Ebola candidate vaccines: Overview of their development

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World Health Organization

information that will be presented

- ☑ Type of vaccine platforms
- ☑ Current level of clinical development
- ☑ Key vaccines attributes
  - Number of doses
  - Targeted viral species

- ☒ Detailed immunogenicity information
- ☒ Safety data profile
- ☒ Specifics of individual candidates regulatory pathways

WHO Target Product Profiles

Ebola Virus Disease (EVD) Vaccine Target Product Profile (Jan 2016)

Reactive/emergency use in the face of an outbreak to prevent EVD in vaccinated individuals as well as interrupt chains of virus transmission to terminate outbreaks.

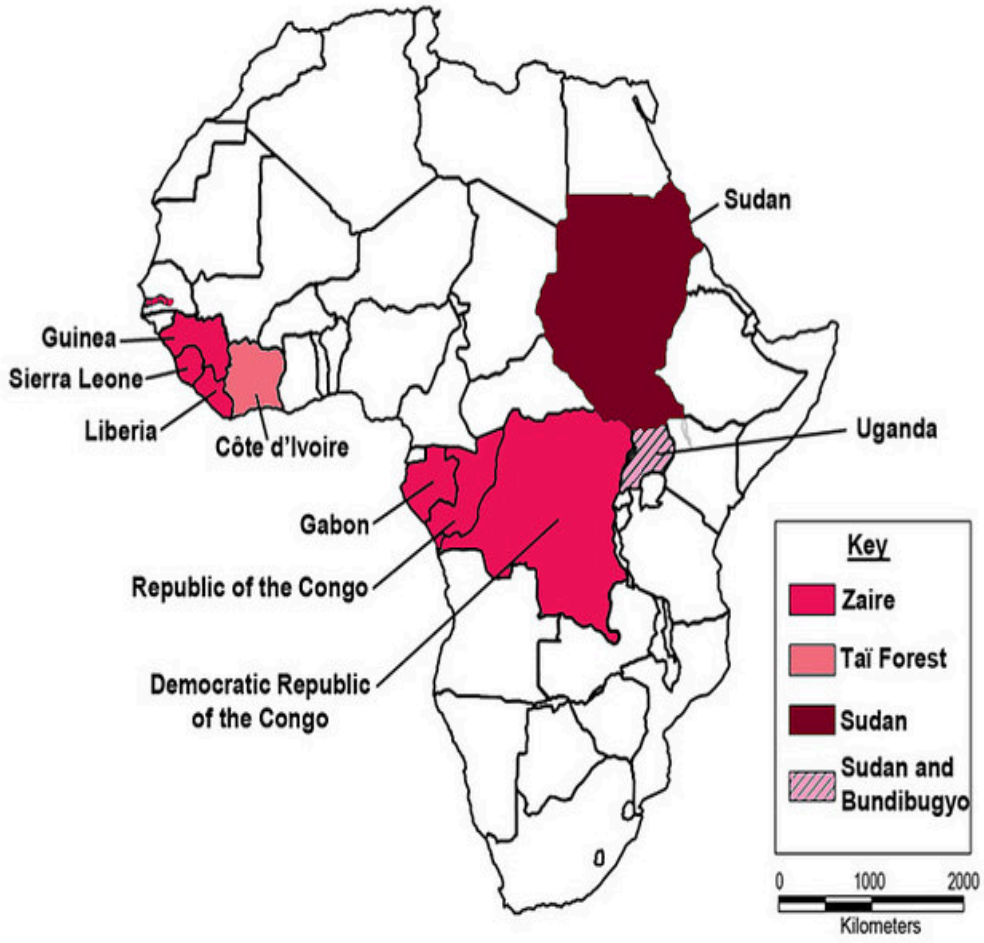
Prophylactic use to protect frontline workers (including healthcare workers, deploying international workers and others at particularly high risk of EVD due to their profession

Multivalent filovirus vaccines: (Nov 2016)

Prophylactic use to protect high-risk groups whether before or during an outbreak.

This target group comprises healthcare workers (HCW) ,frontline workers (FLW) and others at occupational risk, including potentially deployed international workers essential to assist in future outbreaks.

Marburgviruses and ebolaviruses are filoviruses



Family *Filoviridae*

Genus *Marburgvirus*

Species *Marburg marburgvirus*

Virus 1: Marburg virus (MARV)

Virus 2: Ravn virus (RAVV)

Genus *Ebolavirus*

Species *Taï Forest ebolavirus*

Virus: Taï Forest virus (TAFV)

Species *Reston ebolavirus*

Virus: Reston virus (RESTV)

Species *Sudan ebolavirus*

Virus: Sudan virus (SUDV)

