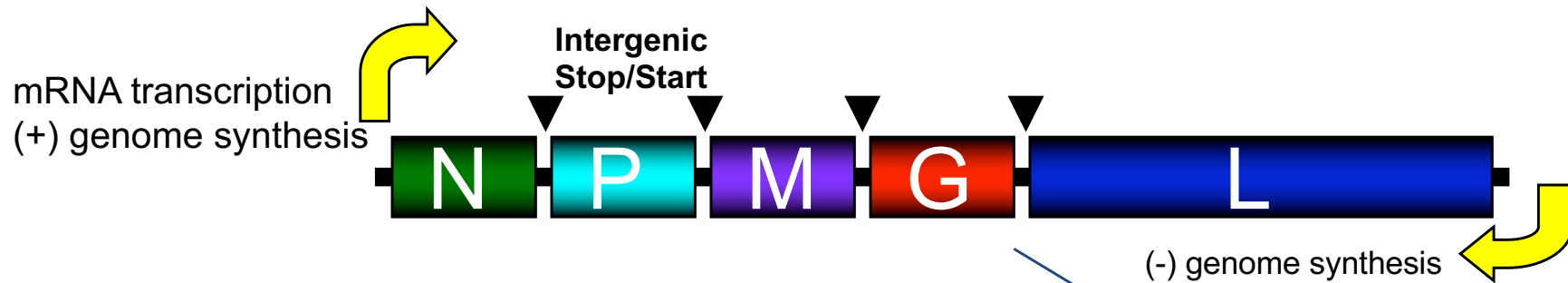


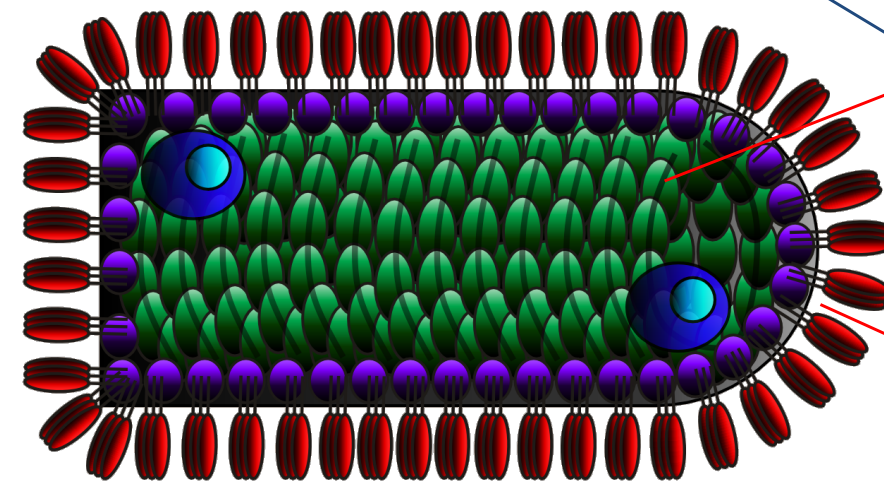
- **John H. Eldridge, Ph.D.**
- Chief Scientific Officer
- 14-Sept-2016

Phase 1 Safety and Immunogenicity of an Attenuated VesiculoVax™ Vectors EBOV Vaccine

VesiculoVax™: A Family of Vaccine Vectors



- Nucleocapsid
- Phosphoprotein
- Matrix protein
- G protein
- Large protein (RNA Pol)



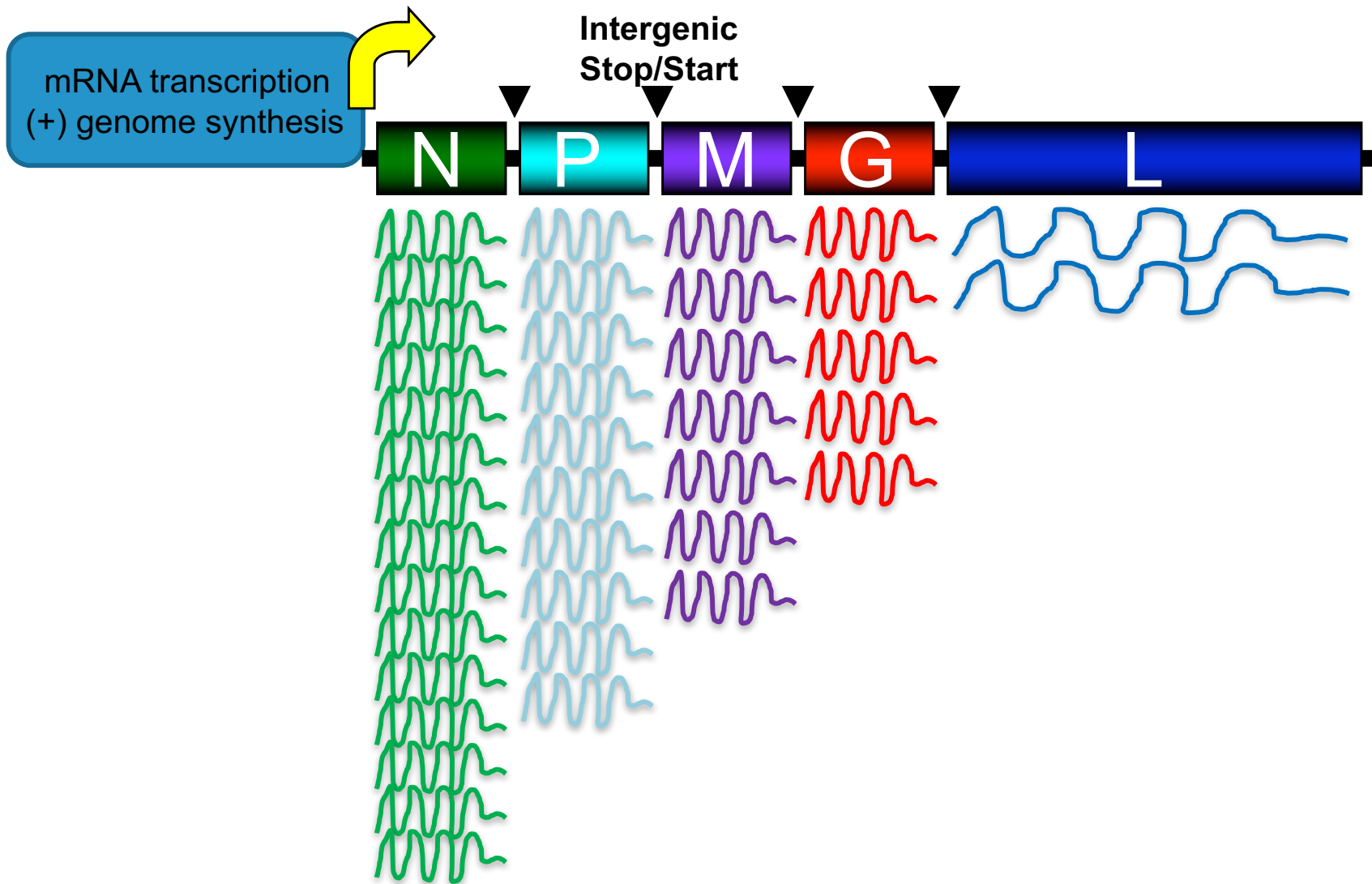
- RNA genome**
- ▶ Nonsegmented,
 - ▶ Single-stranded
 - ▶ Negative-sense

Envelope

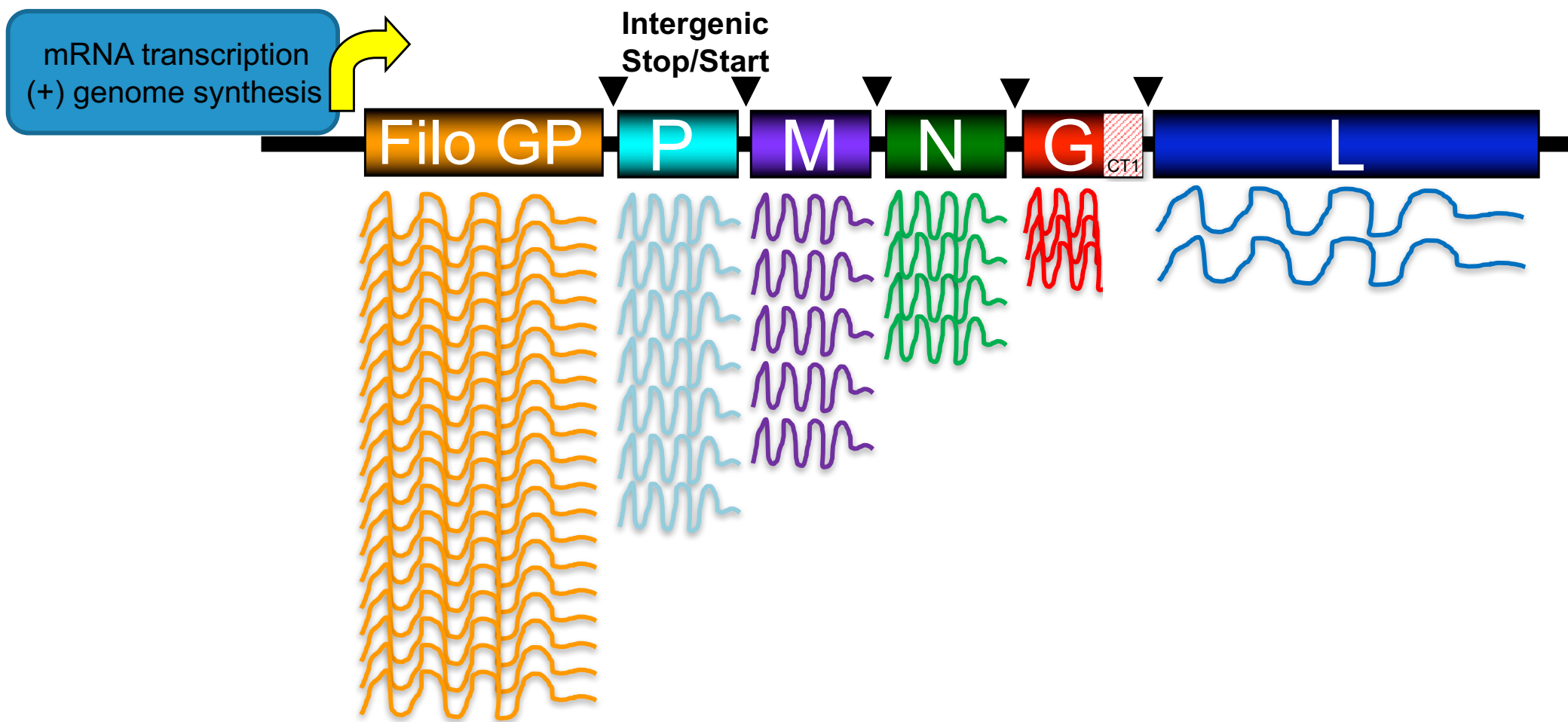
G protein

- ▶ Mediates cell attachment
- ▶ Target of neutralizing antibodies

The Vesiculovirus mRNA Transcriptional Gradient



Using the Vesiculovirus mRNA Transcriptional Gradient to Overexpress a Gene of Interest



