EBV vaccines (mRNA-1189 & mRNA-1195)

Last updated 5/2/24

Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial
Latent	**CMV vaccine**	mRNA-1647					
	EBV vaccine to prevent infectious mononucleosis	mRNA-1189					
	EBV vaccine to address EBV sequelae	mRNA-1195					
Infectious disease vaccines	**HSV vaccine**	mRNA-1608					
	VZV vaccine	mRNA-1468					
	HIV vaccines	mRNA-1644					
		mRNA-1574					
Enteric	**Norovirus vaccines**	mRNA-1403					
		mRNA-1405					
Bacterial	**Lyme vaccines**	mRNA-1975					
		mRNA-1982					
Public health	**Zika vaccine**	mRNA-1893					
	Nipah vaccine	mRNA-1215					
	Mpox vaccine	mRNA-1769					

EBV has several serious health impacts

Infectious mononucleosis

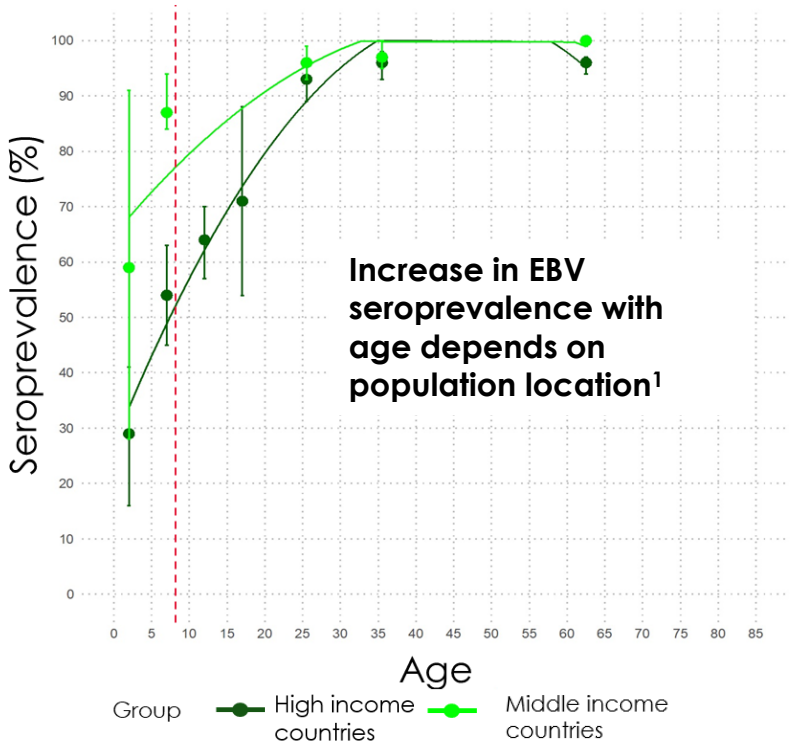
Multiple sclerosis

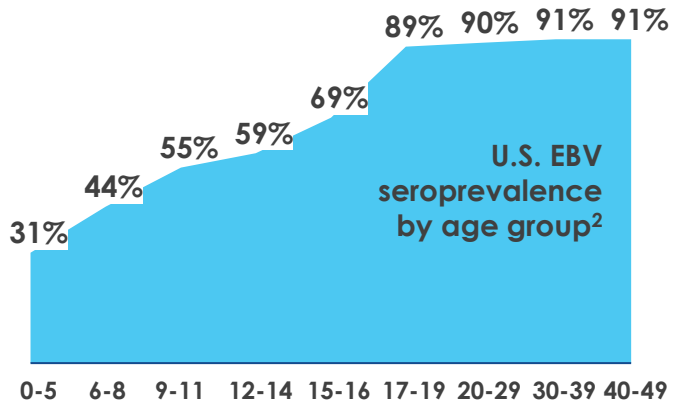
Cancer

moderna

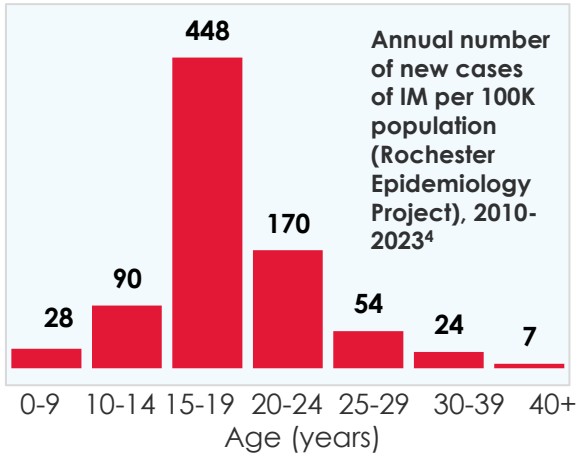
Epidemiology of EBV and infectious mononucleosis (IM)

EBV infects the vast majority of the world population by adulthood (~95% seropositivity)





Studies in Europe and North America show a more gradual increase in seroprevalence which did not exceed 90% until age 22[3]



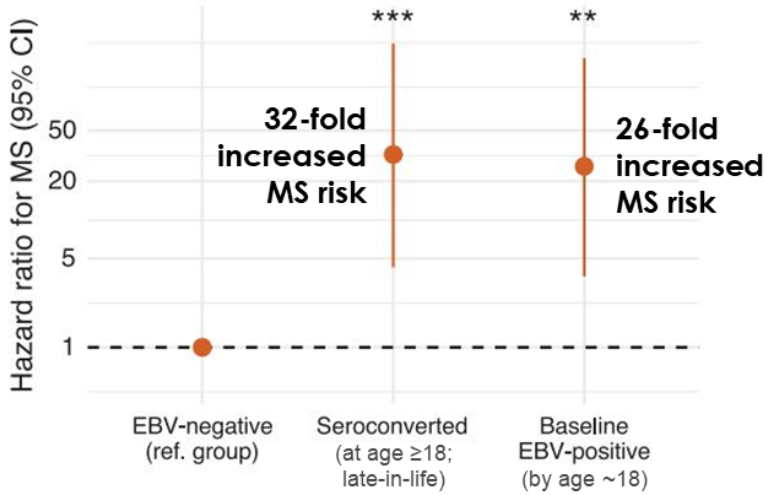
EBV accounts for over 90% of cases of IM[5]. Annual incidence of IM in the general U.S. population is estimated to be at least 45 cases per 100,000[6], with **peak incidence occurring at ages 15-19y[7]**