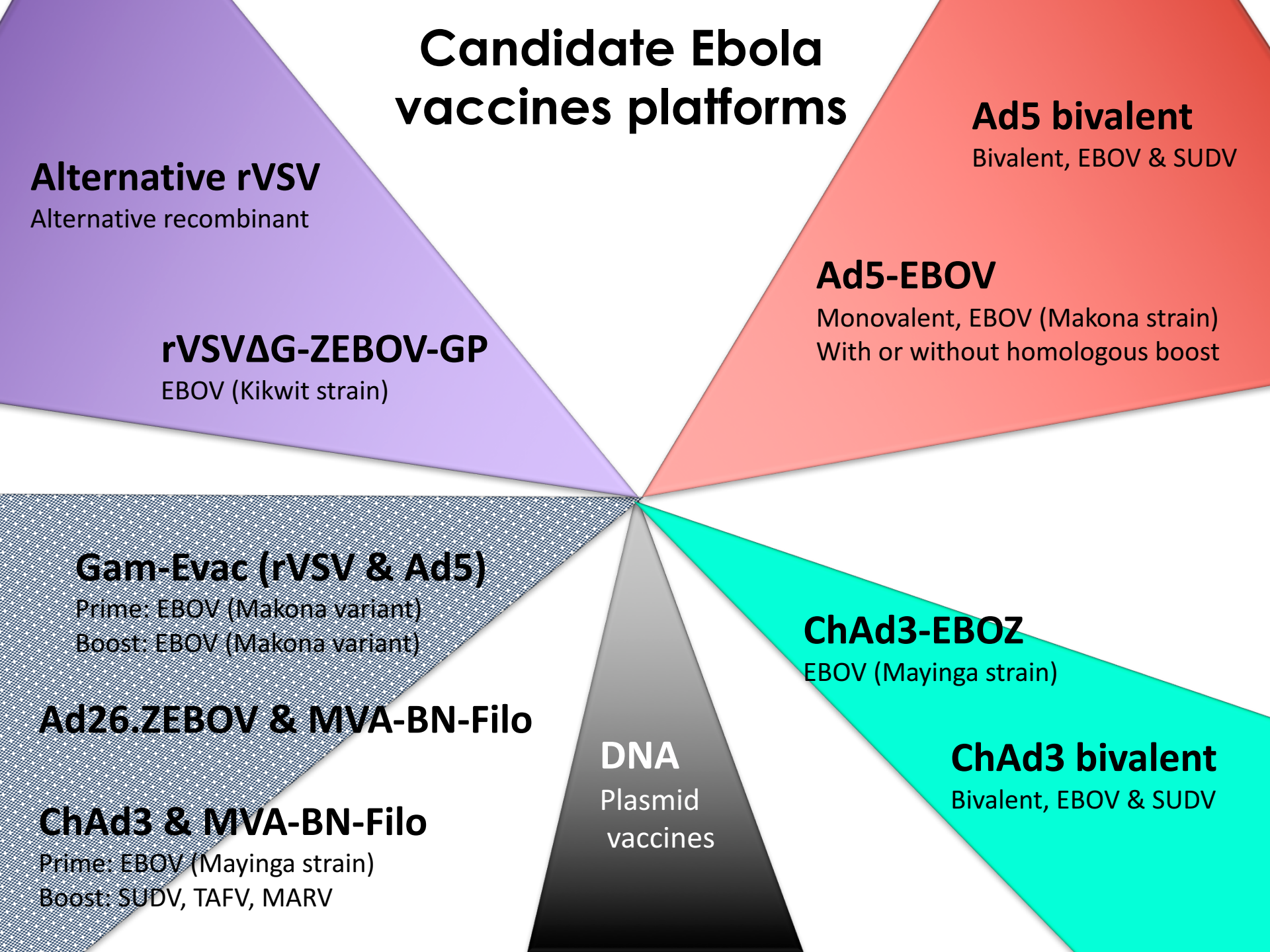
Species *Zaire ebolavirus*

Virus: Ebola virus (EBOV)

Species *Bundibugyo ebolavirus*

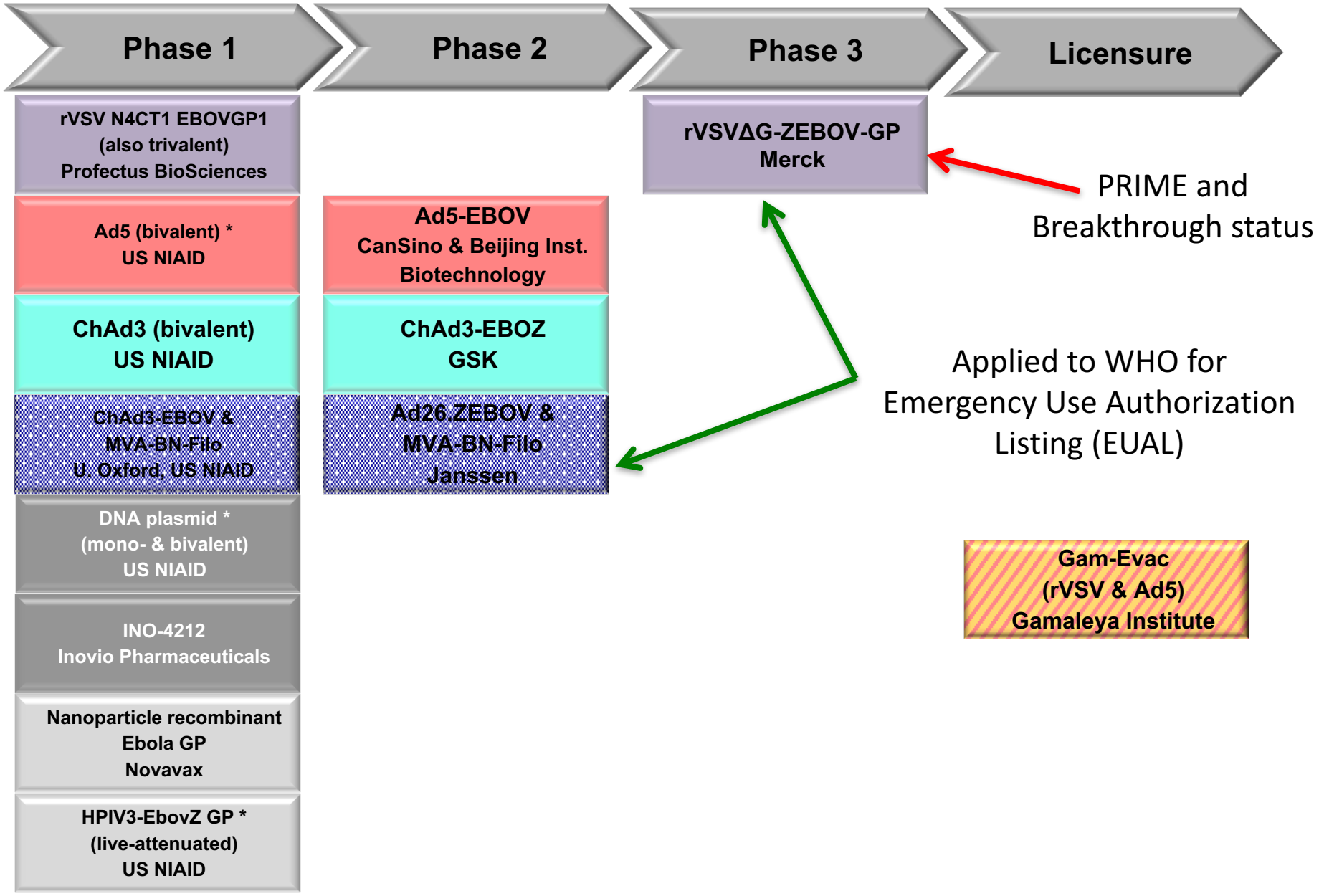
Virus: Bundibugyo virus (BDBV)