VesiculoVax™ Vectored Vaccines

Single Stranded/Non-segmented/Negative-sense RNA Viruses

- Small genomes, but capacity for inserting multiple foreign genes
- Modulation of antigen expression controlled by gene position
- Synergistic attenuating mutations (N gene shuffle & G protein CT truncation)
- **Family of non-cross-reactive (both B and T cell) vectors**
 - Four reduced to practice and three under development

Immunogenicity

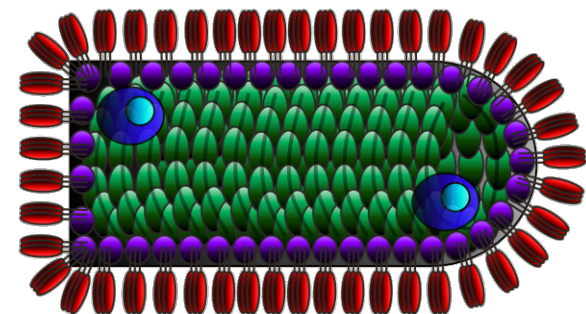
- Replication competent vectors
- Targets antigen-presenting cells
- Attenuating mutations increase immunogenicity

Manufacturing

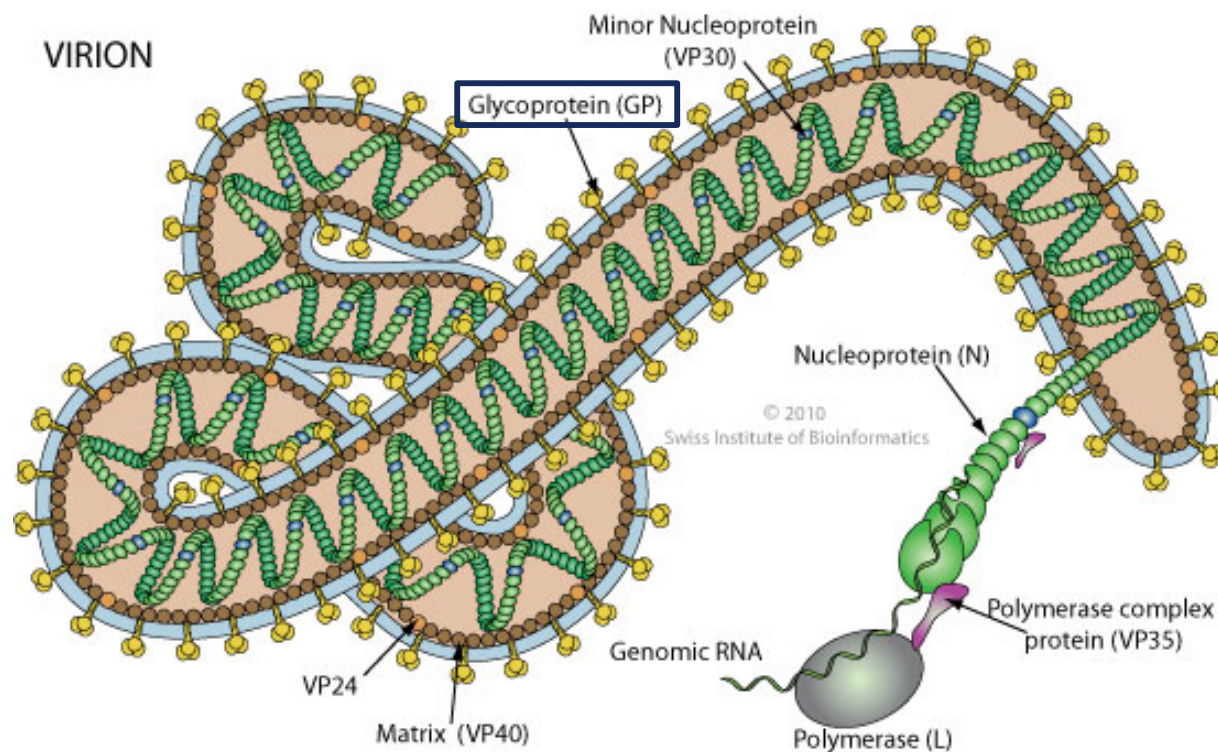
- Propagates efficiently in PBS certified Vero production cell line
- GMP Manufacturing and purification processes in place

Vector Immunity

- Little pre-existing immunity in the human population
- Clinical demonstration of effective homologous boosting

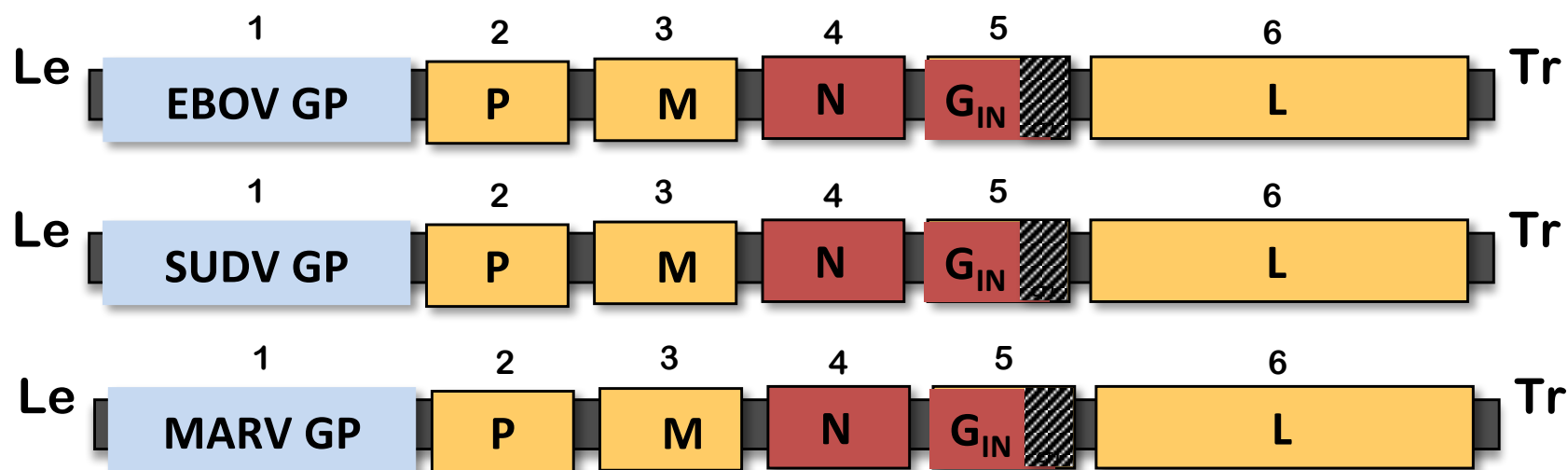


VesiculoVax™ VSV-Vectored Ebola/Marburg Vaccine



rVSV Vectored Tri-Valent Filovirus Vaccine Candidate

rVSVN4CT1-FilovirusGP(a1)



Single Dose NHP Immunogenicity/Efficacy Trial of Tri-Valent rVSVN4CT1-Filovirus Vaccine

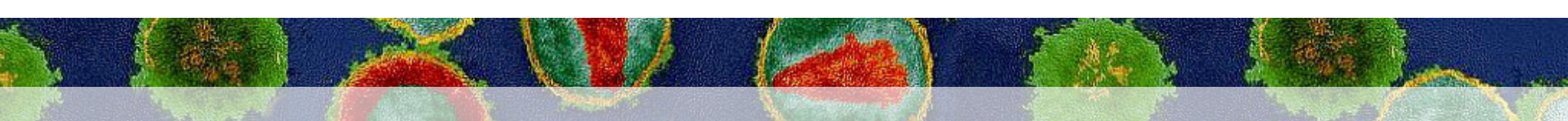
Iteration	Group	Vaccine	Dose (PFU)	Animals		Vacc. Day	1,000 PFU Virus Challenge Day 28
				M	F		
1	1	Tri-val N4CT1GP(a1)	3×10^7	3	2	0	EBOV (Kikwit)
	2	N4CT1-HIVgag(s1)	3×10^7	1	1		
2	3	Tri-val N4CT1GP(a1)	3×10^7	3	2	0	SUDV (Gulu)
	4	N4CT1-HIVgag(s1)	3×10^7	1	1		
3	5	Tri-val N4CT1GP(a1)	3×10^7	3	2	0	MARV (Angola)
	6	N4CT1-HIVgag(s1)	3×10^7	1	1		

Single Dose NHP Trial of Tri-Valent rVSVN4CT1-Filovirus Vaccine: Efficacy

Post challenge clinical signs / outcome

(Data are preliminary and incomplete)

Animal ID	Sex	Weight	Group	Dose Regimen	Post Challenge Clinical Sign / Outcome		
Low Passage 7U EBOV Challenge 1,000 PFU IM	C68105	F	3.387	1	Tri-V N4CT1GP(a1) 3×10^7 (Day 0)	Survived	
	C68581	F	2.969	1		Survived	
	C67794	M	3.569	1		Survived	
	C68349	M	3	1		Survived	
	C68453	M	3.521	1		Survived	
Low Passage SUDV Challenge 1,000 PFU IM	C68525	F	3.262	2	N4CT1-HIVgag(s1) 3×10^7 (Day 0)	Euthanized D7	
	C67091	M	3.371	2		Euthanized D7	
	C68104	F	2.963	3		Tri-V N4CT1GP(a1) 3×10^7 (Day 0)	Survived
	C68568	F	3.843	3			Survived
	C68655	F	3.505	3			Survived
C68335	M	3.07	3	Survived			
C68388	M	3.169	3	Survived			
Low Passage MARV Challenge 1,000 PFU IM	C68585	F	3.062	4	N4CT1-HIVgag(s1) 3×10^7 (Day 0)	Euthanized D6	
	C67058	M	2.953	4		Euthanized D6	
	C66816	F	3.535	5		Tri-V N4CT1GP(a1) 3×10^7 (Day 0)	Survived
	C68645	F	3.36	5			Survived
	C67350	M	2.844	5			Survived
C68328	M	3.288	5	Survived			
C59538	M	3.737	5	Survived			
C62243	F	2.987	6	N4CT1-HIVgag(s1)	rash, ↑ALT, ↑AST, Died D9		
C68329	M	2.946	6	3×10^7 (Day 0)	rash, ↑ALT, ↑AST, Died D8		