Sources: 1. Gequelin, Lucian, et al. Rev Bras Hematol Hemoter (2011), https://doi.org/10.5581/1516-8484.20110103 2. Balfour et al https://pubmed.ncbi.nlm.nih.gov/23868878/, Moderna data on file. 3. Winter et al https://pubmed.ncbi.nlm.nih.gov/32257152/. 4. Moderna data on file, Rochester Epidemiology Project 5 Fugl et al 2019 https://bmcprimcare.biomedcentral.com/articles/10.1186/s12875-019-0954-3 6. Tyring S, Moore AY, Lupi O (2016). *Mucocutaneous Manifestations of Viral Diseases: An Illustrated Guide to Diagnosis and Management* (2 ed.). CRC Press. p. 123. 7. Kuri et al 2020 https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-020-09049-x

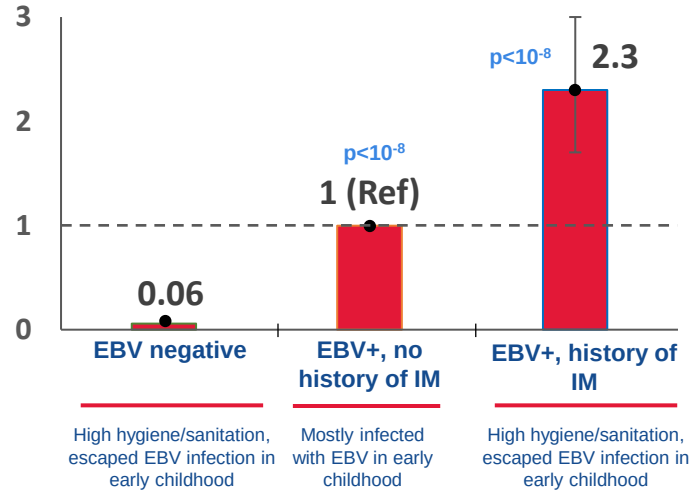
Etiologic link between EBV and multiple sclerosis (MS)

- **Nearly 1M people have MS in the U.S.[1]**
- EBV seropositivity is nearly universal in MS and seronegative individuals have a negligible risk of MS
- Recent landmark study established a **~32 fold increased risk of developing MS following EBV seroconversion[2]**
- It was previously established that **infectious mononucleosis** is an MS risk factor, beyond the contribution of EBV alone; in addition, the epidemiology of IM and MS are similar

MS Risk by EBV serostatus[2]



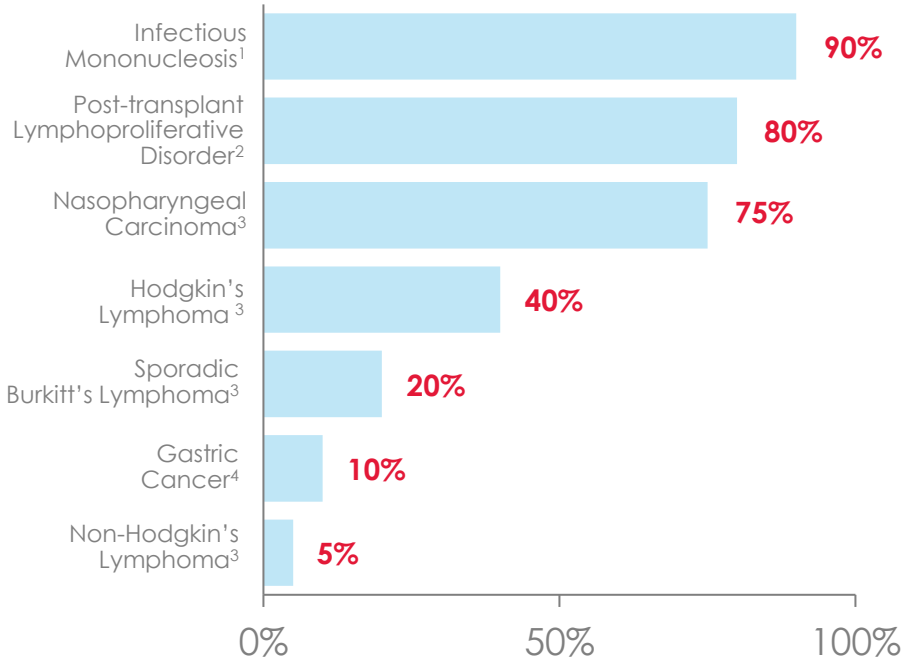
MS Risk by history of IM and EBV serostatus[3]