Candidate Ebola vaccines platforms



Candidate Ebola vaccines in clinical development

(as of April 2017)



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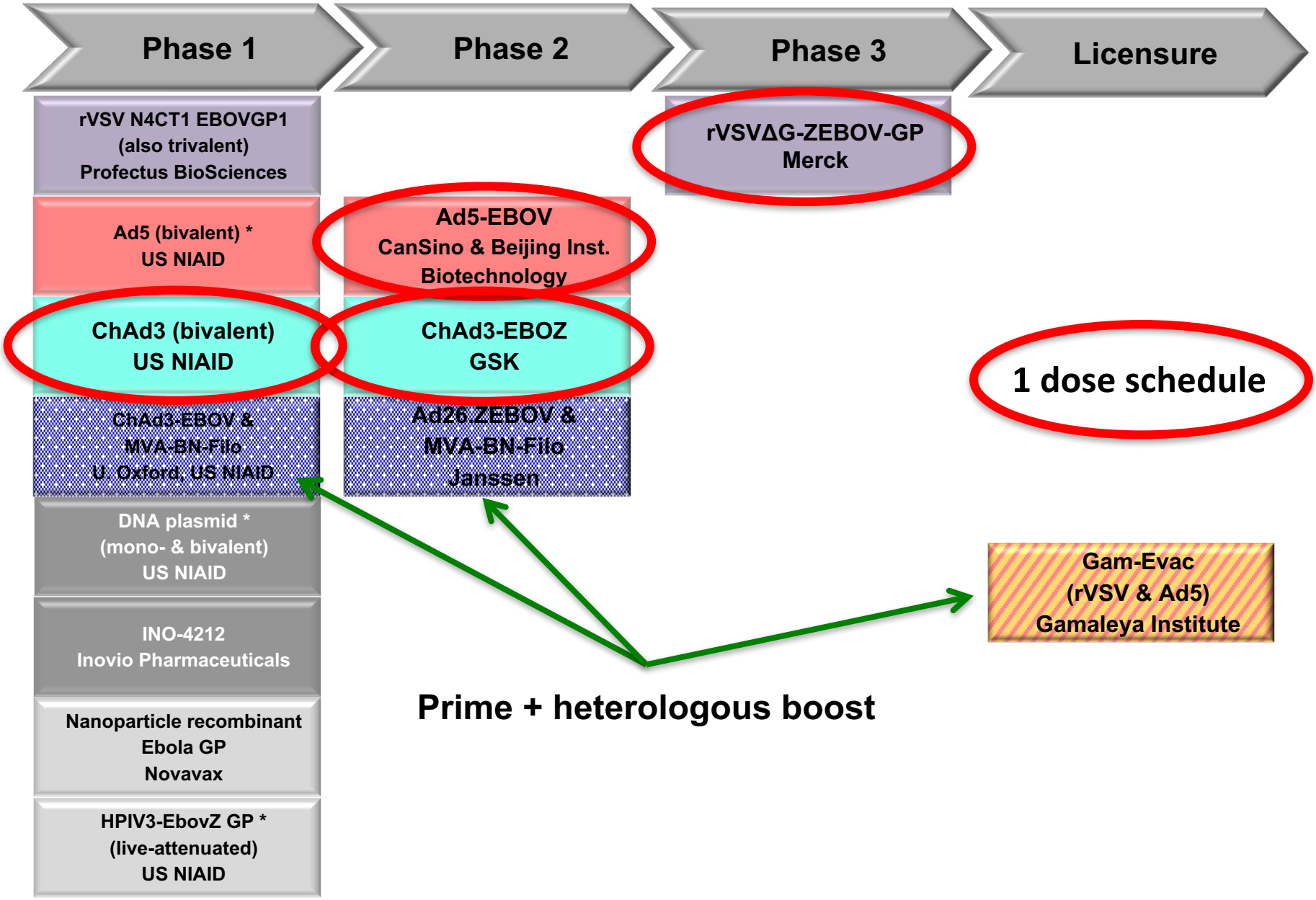