A Phase 1 Clinical Trial to Evaluate the Safety and Immunogenicity of a Monovalent Ebola Zaire Vaccine (rVSVN4CT1-EBOVGP1) Delivered by Intramuscular Injection in Healthy Adult Subjects

IND No.: BB-IND-16670

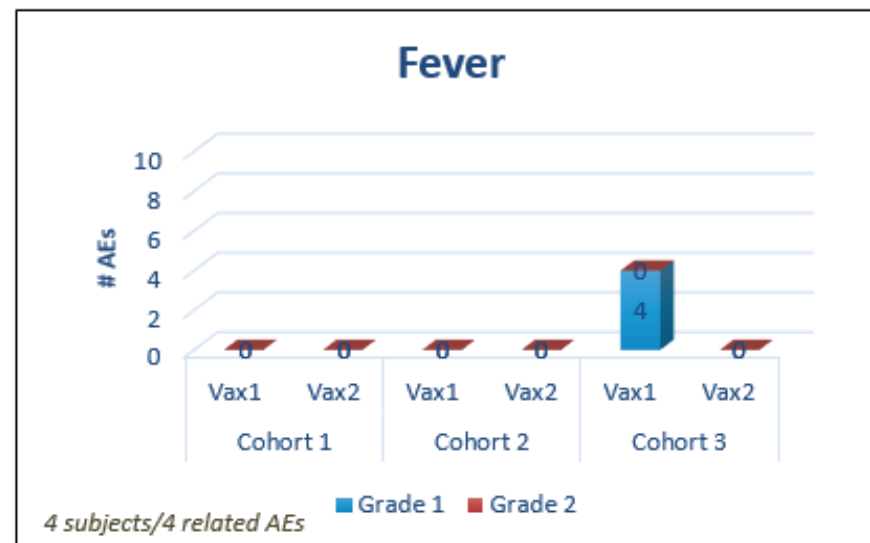
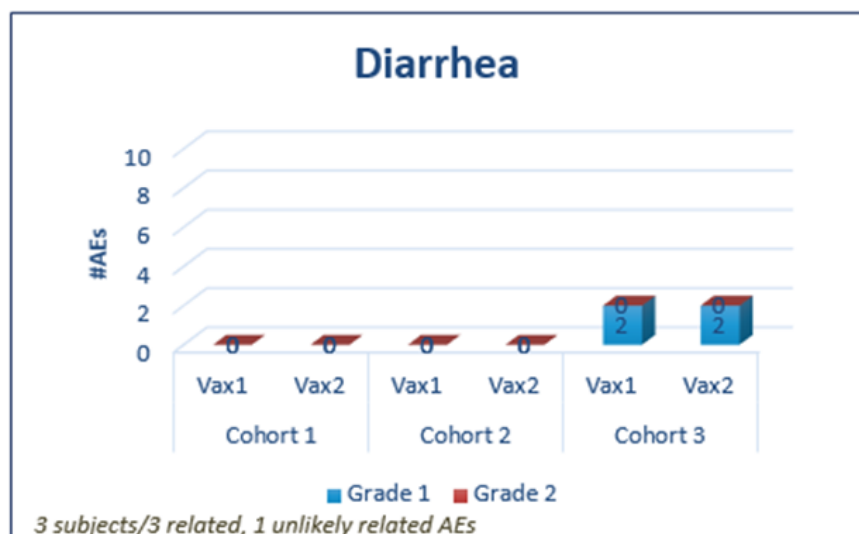
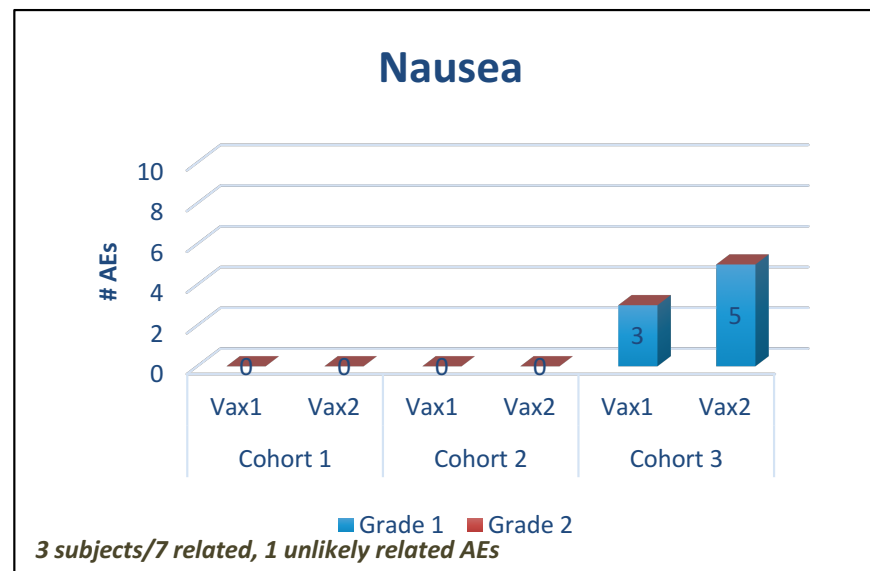
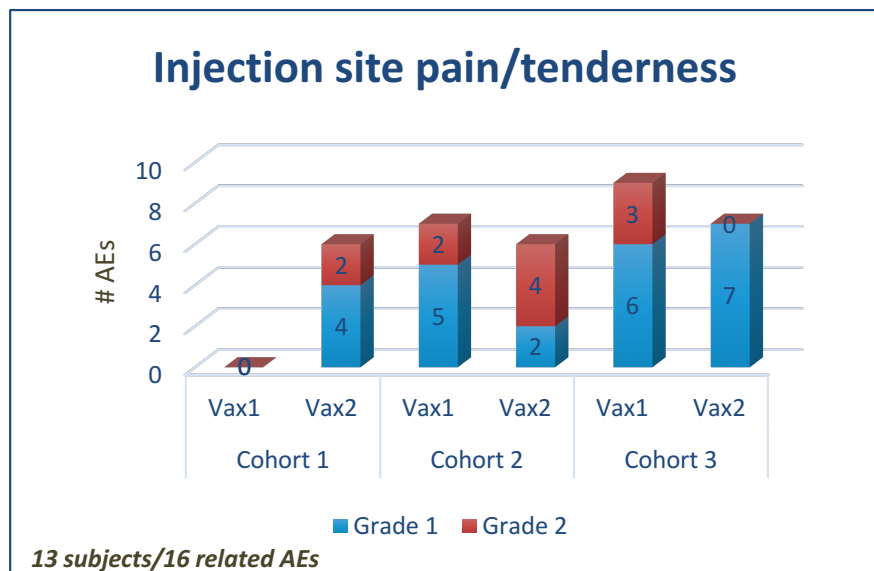
Phase: 1