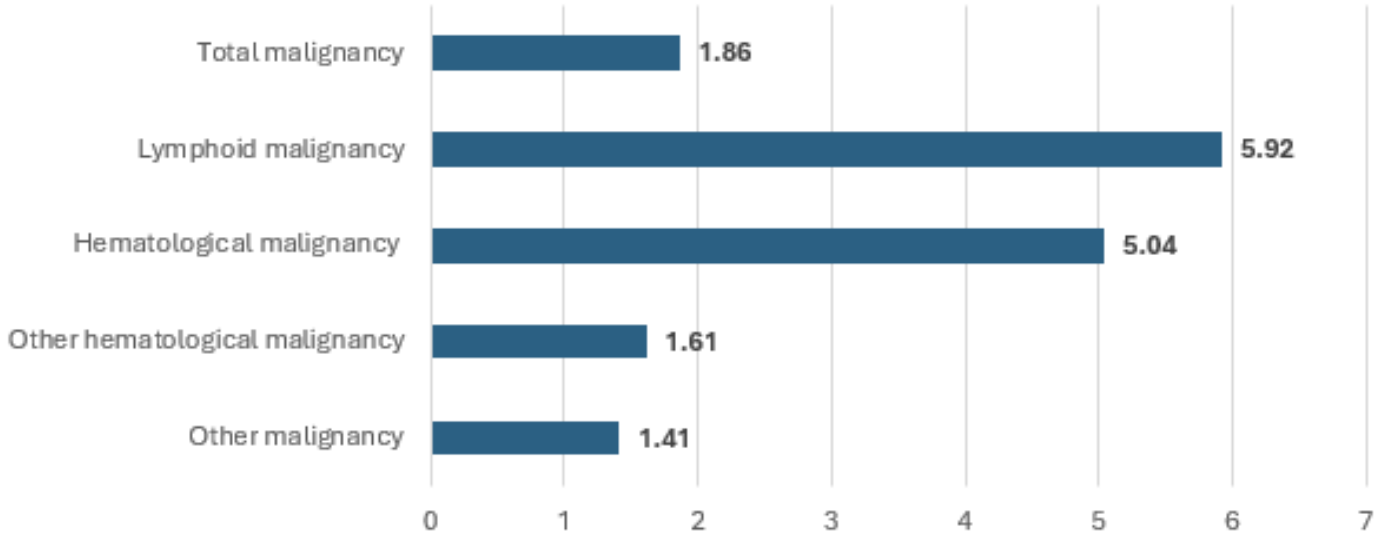
Sources: 1. https://www.nationalmssociety.org/About-the-Society/MS-Prevalence 2 Bjornevik et al https://www.science.org/doi/10.1126/science.abj8222; 3. Ascherio A, Munger KL. Epidemiology of Multiple Sclerosis: From Risk Factors to Prevention-An Update. Semin Neurol. 2016 Apr;36(2):103-14. doi: 10.1055/s-0036-1579693. Epub 2016 Apr 26. PMID: 27116717.

EBV infection is associated with cancer incidence, with increased risk following symptomatic IM

Association of EBV by Indication in the United States



Increased risk following EBV related IM (adjusted risk)[5]

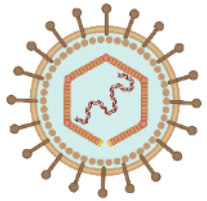


Globally, EBV-associated cancers account for over **200,000** new cases of cancer annually and **150,000** cancer deaths, representing about **1% and 2% of total global cancer incidence and cancer deaths**, respectively[6]

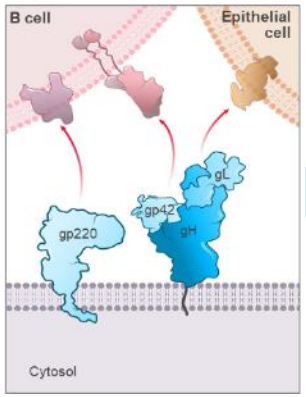
1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6518816/; 2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946499/; 3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3415781/; 4. https://dceg.cancer.gov/research/cancer-types/stomach-gastric/ebv-associated-gastric-cancer; 5. Risk analyses adjusted for gender, parity, maternal age at delivery, maternal education, maternal residence, and paternal malignancy history. Ref: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.991069/full ; 6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8532523/

Moderna's EBV vaccine candidates could tackle multiple EBV-associated conditions

EBV



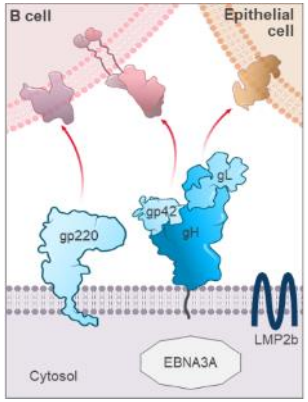
mRNA-1189

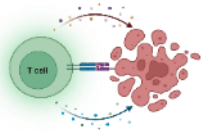


Humoral response to target **lytic** replication and primary infection

- Vaccine composed of **lytic antigens** to build robust **antibody response** against EBV
- **Primary indication: Infectious Mononucleosis**
- **Prophylactic prevention of long-term sequelae**