Candidate Ebola vaccines in clinical development

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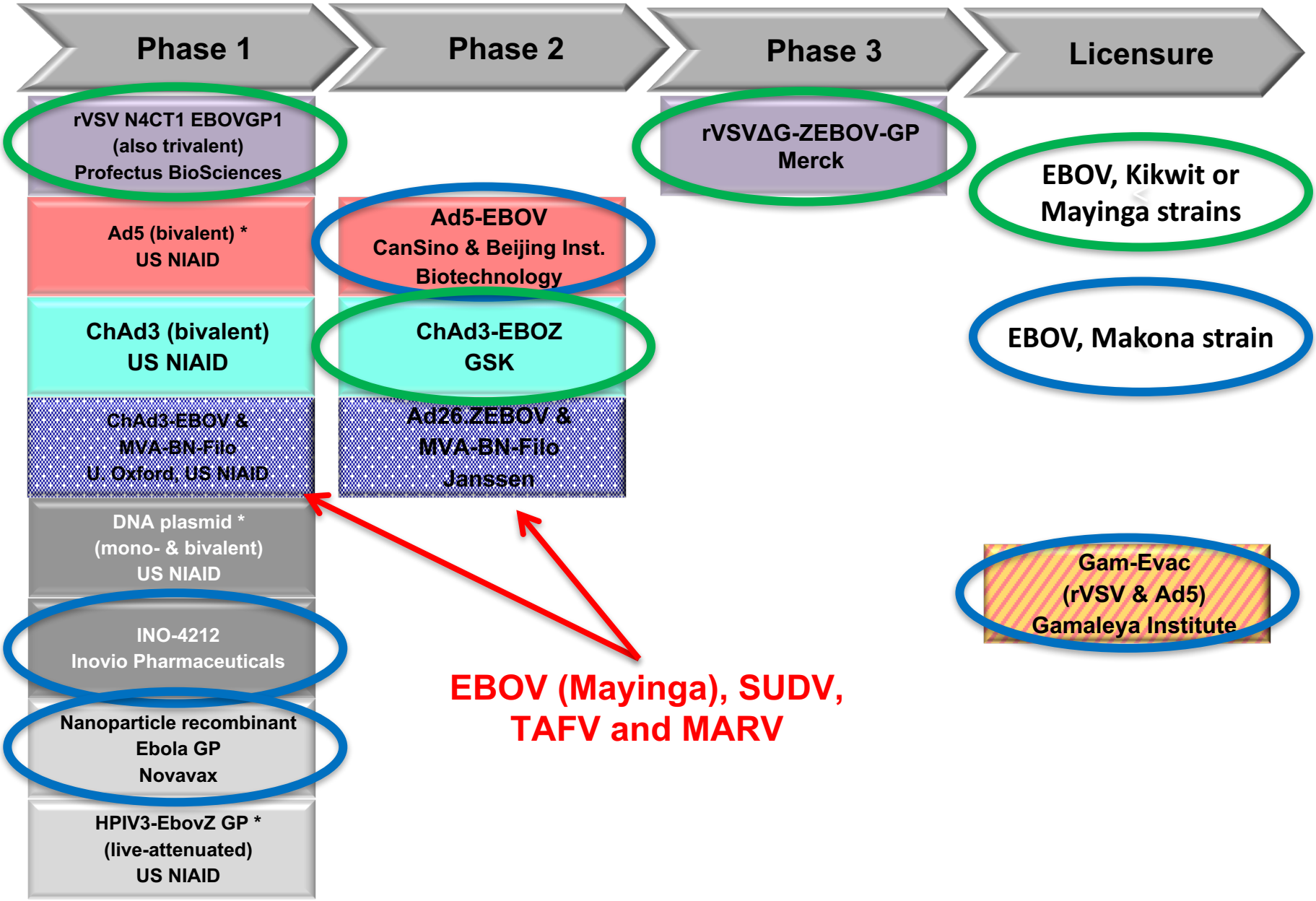


Ad5 expressing envelope GP of Zaire Ebola virus species (Makona variant, monovalent) with or without homologous boost

One Phase 1 study (China) and one Phase 2 study (Sierra Leone).

Glycoprotein (GP) specific antibody titres were significantly increased at Days 14 and Days 28 post vaccination in lower and higher dose vaccine groups.

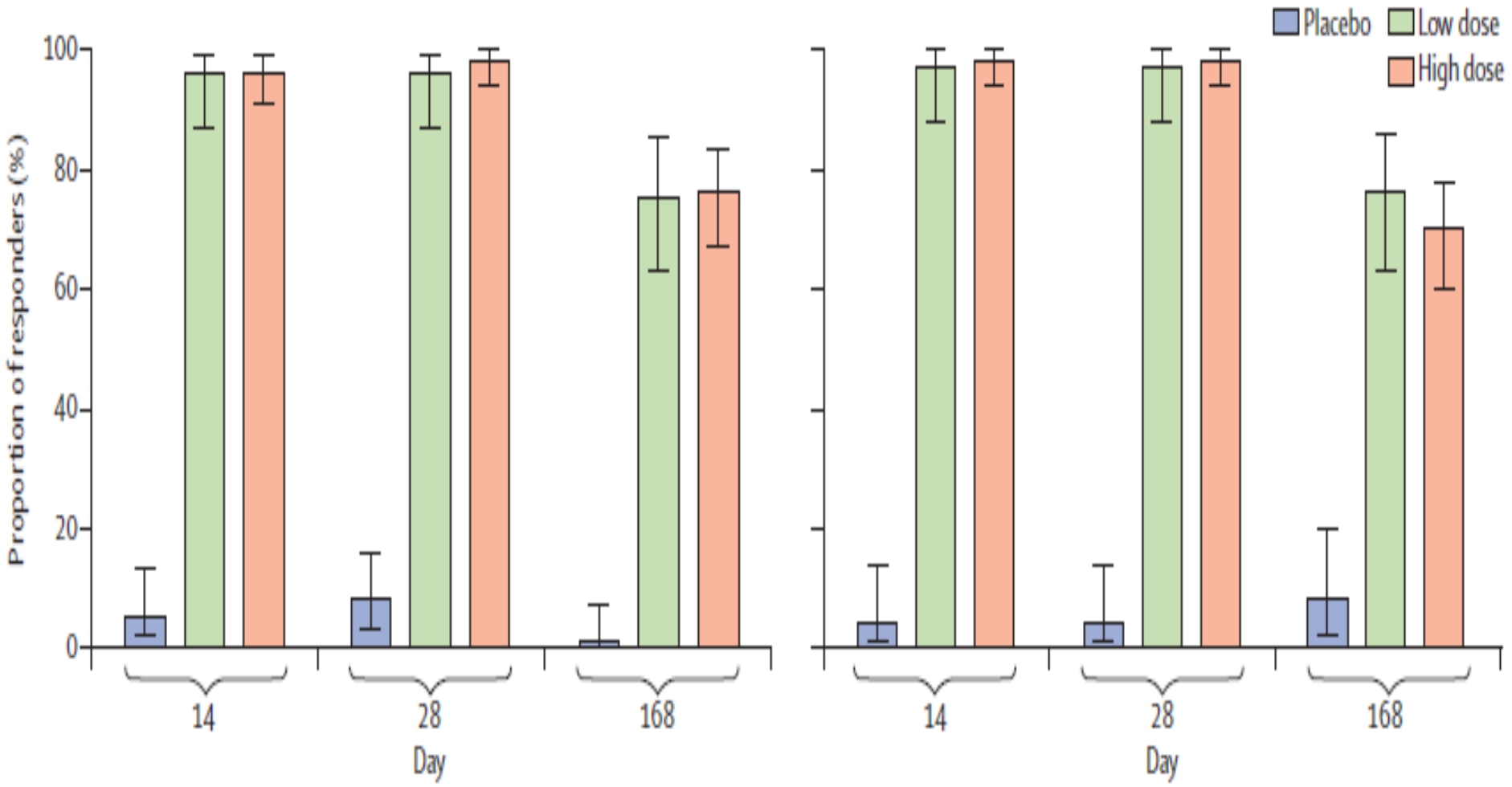
At lower dose, immunogenicity seemed more vulnerable to pre-existing Ad5 immunity.

