, Nigeria and Sierra Leone
- N=24,000
- Enrollment complete, follow up underway (12 and 18 month study visits)
- Incidence of symptomatic LF; sero-prevalence and sero-incidence

IAVI X100 LF Epi study, funded by Wellcome Trust

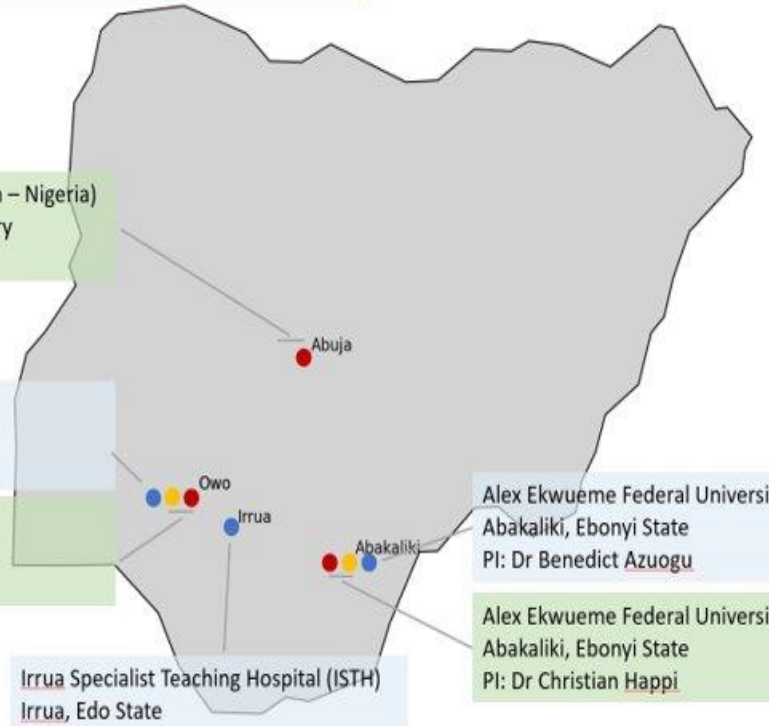
- Sierra Leone (Kenema and Port Loco)
- N=8,010
- Enrollment complete, follow up to start soon (Q4 2022)
- Sero-prevalence and sero-incidence

Walter Reed EID 032

- Nigeria (Owo and Abakaliki)
- N=450
- Enrollment and follow up underway
- Prevalence and incidence

ENABLE and LEAP4WA Consortiums

Nigeria



WRP-N (Walter Reed Program – Nigeria)
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Federal Medical Center
Owu, Ondo State
PI: Dr Olufemi Ayodeji

Federal Medical Center
Owu, Ondo State
PI: Dr Christian Happi

Alex Ekwueme Federal University Teaching Hospital
Abakaliki, Ebonyi State
PI: Dr Benedict Azuogu

Alex Ekwueme Federal University Teaching Hospital
Abakaliki, Ebonyi State
PI: Dr Christian Happi

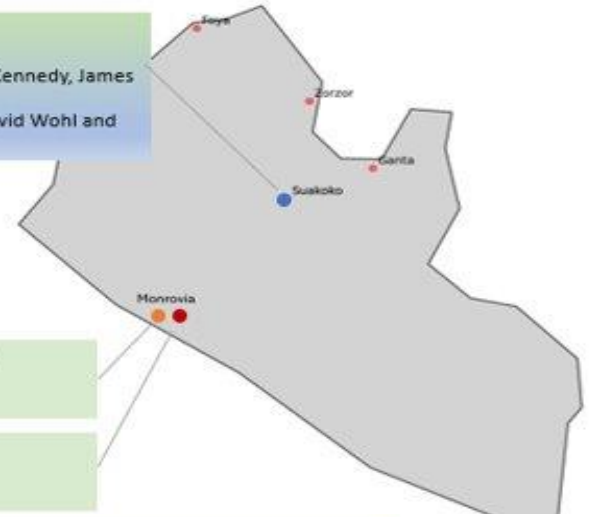
Irrua Specialist Teaching Hospital (ISTH)
Irrua, Edo State
PI: Prof Danny Asogun

Key

- CEPI Enable epidemiology study
- Wellcome-IAVI X100 epidemiology study
- WRAIR EID 032 epidemiology study
- Phase I clinical trial
- Phase II clinical trial (planned)
- ENABLE Consortium
- LEAP4WA Consortium

Liberia

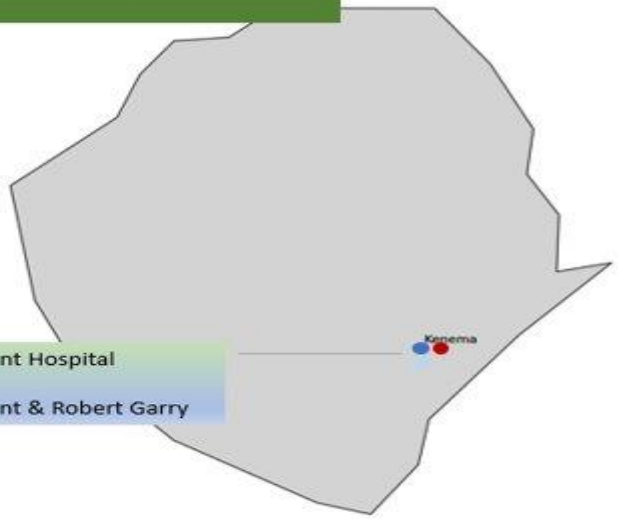
Phebe Hospital
Suakoko
PI: Drs Bernice Dahn, Stephen Kennedy, James Duworko
PI: Dr Jefferson Sibley (UNC: David Wohl and Billy Fischer)



PREVAIL - Redemption Hospital
Monrovia
PI: Dr Mark Kieh

PREVAIL - JFK Hospital
Monrovia
PI: Dr. Johnson

Sierra Leone



Kenema Government Hospital
Kenema District
PIs: Drs Donald Grant & Robert Garry

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