mRNA-1195

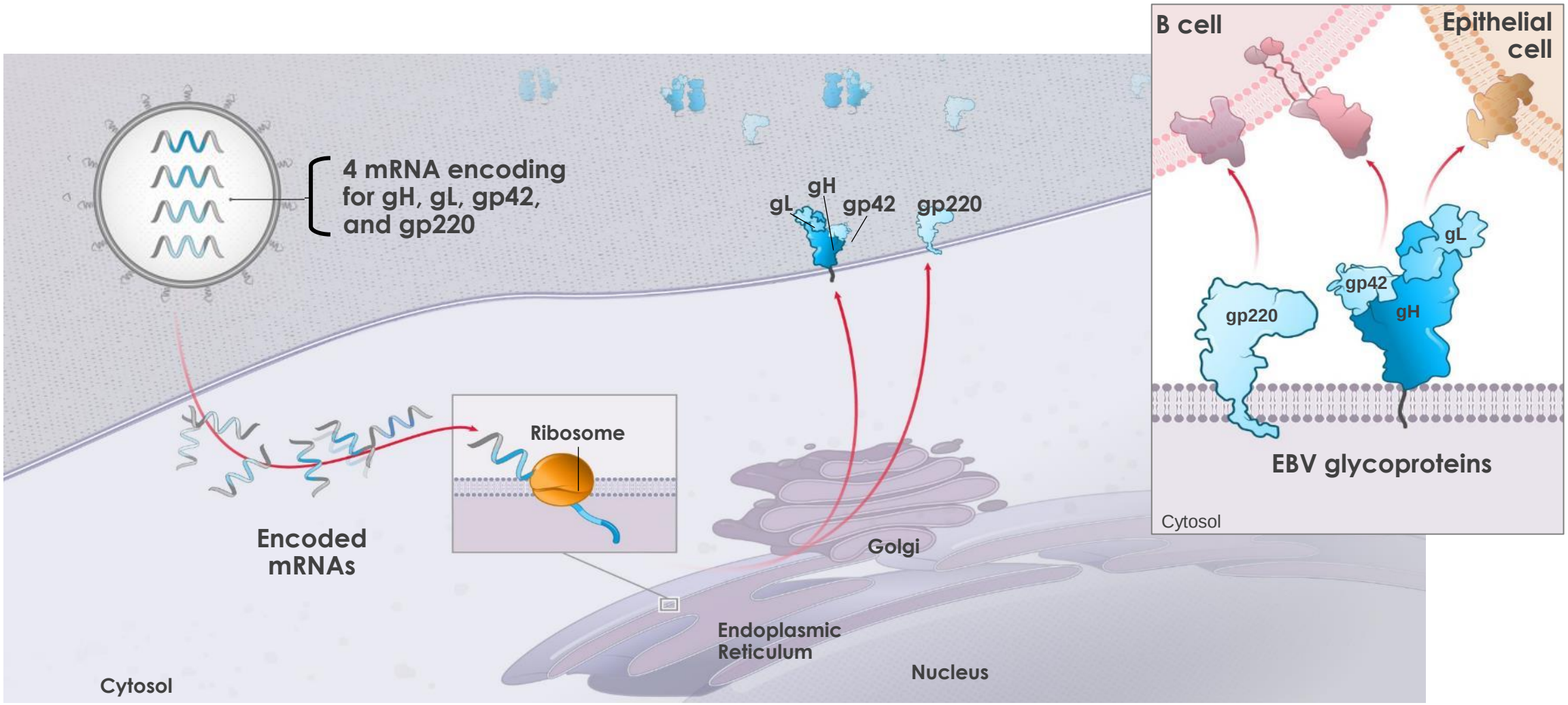




Humoral and **CMI** response to target **lytic** replication and **latent** infection

- Vaccine composed of **lytic** and **latent antigens**
- **Multiple Sclerosis**
  - Immune dysregulation of/by EBV may be one underlying mechanisms of action
  - Vaccine MOA: restoring robust immune control of lytic and latent infection through vaccination
- **Post-transplant Lymphoproliferative Disorder (PTLD)**

EBV vaccine (mRNA-1189) encodes for four antigens



EBV (IM): mRNA-1189 Phase 1 trial design; data from Part A

The Phase 1 was designed to test the safety, reactogenicity, and immunogenicity of 4 different dose levels of mRNA-1189 in participants 12-30 years of age

Design
Randomized equally across 4 arms (Part A) and 5 arms (Part B), observer-blind, placebo-controlled study

Number of participants

Part A: 272 EBV seronegative and EBV seropositive healthy adults (18-30 years old)

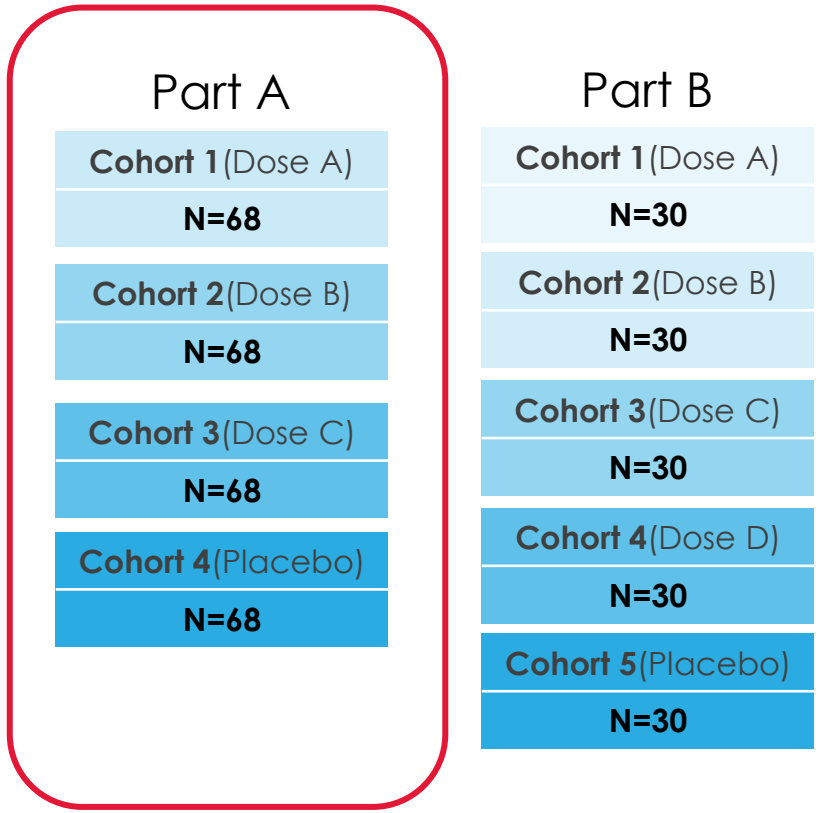
Part B: 150 healthy EBV seronegative adolescents (12-17 years old)