Boosting provided greater antibody response, possibly with longer duration.

Ad5-EBOV immunogenicity in Phase 2 trial, Sierra Leone

Titres of adenovirus type-5 neutralising antibodies at baseline

Low titre (≤1:200) **High titre (>1:200)**



Zhu et al., Lancet 2016, 389:621–628

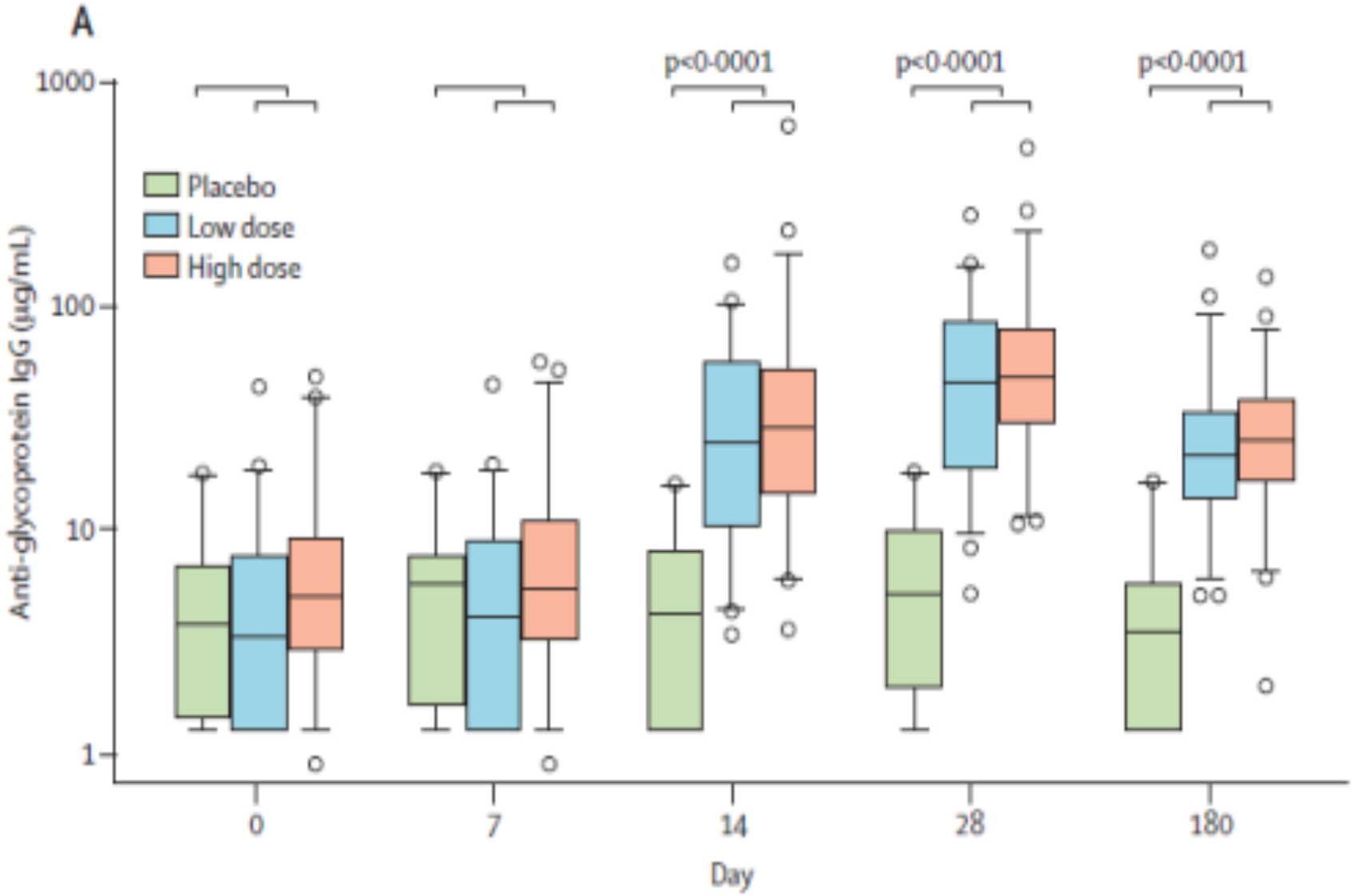
ChAd3 expressing envelope GP of Zaire Ebola virus species (Mayinga variant, monovalent)

One phase 1 (Switzerland) and one phase 2a (USA) clinical trials reported results on the use of a single dose of ChAd3.EBOZ.