Protocol Number: rVSV-EBOV-01

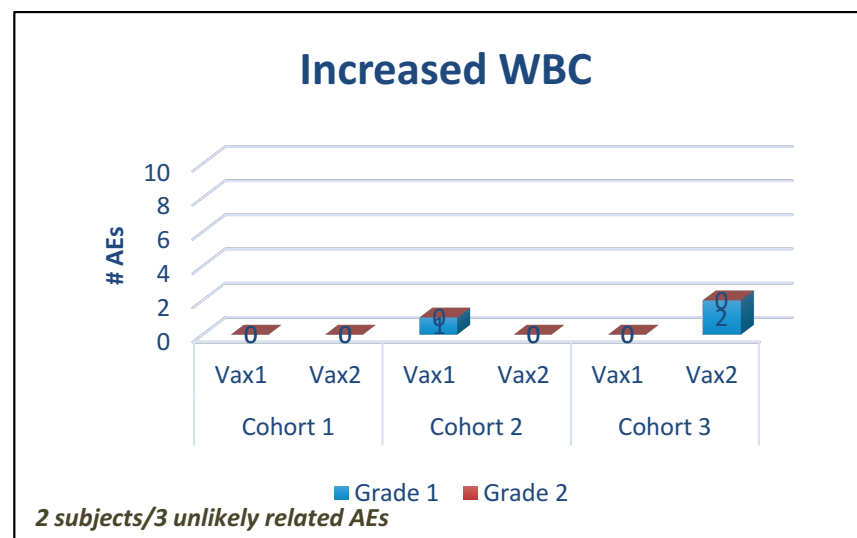
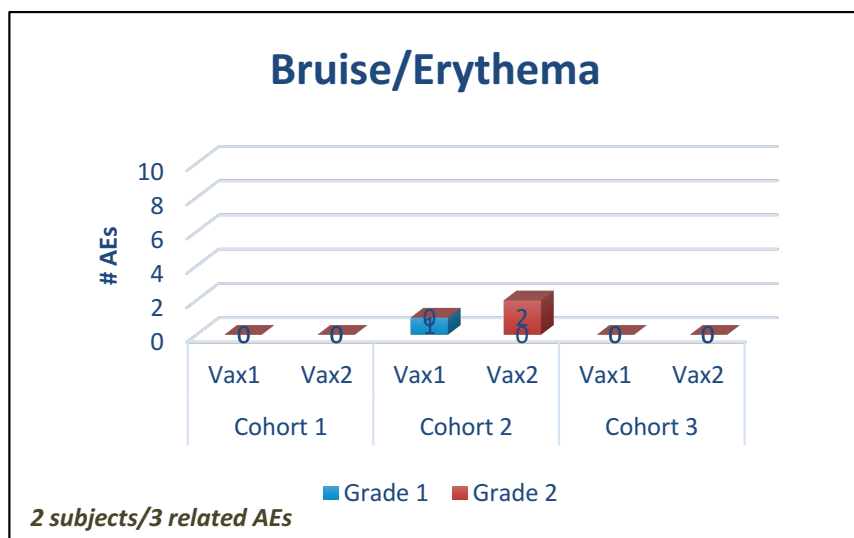
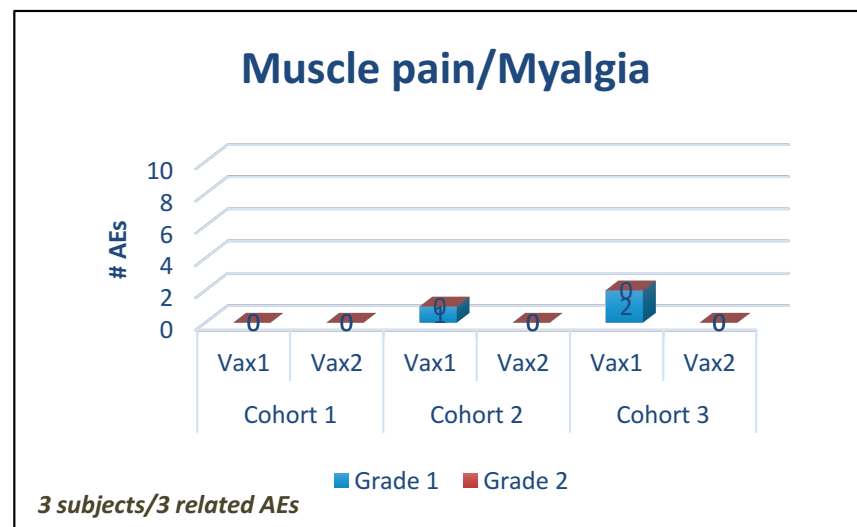
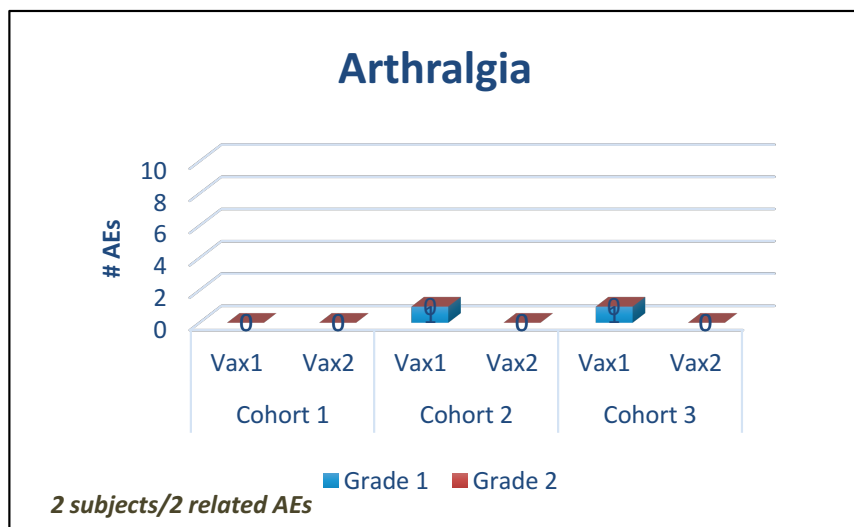
Protocol Number: rVSV-EBOV-01

Phase 1 Dose Escalation and Vaccination Schedule in Months (Days)				
Study Arm	N	Dose	Month 0 (Day 0)	Month 1 (Day 28)
Group 1	10	2.5 x 10 ⁴ PFU	rVSVN4CT1-EBOVGP1	rVSVN4CT1-EBOVGP1
	3	—	control (saline)	control (saline)
Group 2	10	2.5 x 10 ⁵ PFU	rVSVN4CT1-EBOVGP1	rVSVN4CT1-EBOVGP1
	3	—	control (saline)	control (saline)
Group 3	10	2.0 x 10 ⁶ PFU	rVSVN4CT1-EBOVGP1	rVSVN4CT1-EBOVGP1
	3	—	control (saline)	control (saline)
Total	39 (30 vaccine/9 placebo)			
<p>Notes: All immunizations will be administered IM in the deltoid; for Groups 1 and 2 each dose will be delivered bilaterally as 2 x 0.5 mL inoculations, and for Group 3 as 2 x 1.0 ml inoculations; CoA = Certificate of Analysis; PFU = plaques forming units.</p>				

Protocol Number: rVSV-EBOV-01: Adverse Events



Protocol Number: rVSV-EBOV-01: Adverse Events



Protocol Number: rVSV-EBOV-01

Detection of Disseminated Vaccine Virus (Blinded)

Sample Day	Blood		Urine		Saliva	
	PCR	Culture Confirmed ^b	PCR	Culture Confirmed	PCR	Culture Confirmed
0 (Prime)	0/39	NA	0/39	NA	0/39	NA
1	0/39	NA	0/39	NA	0/39	NA
3	0/39	NA	0/39	NA	0/39	NA
7	0/39	NA	0/39	NA	0/39	NA
14	0/39	NA	0/39	NA	0/39	NA
28 (Boost)	0/39	NA	0/39	NA	0/39	NA
29	0/38	NA	0/38	NA	0/38	NA
31	0/38	NA	0/38	NA	0/38	NA
35	0/38	NA	0/38	NA	0/38	NA
42	0/38	NA	0/38	NA	0/38	NA
56	0/38	NA	0/38	NA	0/38	NA

^a2.66 x 10³ copies/mL

^bLOD = 100 PFU



Protocol Number: rVSV-EBOV-01

**EBOV GP and rVSV N-specific cell-mediated immune (CMI) responses
measured in an IFN- γ ELISpot assay.**

Protocol Number: rVSV-EBOV-01

BLINDED EBOV GP and rVSV N-specific cell mediated immune (CMI) Responses by IFN-γ ELISpot assay.

Cohort #1: 2.5×10^4 PFU dose level

V2: baseline
 V5: 1wk post 1st vacc
 V6: 2wk post 1st vacc
 V7: 4wk post 1st vacc
 V10: 1wk post 2nd vacc
 V11: 2wk post 2nd vacc
 V12: 4wk post 2nd vacc
 V13: 22wk post 2nd vacc

Patient ID	Visit No.	Day	EBOV GP-specific IFNγ ELISpot Response	rVSV N-specific IFNγ ELISpot Responses
101-001	V2	0 + D1	12	15
	V5	7	0	13
	V6	14	17	0
	V7	28 + D2	2	7
	V10	35	7	0
	V11	42	13	8
	V12	56	0	0
101-002	V2	0 + D1	0	0
	V5	7	15	3
	V6	14	10	13
	V7	28 + D2	15	12
	V10	35	28	60
	V11	42	17	38
	V12	56	2	18
101-003	V2	0 + D1	0	0
	V5	7	22	22
	V6	14	15	28
	V7	28 + D2	0	0
	V10	35	0	13
	V11	42	132	70
	V12	56	2	10
101-004	V2	0 + D1	35	40
	V5	7	3	17
	V6	14	118	45
	V7	28 + D2	97	63
	V10	35	68	20
	V11	42	23	15
	V12	56	147	12
101-005	V2	0 + D1	15	5
	V5	7	7	18
	V6	14	8	7
	V7	28 + D2	297	533
	V10	35	255	438
	V11	42	200	347
	V12	56	217	380

Patient ID	Visit No.	Day	EBOV GP-specific IFNγ ELISpot Response	rVSV N-specific IFNγ ELISpot Responses
101-006	V2	0 + D1	13	12
	V5	7	0	10
	V6	14	48	25
	V7	28 + D2	340	292
	V10	35	338	392
	V11	42	392	287
	V12	56	245	252
101-007	V2	0 + D1	17	2
	V5	7	33	12
	V6	14	117	30
	V7	28 + D2	103	97
	V10	35	273	175
	V11	42	268	307
	V12	56	165	187
101-008	V2	0 + D1	40	27
	V5	7	50	38
	V6	14	130	178
	V7	28 + D2	22	10
	V10	35	130	150
	V11	42	90	85
	V12	56	45	110
101-009	V2	0 + D1	8	0
	V5	7	28	8
	V6	14	15	13
	V7	28 + D2	13	0
	V10	35	17	17
	V11	42	17	10
	V12	56	27	43

Patient ID	Visit No.	Day	EBOV GP-specific IFNγ ELISpot Response	rVSV N-specific IFNγ ELISpot Responses
101-010	V2	0 + D1	13	20
	V5	7	0	5
	V6	14	85	47
	V7	28 + D2	1228	227
	V10	35	1037	197
	V11	42	1533	333
	V12	56	1137	200
101-011	V2	0 + D1	0	7
	V5	7	0	7
	V6	14	13	13
	V7	28 + D2	32	20
	V10	35	0	0
	V11	42	22	17
	V12	56	2	7
101-012	V2	0 + D1	0	0
	V5	7	17	5
	V6	14	53	42
	V7	28 + D2	8	10
	V10	35	70	68
	V11	42	115	118
	V12	56	30	20
101-013	V2	0 + D1	0	3
	V5	7	2	17
	V6	14	18	17
	V7	28 + D2	55	28
	V10	35	57	55
	V11	42	38	10
	V12	56	7	27

Human ELISpot assay positivity criteria:

- ≥ Assay LOB (80 or 38 SFC/10⁶ PBMCs for EBOV GP or rVSV N respectively)
- ≥ baseline visit 2 response

Protocol Number: rVSV-EBOV-01

BLINDED EBOV GP and rVSV N-specific cell mediated immune (CMI) Responses by IFN-gamma ELISpot assay.