Vaccination schedule
Three doses of mRNA-1189 (0-2-6 month) or placebo

Duration: 18-months
Enrollment period: December 2021–Oct 2023

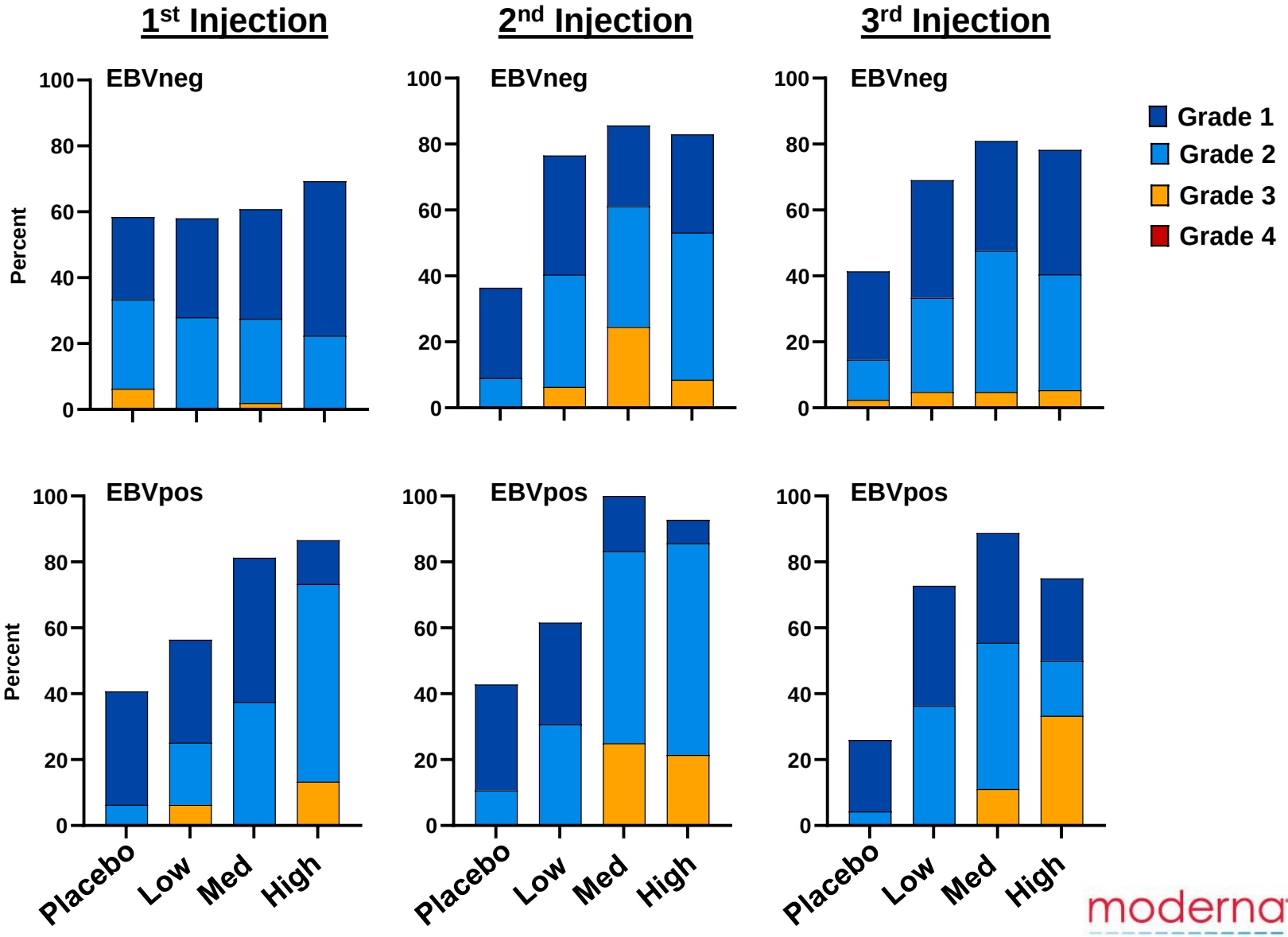
Study participants will be followed up for 12 months after study injection

Site location
US



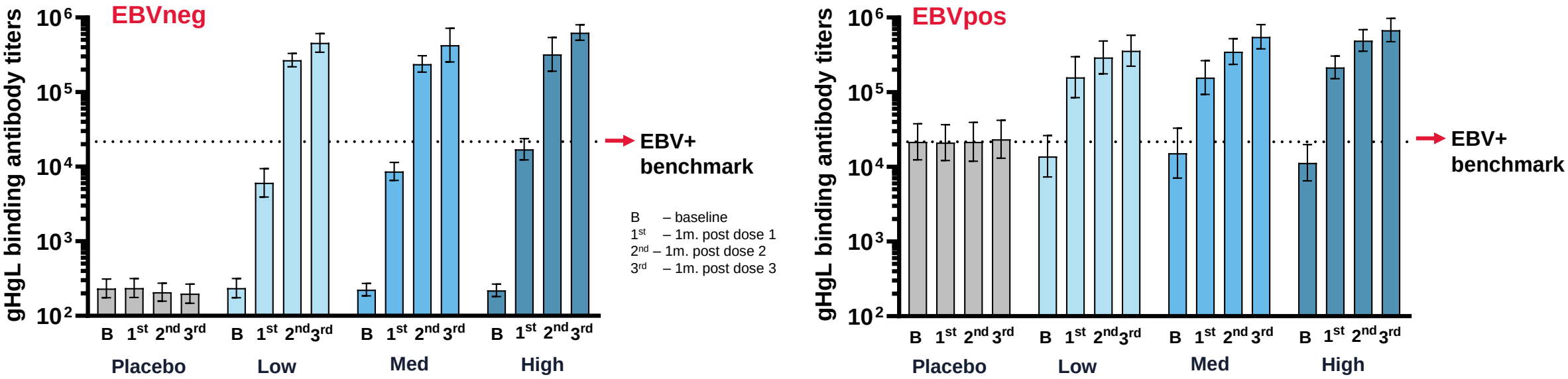
mRNA-1189 was observed to be generally well tolerated following 3 injections