GP-specific antibody response rate in vaccinees was 96% or higher.

Antibody levels peaked at Day 28 and halved by Day 180.

ChAd3-EBOZ immunogenicity in Phase 1 trial



De Santis et al., Lancet Infect Dis 2016, 16:311–320

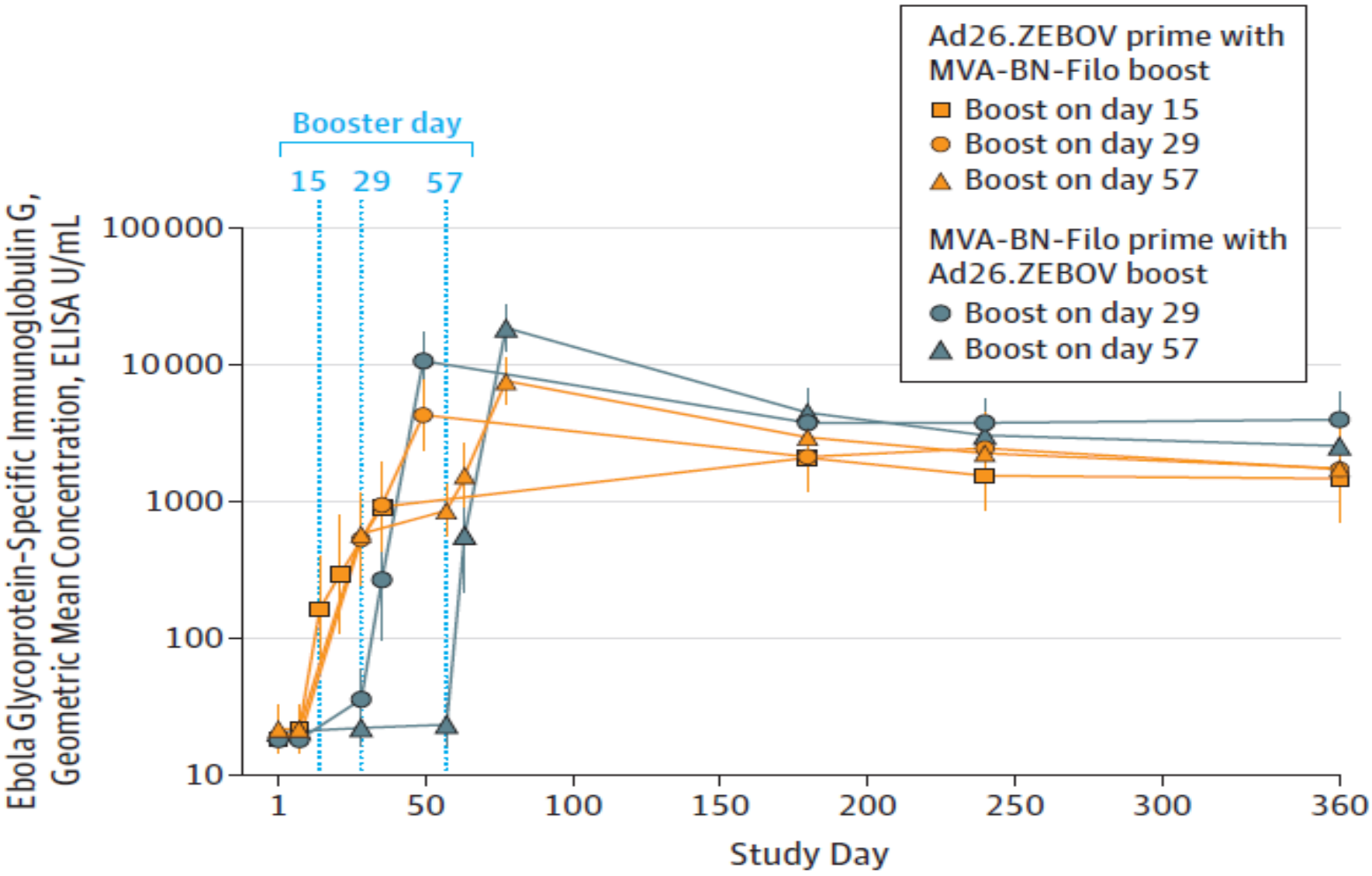
Ad26 and MVA-BN Filo

One phase 1 trial (UK) and one phase 2/3 trial (Sierra Leone) currently recruiting.

In the UK trial, at day 28 seropositivity was 97% and 23% vaccinees primed with Ad26 and MVA, respectively.

All vaccinees had detectable GP-specific IgG at day 21 after boost and at 8 months and 12 months follow-up

Immunogenicity: Ad26/MVA candidate vaccine in Phase 1 trial



Winslow et al., JAMA 2017, 317:1075–1077

rVSV expressing envelope GP of Zaire Ebola virus species (Kikwit variant, rVSVΔG-ZEBOV-GP)

Multi-centric phase I clinical trials across Europe, the UK and Africa were conducted. One phase I trial (USA), one phase I/II (Switzerland) , two phase II trials (Liberia and Sierra Leone) and one phase III trial (Guinea).

In the multi-centric Phase I clinical trial, most vaccinees showed neutralizing antibodies by day 28, with higher titres at higher doses.