Cohort #2: 2.5×10^5 PFU dose level

V2: baseline
 V5: 1wk post 1st vacc
 V6: 2wk post 1st vacc
 V7: 4wk post 1st vacc
 V10: 1wk post 2nd vacc
 V11: 2wk post 2nd vacc
 V12: 4wk post 2nd vacc
 V13: 22wk post 2nd vacc

Patient ID	Visit No.	Day	EBOV GP-specific IFNg ELISpot Response	rVSV N-specific IFNg ELISpot Responses
101-016	V2	0 + D1	18	2
	V5	7	20	20
	V6	14	53	90
	V7	28 + D2	168	122
	V10	35	230	155
	V11	42	173	143
	V12	56	175	137
101-017	V2	0 + D1	0	10
	V5	7	0	30
	V6	14	3	20
	V7	28 + D2	8	18
	V10	35	5	10
	V11	42	20	25
	V12	56	2	25
101-018	V2	0 + D1	5	0
	V5	7	47	7
	V6	14	0	0
	V7	28 + D2	15	18
	V10	35	12	0
	V11	42	43	15
	V12	56	12	22
101-021	V2	0 + D1	28	23
	V5	7	0	0
	V6	14	43	48
	V7	28 + D2	88	137
	V10	35	138	203
	V11	42	60	108
	V12	56	48	52

Patient ID	Visit No.	Day	EBOV GP-specific IFNg ELISpot Response	rVSV N-specific IFNg ELISpot Responses
101-022	V2	0 + D1	5	0
	V5	7	2	0
	V6	14	152	42
	V7	28 + D2	110	163
	V10	35	223	208
	V11	42	117	125
	V12	56	123	117
101-023	V2	0 + D1	38	8
	V5	7	48	30
	V6	14	105	37
	V7	28 + D2	95	25
	V10	35	22	5
	V11	42	158	50
	V12	56	138	68
101-024	V2	0 + D1	35	20
	V5	7	20	0
	V6	14	38	22
	V7	28 + D2	72	60
	V10	35	47	70
	V11	42	2	0
	V12	56	23	18
101-025	V2	0 + D1	7	0
	V5	7	10	17
	V6	14	30	7
	V7	28 + D2	163	172
	V10	35	108	145
	V11	42	138	152
	V12	56	43	58

Patient ID	Visit No.	Day	EBOV GP-specific IFNg ELISpot Response	rVSV N-specific IFNg ELISpot Responses
101-026	V2	0 + D1	7	10
	V5	7	8	0
	V6	14	13	17
	V7	28 + D2	13	3
	V10	35	5	0
	V11	42	0	0
	V12	56	3	0
101-027	V2	0 + D1	0	7
	V5	7	33	53
	V6	14	363	265
	V7	28 + D2	333	325
	V10	35	5	0
	V11	42	162	165
	V12	56	218	238
101-029	V2	0 + D1	0	0
	V5	7	55	80
	V6	14	57	113
	V7	28 + D2	127	90
	V10	35	380	277
	V11	42	380	258
	V12	56	262	183
101-030	V2	0 + D1	45	37
	V5	7	115	33
	V6	14	38	17
	V7	28 + D2	237	95
	V10	35	172	78
	V11	42	148	75
	V12	56	148	87

Human ELISpot assay positivity criteria:

- \geq Assay LOB (80 or 38 SFC/ 10^6 PBMCs for EBOV GP or rVSV N respectively)
- \geq baseline visit 2 response

Protocol Number: rVSV-EBOV-01

BLINDED EBOV GP and rVSV N-specific cell mediated immune (CMI) Responses by IFN-gamma ELISpot assay.

Cohort #3: 2.0×10^6 PFU dose level

V2: baseline
 V5: 1wk post 1st vacc
 V6: 2wk post 1st vacc
 V7: 4wk post 1st vacc
 V10: 1wk post 2nd vacc
 V11: 2wk post 2nd vacc
 V12: 4wk post 2nd vacc
 V13: 22wk post 2nd vacc

Patient ID	Visit No.	Day	EBOV GP-specific IFNg ELISpot Response	rVSV N-specific IFNg ELISpot Responses
101-032	V2	0 + D1	27	22
	V5	7	32	28
	V6	14	73	67
	V7	28 + D2	93	70
	V10	35	65	135
	V11	42	103	185
	V12	56	118	162
	V13			
101-034	V2	0 + D1	0	18
	V5	7	0	17
	V6	14	5	57
	V7	28 + D2	18	13
	V10	35	0	0
	V11	42	8	0
	V12	56	7	0
	V13			
101-035	V2	0 + D1	5	0
	V5	7	0	2
	V6	14	135	173
	V7	28 + D2	52	60
	V10	35	132	163
	V11	42	110	130
	V12	56	80	142
	V13			
101-036	V2	0 + D1	17	0
	V5	7	78	10
	V6	14	37	33
	V7	28 + D2	75	48
	V10	35	90	185
	V11	42	120	148
	V12	56	80	122
	V13			
101-037	V2	0 + D1	20	10
	V5	7	18	0
	V6	14	28	33
	V7	28 + D2	143	277
	V10	35	63	118
	V11	42	112	192
	V12	56	127	183
	V13			

Patient ID	Visit No.	Day	EBOV GP-specific IFNg ELISpot Response	rVSV N-specific IFNg ELISpot Responses
101-038	V2	0 + D1	0	10
	V5	7	23	43
	V6	14	173	180
	V7	28 + D2	90	123
	V10	35	110	127
	V11	42	298	397
	V12	56	235	352
	V13			
101-039	V2	0 + D1	7	8
	V5	7	18	12
	V6	14	20	28
	V7	28 + D2	20	98
	V10	35	58	335
	V11	42	53	328
	V12	56	75	408
	V13			
101-042	V2	0 + D1	23	23
	V5	7	18	28
	V6	14	80	88
	V7	28 + D2	63	140
	V10	35	178	258
	V11	42	93	158
	V12	56	102	122
	V13			
101-043	V2	0 + D1	25	23
	V5	7	29	19
	V6	14	5	3
	V7	28 + D2	15	1
	V10	35	0	0
	V11	42	0	0
	V12	56	13	6
	V13			

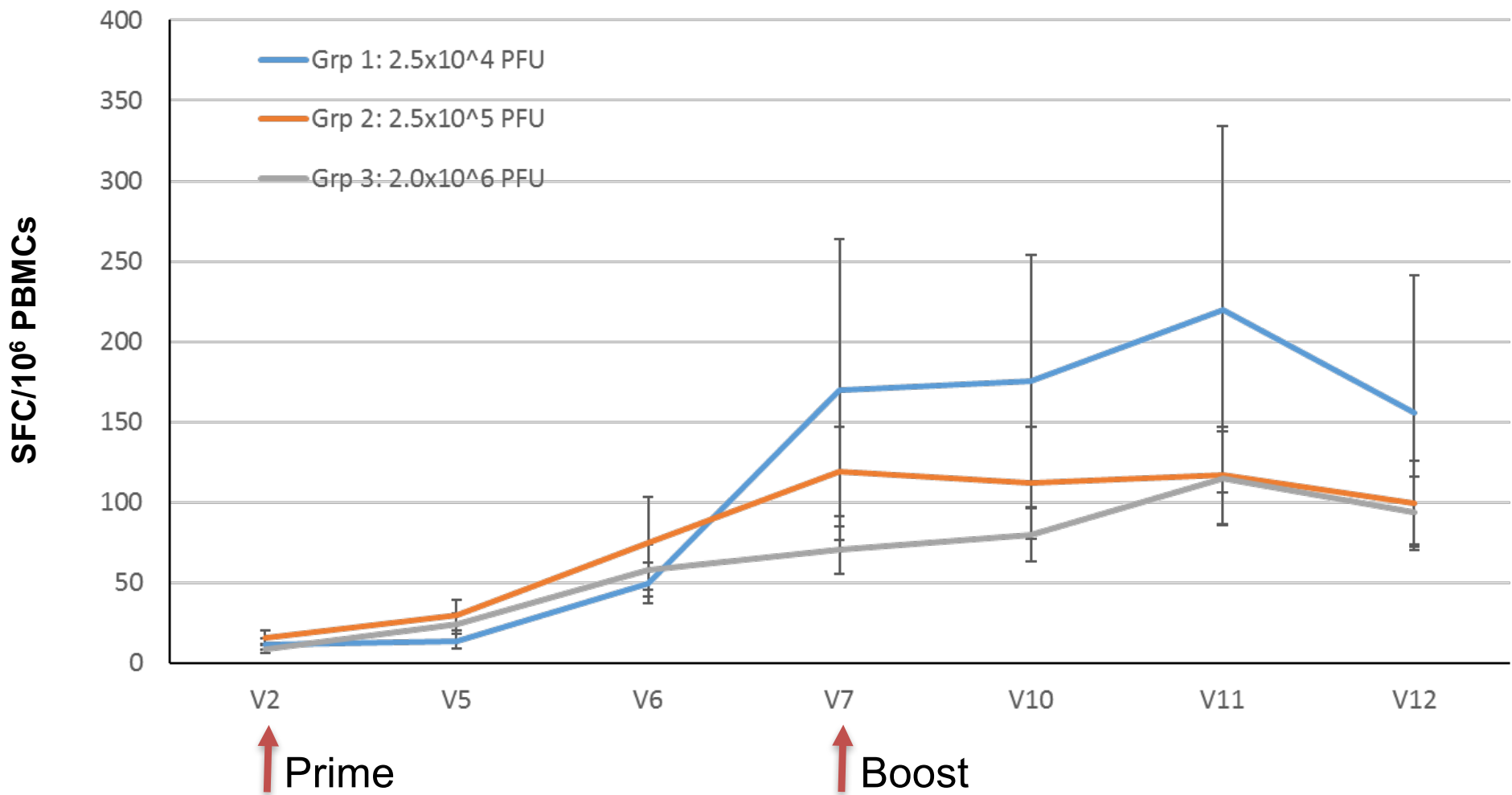
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101-044	V2	0 + D1	2	0
	V5	7	0	38
	V6	14	12	12
	V7	28 + D2	12	7
	V10	35	0	0
	V11	42	7	0
	V12	56	8	17
	V13			
101-045	V2	0 + D1	7	0
	V5	7	48	42
	V6	14	108	105
	V7	28 + D2	112	138
	V10	35	137	125
	V11	42	328	442
	V12	56	255	412
	V13			
101-046	V2	0 + D1	0	25
	V5	7	35	27
	V6	14	88	20
	V7	28 + D2	177	43
	V10	35	77	25
	V11	42	163	67
	V12	56	80	32
	V13			
101-049	V2	0 + D1	0	0
	V5	7	27	18
	V6	14	1	13
	V7	28 + D2	68	188
	V10	35	112	320
	V11	42	85	192
	V12	56	68	202
	V13			

Human ELISpot assay positivity criteria:

- \geq Assay LOB (80 or 38 SFC/10⁶ PBMCs for EBOV GP or rVSV N respectively)
- \geq baseline visit 2 response