- mRNA-1189 was observed to be generally well tolerated in the Phase 1 study
- The low dose group exhibited the lowest rate of systemic reactogenicity
- The frequency and severity of systemic SARs increased after the second and third injections regardless of EBV serostatus
- **Local reactogenicity:** pain was the most common local reaction at injection site, with frequency similar to other mRNA vaccines



Data from mRNA-1189-P101 Part A (Adults 18-30Y)

gHgL binding antibody titers elicited by mRNA-1189 are numerically higher than those induced by natural infection



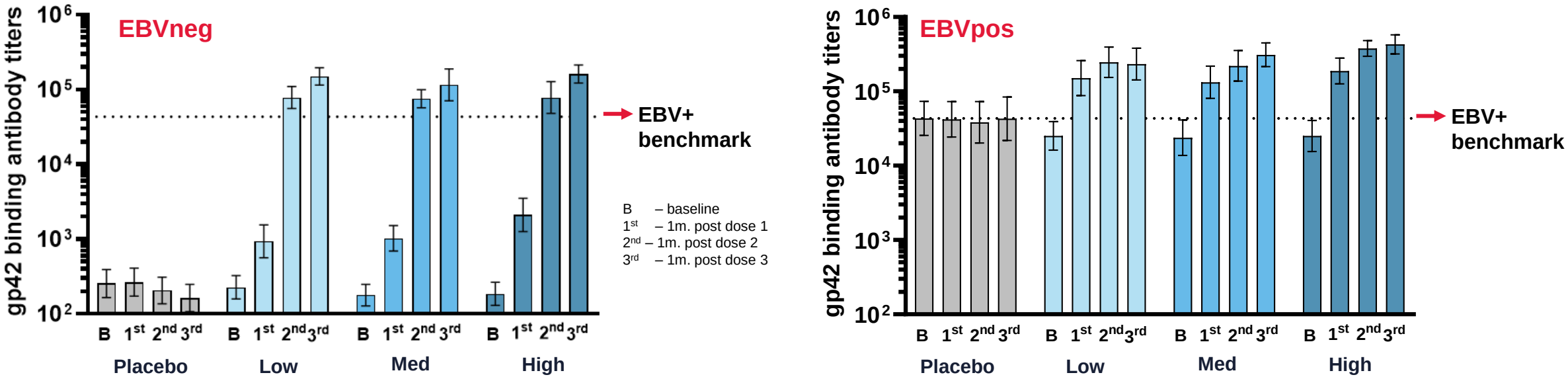
Data from mRNA-1189-P101 Part A (Adults 18-30Y)

Binding antibody titers to gHgL increased after each injection in both EBV seronegatives and EBV seropositives

There was no obvious dose response after 3 injections, regardless of serostatus

After 3 injections, gHgL titers in seronegative recipients were numerically higher than those in EBV seropositives at baseline

gp42 binding antibody titers elicited by mRNA-1189 are numerically higher than those induced by natural infection



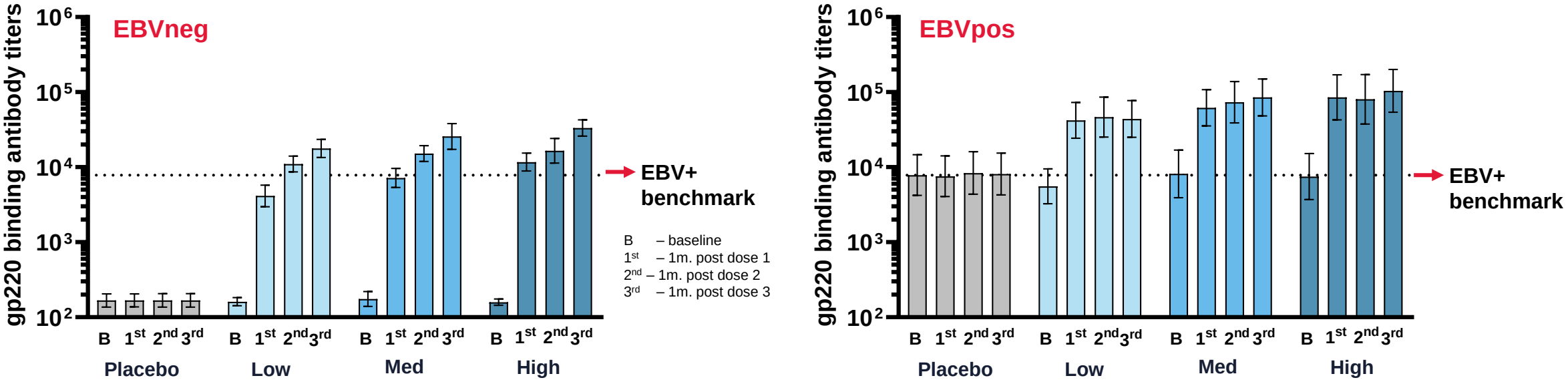
Data from mRNA-1189-P101 Part A (Adults 18-30Y)

Binding antibody titers to gp42 increased after each injection in both EBV seronegatives and EBV seropositives

There was no obvious dose response after 3 injections, regardless of serostatus

After 3 injections, gp42 titers in seronegative recipients were numerically higher than those in EBV seropositives at baseline

gp220 binding antibody titers elicited by mRNA-1189 are numerically higher than those induced by natural infection