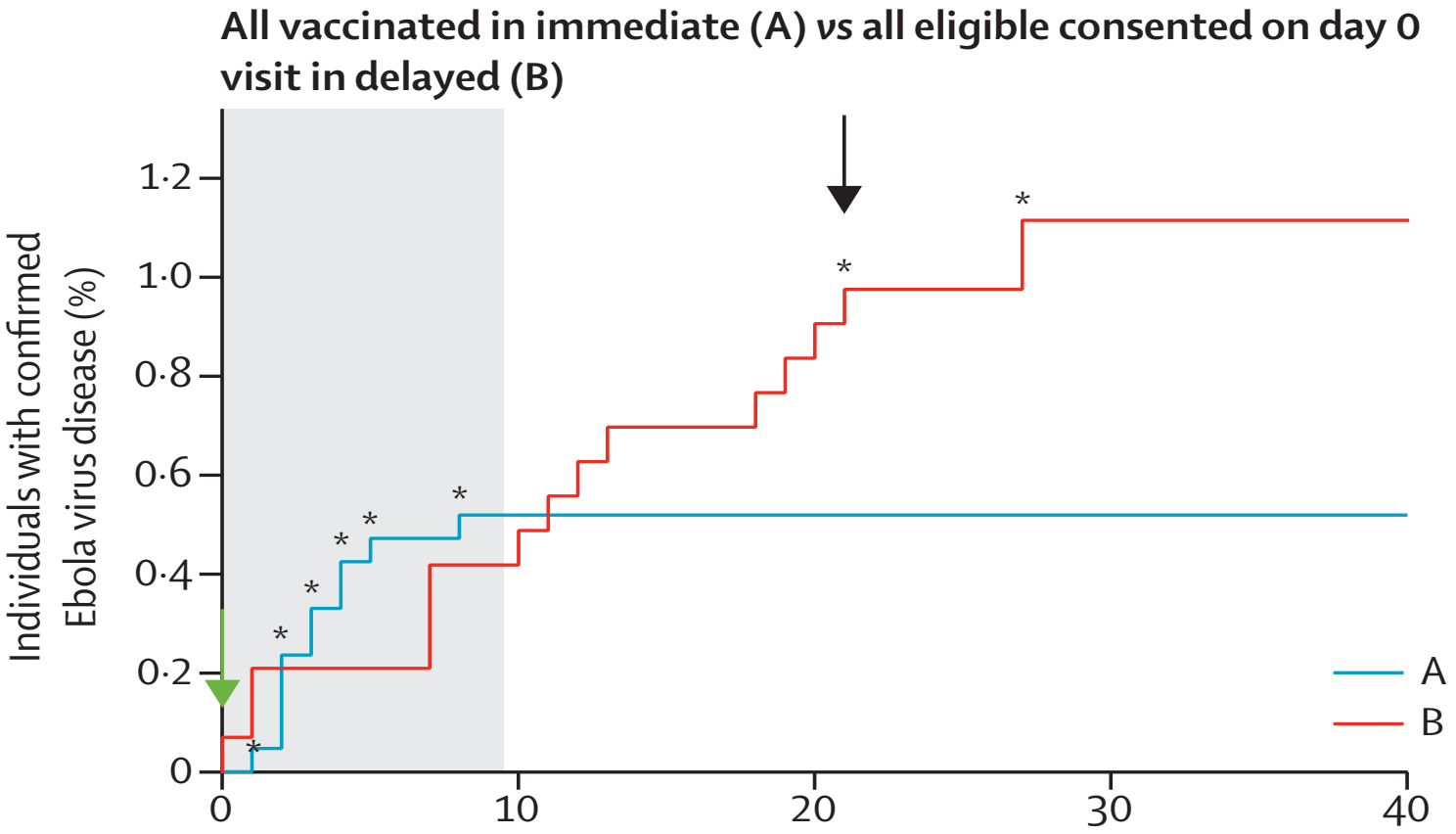
In Liberia, 94 percent of the volunteers who received the rVSV-ZEBOV vaccine had demonstrable antibodies after one month.

Effect of rVSVΔG-ZEBOV-GP on cases of Ebola virus disease in different study populations—Guinea and Sierra Leone, 2015

	All clusters*				Randomised clusters†			
	1	2	3	4	5	6	7	8
	All vaccinated in immediate (group A) *vs* all contacts and contacts of contacts in delayed plus all never-vaccinated in immediate or non-randomised (group B)	All vaccinated in immediate (group A) *vs* all eligible in delayed plus all eligible never-vaccinated in immediate (group B)	All contacts and contacts of contacts in immediate (group A) *vs* delayed (group B)	All vaccinated in immediate (group A) *vs* all eligible never vaccinated in immediate (group B)	All vaccinated in immediate (group A) *vs* all eligible and consented on day 0 visit in delayed (group B)	All vaccinated in immediate (group A) *vs* all eligible in delayed (group B)	All eligible in immediate (group A) *vs* all eligible delayed (group B)	All contacts and contacts of contacts in immediate (group A) *vs* all contacts and contacts of contacts in delayed (group B)
Group A								
Number of individuals (clusters)	3775 (70)	3775 (70)	7241 (70)	3775 (70)	2108 (51)	2108 (51)	3212 (51)	4513 (51)
Cases of Ebola virus disease (clusters affected)	0 (0)	0 (0)	12 (7)	0 (0)	0 (0)	0 (0)	7 (4)	10 (5)
Attack rate	0%	0%	0·17%	0%	0%	0%	0·22%	0·22%
Group B								
Number of individuals (clusters)	7995 (116)	4507 (104)	4529 (47)	1432 (57)	1429 (46)	3075 (47)	3075 (47)	4529 (47)
Cases of Ebola virus disease (clusters affected)	34 (15)	23 (11)	22 (8)	7 (4)	10 (4)	16 (7)	16 (7)	22 (8)
Attack rate	0·43%	0·51%	0·49%	0·49%	0·7%	0·52%	0·52%	0·49%
Vaccine effect								
Vaccine efficacy/ effectiveness‡ (%, 95% CI)	100% (77·0 to 100·0)	100% (79·3 to 100·0)	70·1% (−4·9 to 91·5)	100% (−51·5 to 100·0)	100% (63·5 to 100·0)	100% (68·9 to 100·0)	64·6% (−46·5 to 91·4)	64·6% (−44·2 to 91·3)
p value§	0·0012	0·0033	0·2759	0·125	0·0471	0·0045	0·344	0·3761

Henao-Restrepo et al., Lancet 2017, 389:505–18

Effect of rVSVΔG-ZEBOV-GP on cases of Ebola virus disease in different study populations —Guinea and Sierra Leone, 2015