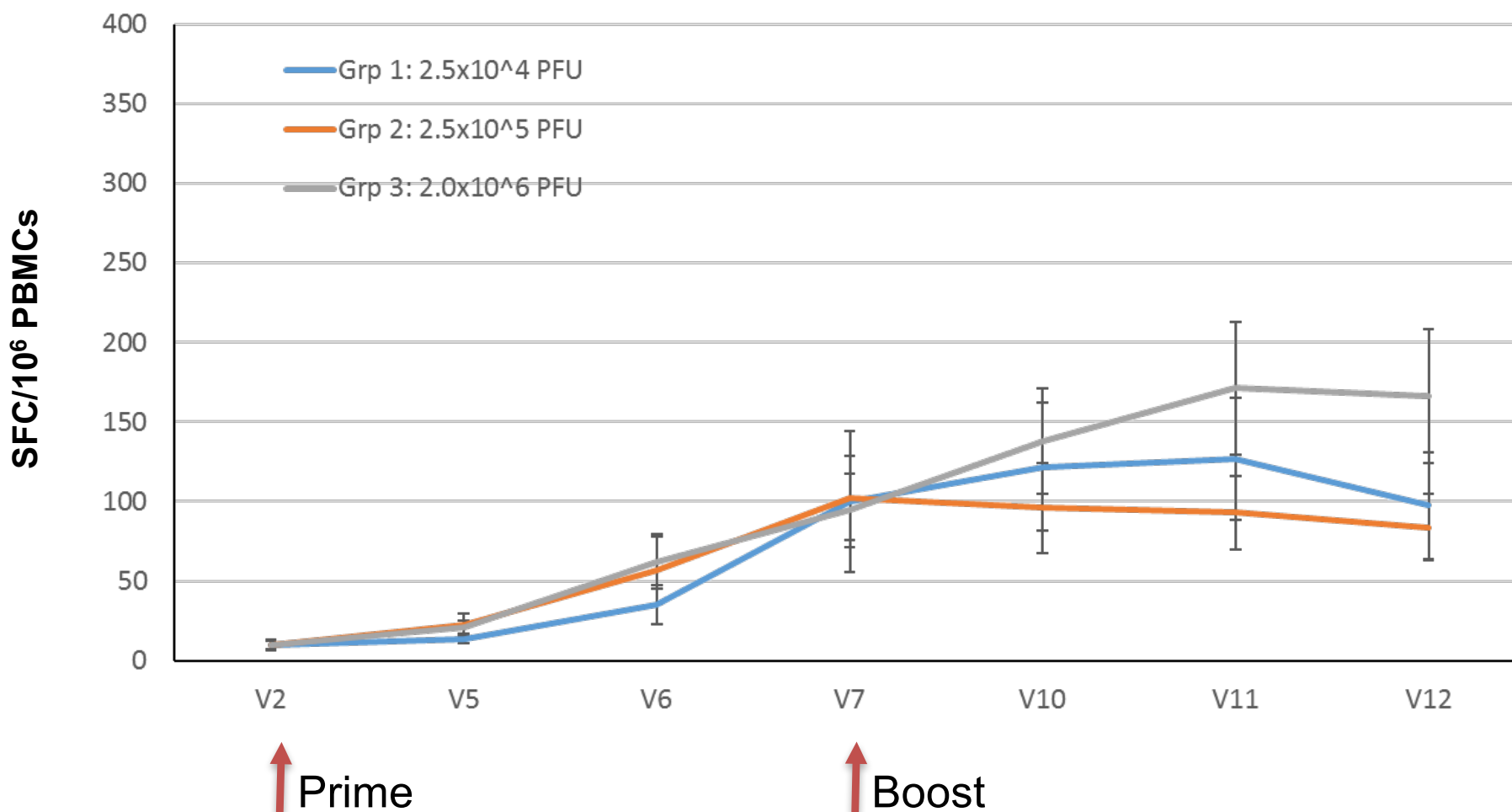
Protocol Number: rVSV-EBOV-01

BLINDED EBOV GP-specific cell mediated immune (CMI) responses by IFN-gamma ELISpot assay over time



Protocol Number: rVSV-EBOV-01

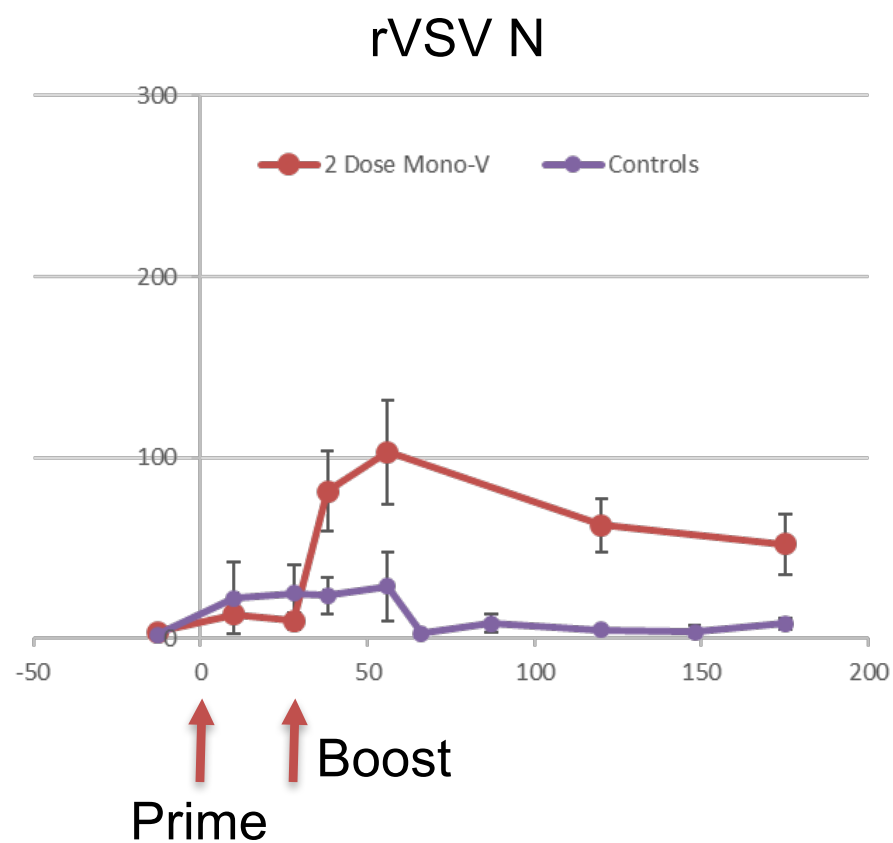
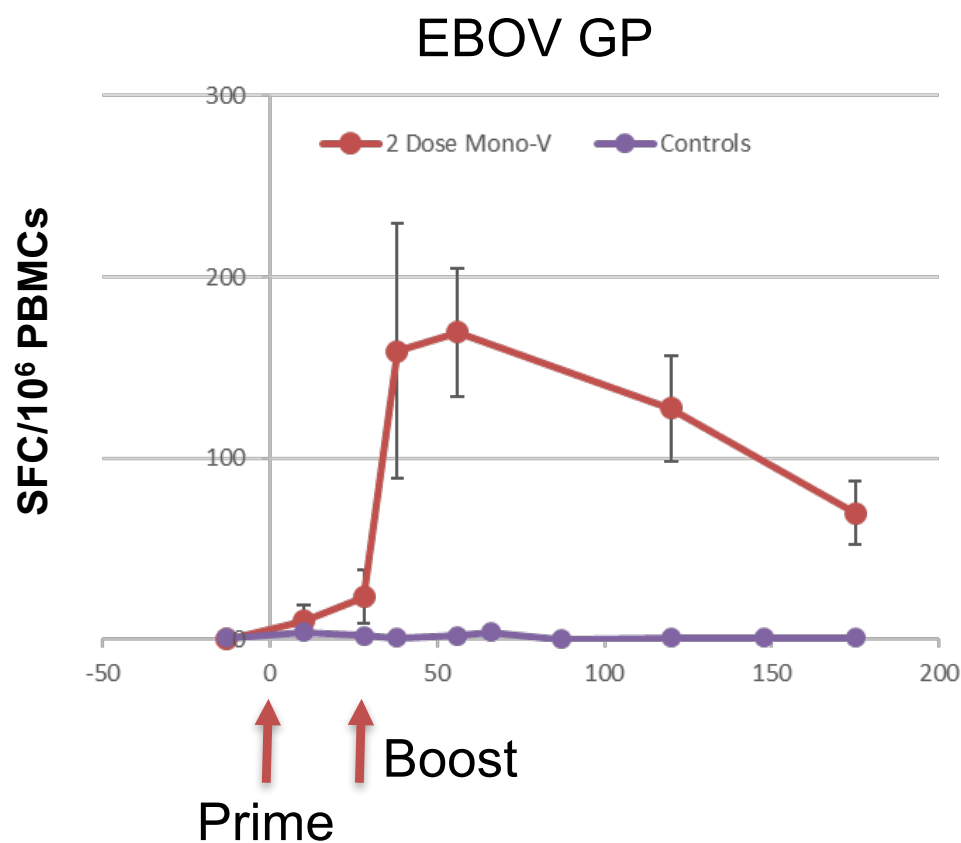
BLINDED rVSV N-specific cell mediated immune (CMI) responses by IFN-gamma ELISpot assay over time



Battelle Study 05400:

Magnitude of the EBOV GP and rVSV N-specific cell mediated immune (CMI) responses in NHP by the IFN- γ ELISpot assay.