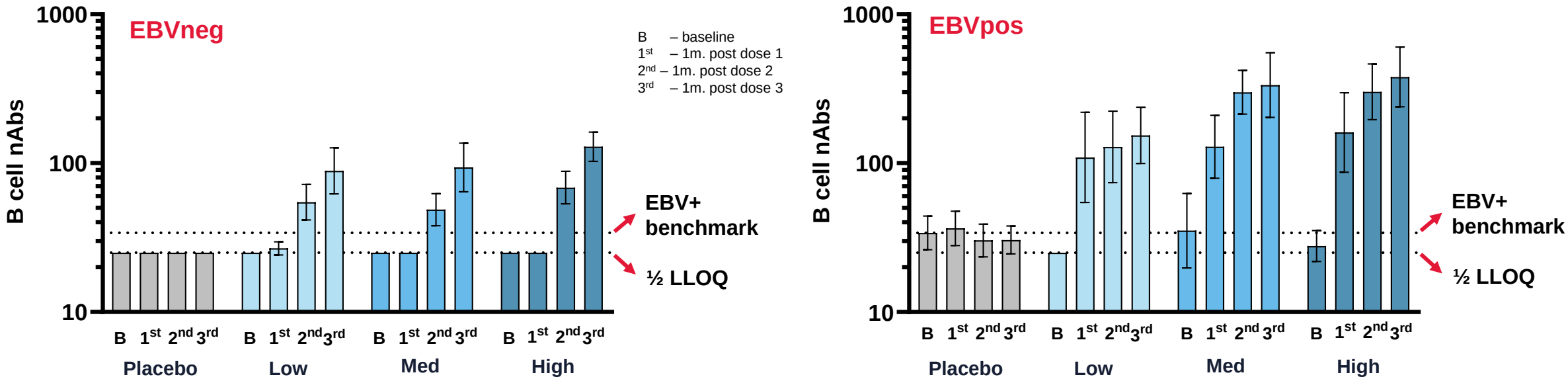
Data from mRNA-1189-P101 Part A (Adults 18-30Y)

Binding antibody titers to gp220 increased after each injection in EBV seronegatives while the fold rise was less obvious in EBV seropositives with the 2nd and 3rd injection

There was no obvious dose response after 3 injections, regardless of serostatus

After 3 injections, gp220 titers in seronegative recipients were numerically higher than those in EBV seropositives at baseline

B cell neutralizing antibody titers elicited by mRNA-1189 are numerically higher than those induced by natural infection



Data from mRNA-1189-P101 Part A (Adults 18-30Y)

B cell nAbs were below detection in all EBV seronegative and most EBV seropositive participants at baseline, indicating a low response even in previously infected healthy individuals

Regardless of serostatus, participants across mRNA-1189 dose groups showed increases in B-cell nAbs from Baseline following 3 injections

Though titers were similar across the 3 dose levels, the highest titers were observed in the highest dose group

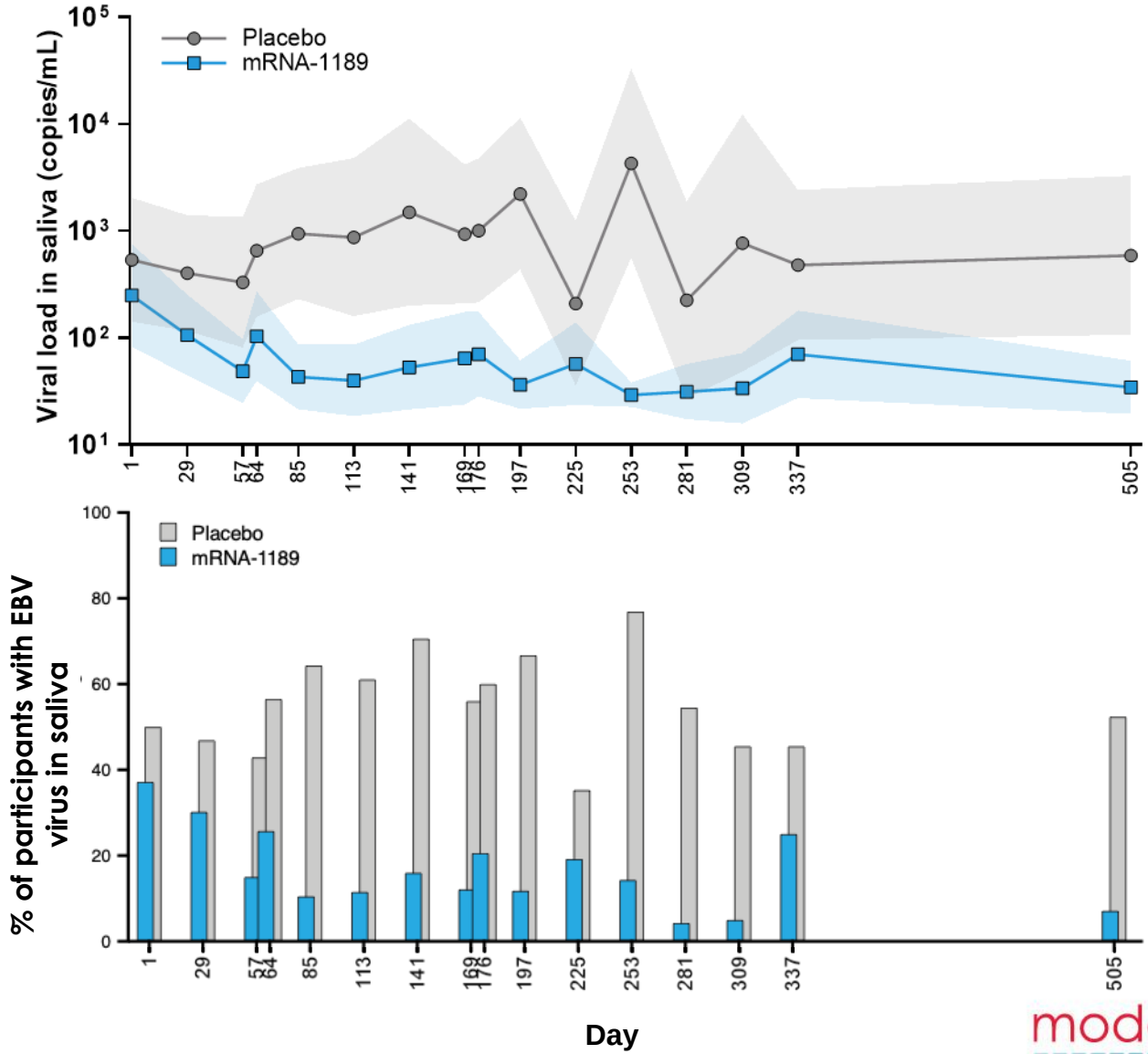
A larger impact of the 3rd injection on B cell nAbs was noted in the EBV seronegative group compared to the EBV seropositive group