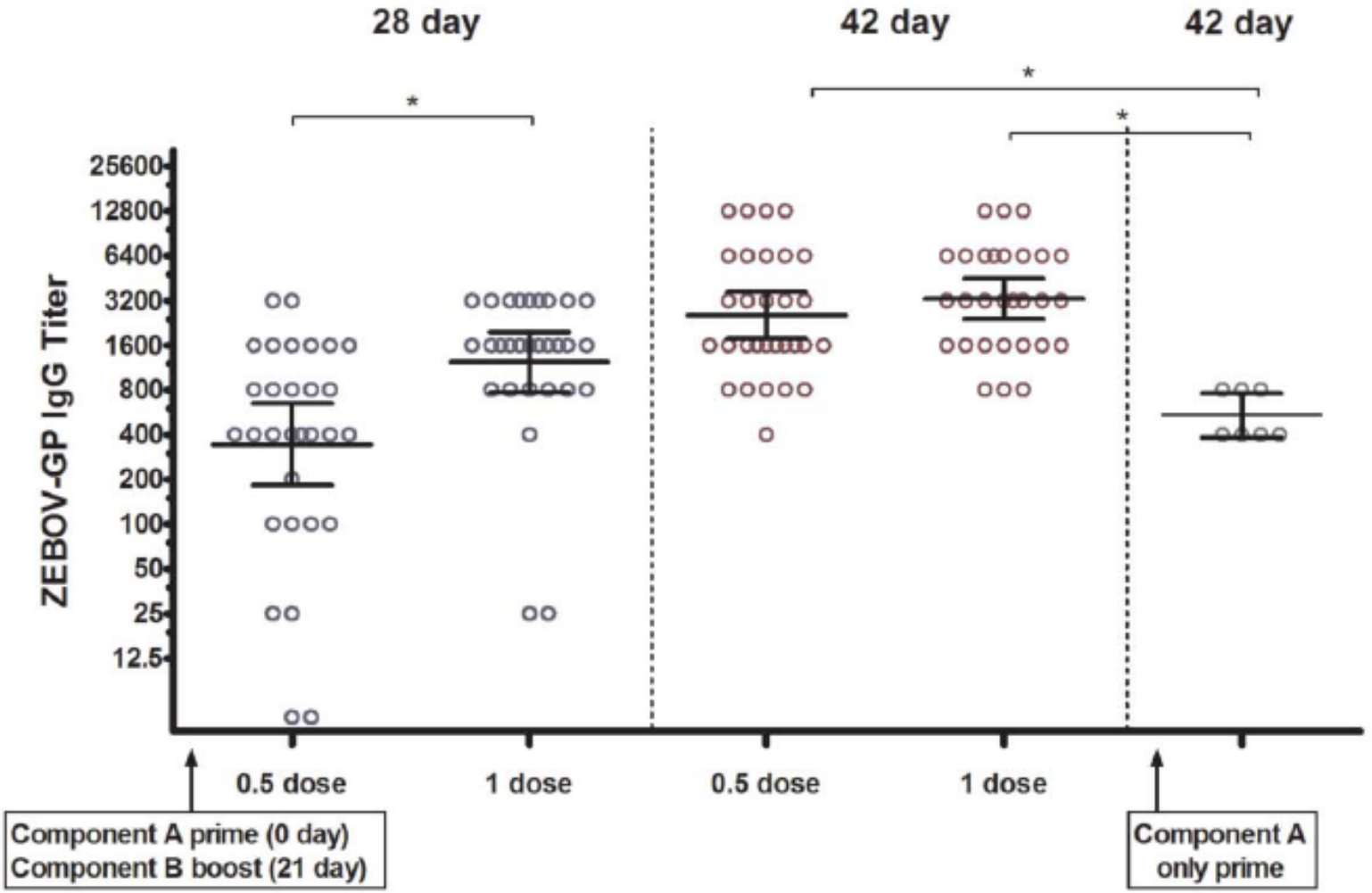
Number at risk					
Immediate vaccination	2119	2108	2108	2108	2108
Delayed vaccination	1434	1428	1422	1419	1419

rVSV & Ad5, prime & heterologous boost expressing Zaire Ebola virus species (Makona variant)

One phase 1/2 trial (Russia) reporting results.
One phase 4 study in Russia (recruiting) and a Phase 2 Guinea (not yet recruiting)

The Phase1/2 trial reported 100% prime-boost vaccinees of half dose and full dose groups showed GP-specific immune response at day 42.
Titres were 1.25-fold greater in full-dose vaccinees at day 42 compared to half-dose vaccinees.

Gam-Evac (rVSV & Ad5) immunogenicity in Phase I trial



Dolzhikova et al., Hum Vaccin Immunother 2017, 13:613–620

Overview of regulatory status

LICENSURE - rVSV & Ad5 is licensed in the Russian Federation but no information package has been submitted to WHO for assessment for prequalification.

EUAL WHO Emergency Use Assessment and Listing documentation submitted for

- rVSVΔG-ZEBOV-GP and
- Ad26.ZEBOV/MVA-BN-Filo

Review by ad-hoc Committee planned for Q2/3 of 2017

PRIME status (EMA) and Breakthrough Therapy designation (US FDA)-granted to rVSVΔG-ZEBOV-GP

Various licensure pathways exist for candidate vaccines; developers are consulting individually with regulatory agencies to define the documentation and evidence that is needed

Summary

- A dozen candidate vaccines underwent or are actively undergoing clinical development at different trial phases
- The Phase 3 trial for rVSVΔGZEBOV-GP undertaken in Guinea reported clinical efficacy and effectiveness.
- rVSV & Ad5 is licensed in the Russian Federation
- No vaccine has been WHO-prequalified or completed the WHO Emergency Use Assessment and Listing (EUAL) procedure.


Thank you