Grp 3: 1.0×10^7 PFU dose level (PBS potency assay)





Protocol Number: rVSV-EBOV-01

EBOV GP-specific ELISA analysis conducted by Battelle

Serum was collected at the following time points for ELISA analysis:

- Visit 2:** Day of 1st vaccination
- Visit 5:** 1 week post 1st vaccination
- Visit 6:** 2 weeks post 1st vaccination
- Visit 7:** Day of 2nd vaccination
- Visit 10:** 1 week post 2nd vaccination
- Visit 11:** 2 weeks post 2nd vaccination
- Visit 12:** 4 weeks post 2nd vaccination
- Visit 13:** 22 weeks post 2nd vaccination

Protocol Number: rVSV-EBOV-01

EBOV GP-specific ELISA responses

Cohort #1: 2.5×10^4 PFU dose level

V2: baseline

V5: 1wk post 1st vacc

V6: 2wk post 1st vacc

V7: 4wk post 1st vacc

V10: 1wk post 2nd vacc

V11: 2wk post 2nd vacc

V12: 4wk post 2nd vacc

V13: 22wk post 2nd vacc

SAMPLE ID	Zaire (ELISA Units/mL)						
	Visit 2	Visit 5	Visit 6	Visit 7	Visit 10	Visit 11	Visit 12
101-001	0	0	0	0	0	0	0
101-002	0	0	0	101	297	359	224
101-003	0	0	0	0	0	0	0
101-004	0	0	0	94	1,151	1,368	989
101-005	0	0	0	77	835	1,156	912
101-006	0	0	0	336	1,235	1,222	1,582
101-007	0	0	0	0	843	1,449	754
101-008	0	0	0	235	1,067	2,425	1,677
101-009	0	0	0	0	2,012	1,937	647
101-010	0	0	0	651	1,785	2,503	3,125
101-011	0	0	0	0	0	0	0
101-012	0	0	55	206	2,386	3,163	1,536
101-013	0	0	0	0	217	447	415

AVG	0	0	4	131	910	1,233	912
SE	0	0	4	53	222	292	249

Protocol Number: rVSV-EBOV-01

EBOV GP-specific ELISA responses

Cohort #2: 2.5×10^5 PFU dose level

V2: baseline

V5: 1wk post 1st vacc

V6: 2wk post 1st vacc

V7: 4wk post 1st vacc

V10: 1wk post 2nd vacc

V11: 2wk post 2nd vacc

V12: 4wk post 2nd vacc

V13: 22wk post 2nd vacc

Zaire (ELISA Units/mL)							
SAMPLE ID	Visit 2	Visit 5	Visit 6	Visit 7	Visit 10	Visit 11	Visit 12
101-015	0	0	0	120	---	---	---
101-016	0	0	0	286	677	1,002	634
101-017	0	0	0	0	0	0	0
101-018	0	0	0	0	0	0	0
101-021	0	0	0	172	1,712	2,726	2,156
101-022	0	0	0	156	1,929	3,897	2,053
101-023	72	90	163	274	2,490	3,833	1,800
101-024	72	90	163	274	2,490	3,833	1,800
101-025	0	0	0	0	136	246	276
101-026	0	0	0	0	0	0	0
101-027	0	0	197	1,294	7,728	5,015	3,718
101-029	0	0	0	474	2,793	4,612	2,869
101-030	0	0	0	330	842	1,090	664

AVG	11	14	40	260	1,733	2,188	1,331
SE	7	9	21	96	601	550	345

Protocol Number: rVSV-EBOV-01

EBOV GP-specific ELISA responses

Cohort #3: 2.0x10⁶ PFU dose level

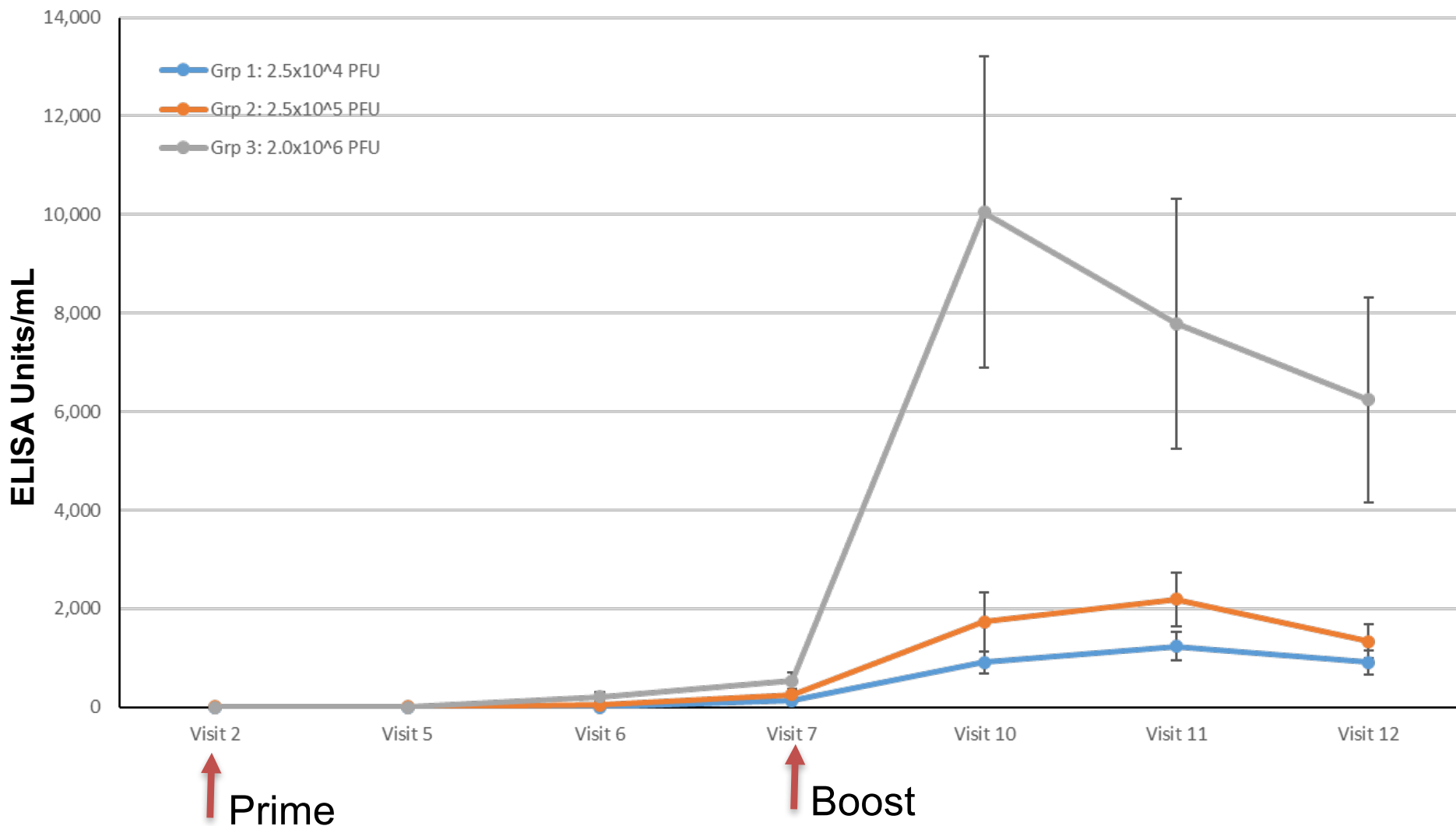
V2: baseline
V5: 1wk post 1st vacc
V6: 2wk post 1st vacc
V7: 4wk post 1st vacc
V10: 1wk post 2nd vacc
V11: 2wk post 2nd vacc
V12: 4wk post 2nd vacc
V13: 22wk post 2nd vac

Zaire (ELISA Units/mL)							
SAMPLE ID	Visit 2	Visit 5	Visit 6	Visit 7	Visit 10	Visit 11	Visit 12
101-032	0	0	75	159	2,900	5,874	5,918
101-034	0	0	0	0	0	0	0
101-035	0	0	220	594	23,406	6,059	4,414
101-036	0	0	141	391	8,953	34,706	15,424
101-037	0	0	82	317	2,382	4,543	1,953
101-038	0	0	65	152	3,284	2,464	2,046
101-039	0	0	1,225	1,366	14,571	6,983	6,354
101-042	0	0	0	156	2,707	5,911	2,959
101-043	0	0	0	0	0	0	0
101-044	0	0	0	0	0	0	0
101-045	0	0	457	971	31,027	11,182	26,349
101-046	0	0	380	1,268	30,173	13,304	10,085
101-049	0	0	146	1,614	11,170	10,175	5,596

AVG	0	0	215	538	10,044	7,785	6,238
SE	0	0	93	159	3,161	2,537	2,074

Protocol Number: rVSV-EBOV-01

BLINDED Mean EBOV GP-specific ELISA responses over time



Safety and Immunogenicity of Novel Adenovirus Type 26- and Modified Vaccinia Ankara-Vectored Ebola Vaccines A Randomized Clinical Trial

Iain D. Milligan, MRCP; Malick M. Gibani, MRCP; Richard Sewell, BA; Elizabeth A. Clutterbuck, PhD; Danielle Campbell, BScN; Emma Pilested; Elizabeth Nuthall, BSc; Merryn Voysey, MBIostat; Laura Silva-Reyes, MSc; M. Juliana McElrath, MD, PhD; Stephen C. De Rosa, MD; Nicole Frahm, PhD; Kristen W. Cohen, PhD; Georgi Shukarev, MD; Nicola Orzabal, BSc; Wilbert van Duijnhoven, MSc; Carla Truysers, PhD; Nora Bachmayer, PhD; Daniel Splinter, PhD; Nathaly Samy, MD; Maria Grazia Pau, PhD; Hanneke Schuitemaker, PhD; Kerstin Luhn, PhD; Benoit Calendret, PhD; Johan Van Hoof, MD; Macaya Dougouh, MD, MPH; Katie Ewer, PhD; Brian Angus, MD; Andrew J. Pollard, FRCPCH, PhD; Matthew D. Snape, FRCPCH, MD

JAMA. 2016; 315(15):1610-1623. doi:10.1001/jama.2016.4218

Total IgG responses against Ebola glycoprotein were assessed by enzyme-linked immunosorbent assay (ELISA) at Battelle Biomedical Research Center. Purified recombinant glycoprotein from the Ebola virus Kikwit variant provided by the Joint Vaccine Acquisition Program was immobilized on a 96-well microtiter plate. Test samples were serially diluted and Ebola-specific antibodies were detected with antihuman IgG antibodies conjugated with horseradish peroxidase followed by a colorimetric reaction.