Pooled mRNA-1189 dose levels were observed to reduce viral shedding as compared to placebo

Due to small sample size, results across the three mRNA-1189 dose levels were consolidated and analyzed together to provide better qualitative description of the viral shedding data

At each timepoint, all dose levels of mRNA-1189 delivered a measurable reduction in detectable EBV viral DNA in saliva sampled at monthly intervals when compared to placebo

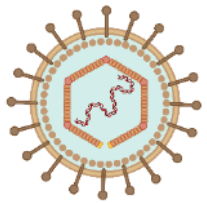
Though limited in sample size, this impact continues to be observed at 6 months (D337) and 1 year (D505) after the last injection



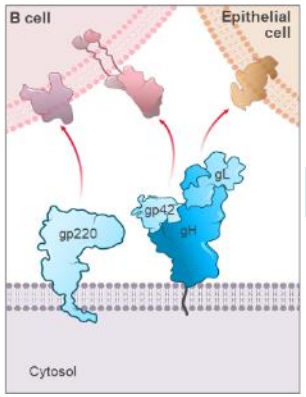
Data from mRNA-1189-P101 Part A (Adults 18-30Y)

Moderna's EBV vaccine candidates could tackle multiple EBV-associated conditions

EBV



mRNA-1189



Humoral response to target **lytic** replication and primary infection

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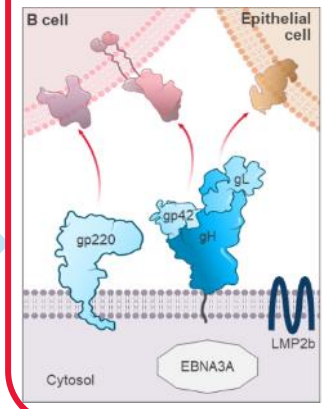
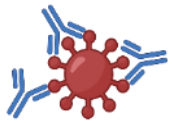
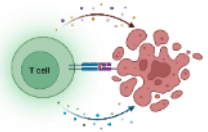
mRNA-1195







Humoral and **CMI** response to target **lytic** replication and **latent** infection

- Vaccine composed of **lytic** and **latent antigens**
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EBV vaccine (mRNA-1195) Phase 1 part A trial design; fully enrolled

The Phase 1 Part A was designed to test the safety, reactogenicity, and immunogenicity of mRNA-1195 (4 different dose levels) in healthy EBV seropositive participants 18-55 years of age

Design
Randomized equally across 10 arms, observer-blind, placebo-controlled study

Number of participants
350 healthy EBV seropositive adults (18-55 years old)

Vaccination schedule
Three doses of mRNA-1195 (0-2-6 month) or placebo

Duration: 12-months
Enrollment period: Apr – Jul 2023

Study participants will be followed up for 6 months after study injection

Site location
US

Part A (18-55 Y)
Total N = 350
Randomization Ratio = 1:1:1:1:1:1:1:1:1:1

Cohort 1(1195.1; Dose A) **N=35**	**Cohort 2**(1195.2; Dose A) **N=35**
Cohort 3(1195.1; Dose B) **N=35**	**Cohort 4**(1195.2; Dose B) **N=35**
Cohort 5(1195.1; Dose C) **N=35**	**Cohort 6**(1195.2; Dose C) **N=35**
Cohort 7(1195.1; Dose D) **N=35**	**Cohort 8**(1195.2; Dose D) **N=35**
Cohort 9(1189; Dose E) **N=35**	**Cohort 10**(Placebo) **N=35**

EBV vaccine summary and next steps

Disease burden	• EBV infects more than 90% of the world's adult population; it causes serious health conditions including infectious mononucleosis, several cancers and autoimmune disorders like multiple sclerosis
Safety	• mRNA-1189 is generally well tolerated in adults 18-30 yrs
Immunogenicity	• Phase 1 interim analysis data from mRNA-1189 demonstrate binding antibody titers for glycoproteins (gHgL, gp42, gp220) were boosted regardless of serostatus • Regardless of serostatus, participants across mRNA-1189 dose groups showed increases in B-cell nAbs from Baseline following 3 injections • Following 3 injections, titers in mRNA-1189 recipients crossed baseline EBV seropositive threshold • mRNA-1189 reduced measurable viral shedding in saliva of EBV seropositive recipients
Next steps	• mRNA-1189: advancing toward pivotal development • mRNA-1195: ongoing Phase 1 study in healthy volunteers

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding: development candidate activities and clinical trials; the potential for Moderna's EBV vaccines to prevent infectious mononucleosis and to address EBV sequelae; and expected market opportunity. In some cases, forward-looking statements can be identified by terminology such as "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward -looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include those described in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date referenced on the first page.