Table 3. Ebola Glycoprotein-Specific Antibody Responses Detected by ELISA^a

	Prime on Day 1, Boost on Day 29		
	MVA-BN-Filo, Then Ad26.ZEBOV	Ad26.ZEBOV, Then MVA-BN-Filo	Placebo
Day 50			
No. of participants	15	15	6
Geometric mean concentration (95% CI), ELISA units/mL	10 573.1 (6451.8-17 326.8)	4274.0 (2349.6-7774.7)	23.3 (12.5-43.1)
Responders, No. (%) ^b	15 (100)	15 (100)	1 (16.7)
95% CI	78.2-100	78.2-100	0.4-64.1

In the mono-V EBOV clinical study, Grp 3 (2.0x10⁶ PFU) had a peak mean ELISA responses of **13,057** ELISA units/mL



Protocol Number: rVSV-EBOV-01

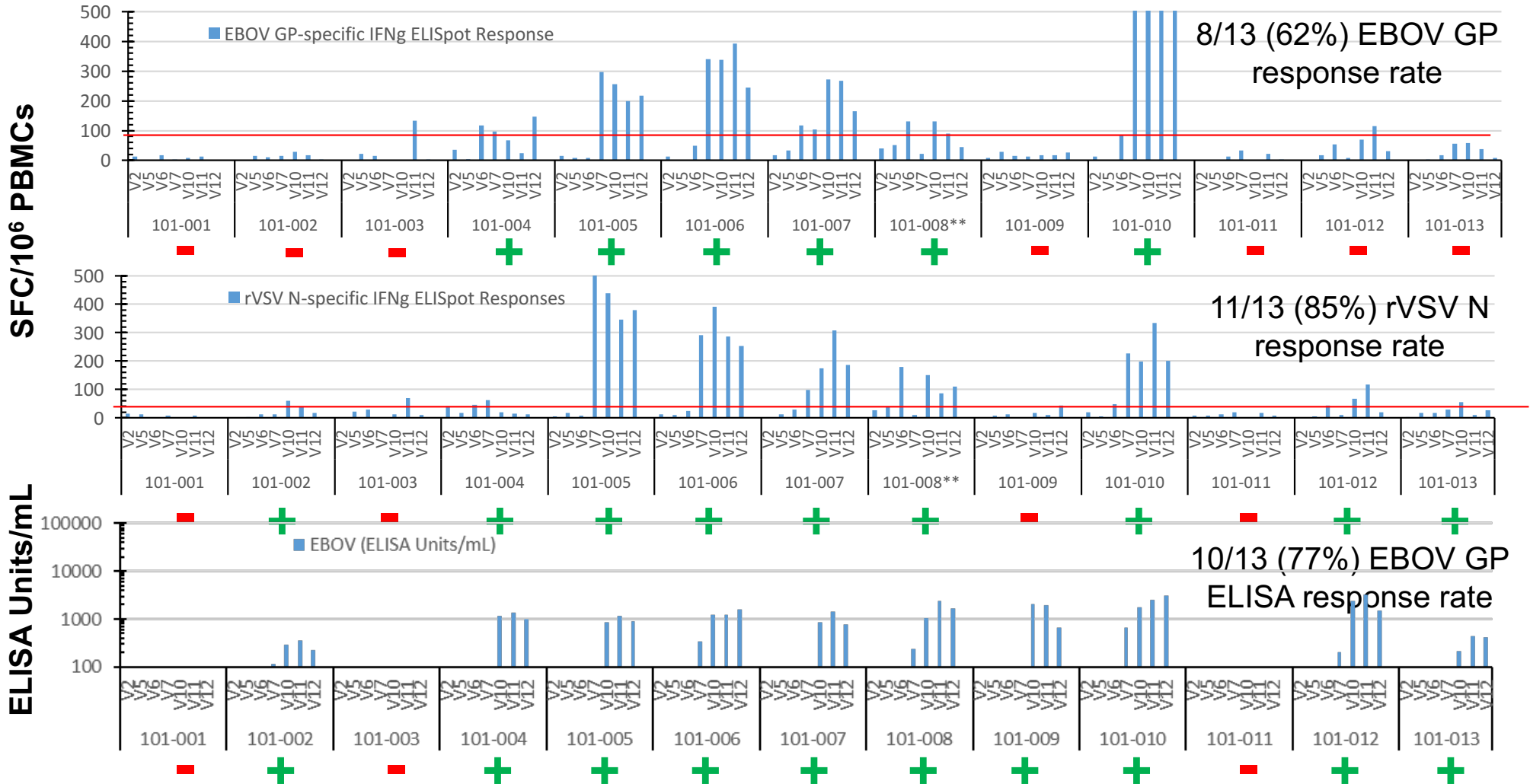
Alignment of ELISpot and ELISA Responses

Protocol Number: rVSV-EBOV-01

EBOV GP and rVSV N-specific cell mediated immune (CMI) responses by IFN-gamma ELISpot assay.

Cohort #1: 2.5×10^4 PFU dose level

V2: baseline
 V5: 1wk post 1st vacc
 V6: 2wk post 1st vacc
 V7: 4wk post 1st vacc
 V10: 1wk post 2nd vacc
 V11: 2wk post 2nd vacc
 V12: 4wk post 2nd vacc
 V13: 22wk post 2nd vacc

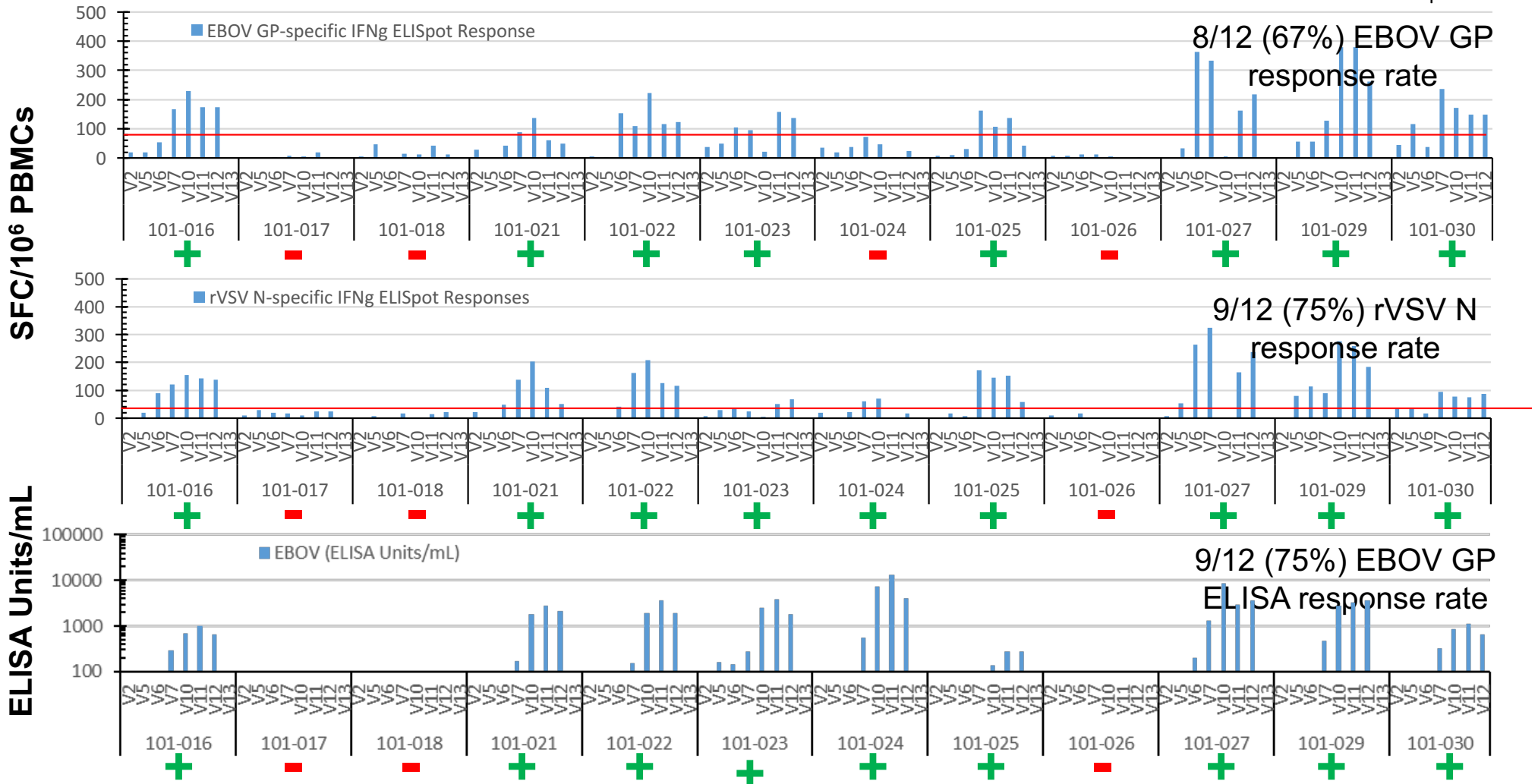


Protocol Number: rVSV-EBOV-01

EBOV GP and rVSV N-specific cell mediated immune (CMI) responses by IFN-gamma ELISpot assay.

Cohort #2: 2.5×10^5 PFU dose level

- V2: baseline
- V5: 1wk post 1st vacc
- V6: 2wk post 1st vacc
- V7: 4wk post 1st vacc
- V10: 1wk post 2nd vacc
- V11: 2wk post 2nd vacc
- V12: 4wk post 2nd vacc
- V13: 22wk post 2nd vac



Protocol Number: rVSV-EBOV-01

EBOV GP and rVSV N-specific cell mediated immune (CMI) responses by IFN-gamma ELISpot assay.

Cohort #3: 2.0×10^6 PFU dose level

- V2: baseline
- V5: 1wk post 1st vacc
- V6: 2wk post 1st vacc
- V7: 4wk post 1st vacc
- V10: 1wk post 2nd vacc
- V11: 2wk post 2nd vacc
- V12: 4wk post 2nd vacc
- V13: 22wk post 2nd vac





Filovirus Vaccines: Summary and Plans

- **rVSV-EBOV-01**

- **Safe and well-tolerated at all tested doses**

- No vaccine-related AEs greater than grade 2
 - 13/39 reported mild to moderate injection site tenderness
 - No other AEs reported in more than 5/39 subjects
 - 1 blood sample PCR positive, culture negative
 - PCR and culture of urine, universally negative

- **Immunogenic at all tested doses and blinded data consistent with:**

- CMI responses by INF- γ ELISpot
 - Response rates of 60-80% post dose 1 and 80-90% post dose 2
 - Antibody responses by ELISA
 - Response rates of 70-100% post dose 1 and 100% post dose 2

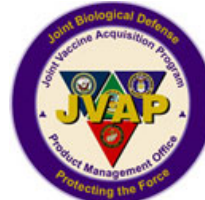
- **Work in-progress and Plans**

- rVSV-EBOV and rVSV-MARV lyophilized with ~75% retention of potency
 - rVSV-SUDV lyophilization development in progress
 - rVSV-MARV-01 planned start 15-Jan-2017

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