

# Epstein-Barr virus (EBV) vaccine (mRNA-1647)

Last program update: February 26, 2020

Modality	ID #	Program		Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
 Prophylactic vaccines	mRNA-1647	Cytomegalovirus (CMV) vaccine						Worldwide
	mRNA-1893	Zika vaccine						Worldwide <i>BARDA funded</i>
	mRNA-1172/ Merck V172	Respiratory syncytial virus (RSV) vaccine						Merck to pay milestones and royalties
	mRNA-1177	Respiratory syncytial virus (RSV) vaccine						
	mRNA-1653	hMPV/PV3 vaccine		Phase 1 (healthy volunteers)	Phase 1b (Age de-escalation) Seropositives			Worldwide
	mRNA-1345	Pediatric respiratory syncytial virus (RSV) vaccine <i>Future respiratory combo</i>						Worldwide
	<b>mRNA-1189</b>	<b>Epstein-Barr virus (EBV) vaccine</b>						Worldwide
	mRNA-1851	Influenza H7N9 vaccine						Worldwide <i>Advancing subject to funding</i>
	mRNA-1273	Novel coronavirus (SARS-CoV-2) vaccine						Worldwide <i>CEPI funded</i>

# Epstein-Barr virus (EBV) overview

- EBV is a member of the herpesvirus family that includes CMV, is spread through bodily fluids (e.g., saliva) and contracted primarily by young children and adolescents
- **Disease burden:** EBV is a major cause of infectious mononucleosis (IM) in the U.S., accounting for over 90% of the ~1+ million cases annually
  - IM can debilitate patients for weeks to months, can lead to hospitalization and (rarely) splenic rupture
  - EBV infection is also associated with certain lymphoproliferative disorders, cancers and autoimmune diseases
  - IM and EBV infection are associated with increased risk of developing multiple sclerosis (MS)
- **Unmet need:** No approved vaccine

## EBV infection sequelae

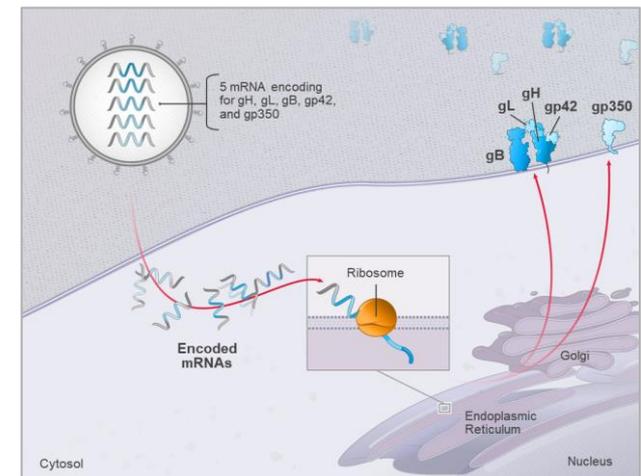
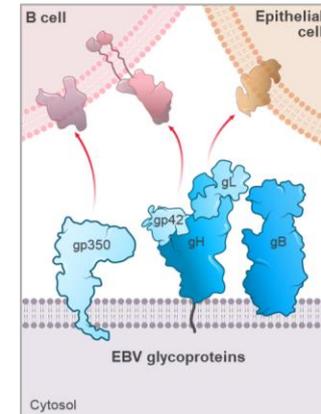
<b>Adolescents and young adults</b>	<i>Infectious Mononucleosis</i> <ul style="list-style-type: none"><li>• Sore throat</li><li>• Lymphadenopathy</li><li>• Fever</li><li>• Body aches</li><li>• Fatigue</li></ul>
<b>Lifetime associated risks</b>	Increased risk of developing cancer and multiple sclerosis

**Moderna product concept: Develop a multi-antigen vaccine to prevent IM and EBV infection, with long-term potential to impact EBV-associated diseases**

# EBV vaccine (mRNA-1189)

## Encodes for five glycoproteins to inhibit both mechanisms for viral entry

- EBV lifecycle has lytic and latent stages, similar to other herpesviruses like CMV
- EBV has multiple surface (envelope) glycoproteins that mediate virus entry in different cell types<sup>1</sup>
  - **gp350** and **gp42/gH/gL complex** primarily mediate B cell infection
  - **gH/gL complex** primarily mediate epithelial cell infection
  - **gB** drives viral fusion for all cell types
- Vaccination with *only* gp350 (partial B cell protection) reduced the rate of IM by 78% in a clinical trial, but did not prevent infection<sup>2</sup>
- Our vaccine encodes five glycoproteins to inhibit both mechanisms for viral entry into **B cells (gp350 plus gH/gL/gp42)**, adds protection for **epithelial cells (gH/gL)**, and includes **gB** for protection of all cells
- We believe that by protecting both cell types our vaccine will **reduce the rate of IM, and possibly prevent EBV infection**



<sup>1</sup>Balfour. *Pediatr Res.* 2020 Jan;87(2):345-352

<sup>2</sup>Sokal. *The Journal of Infectious Diseases*, Volume 196, Issue 12, 15 December 2007, Pages 1749–1753

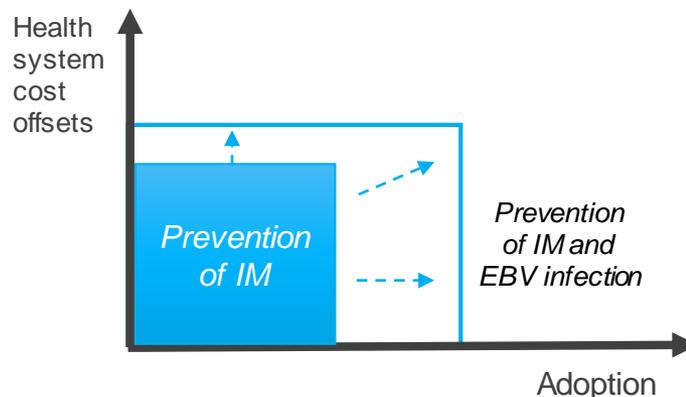
<sup>3</sup>Nielsen. *Arch Neurol.* 2007; 64:72; Ascherio. *Semin Neurol.* 2016; 36:103

<sup>4</sup>*Semin Neurol* 2016; 36(02): 103-114

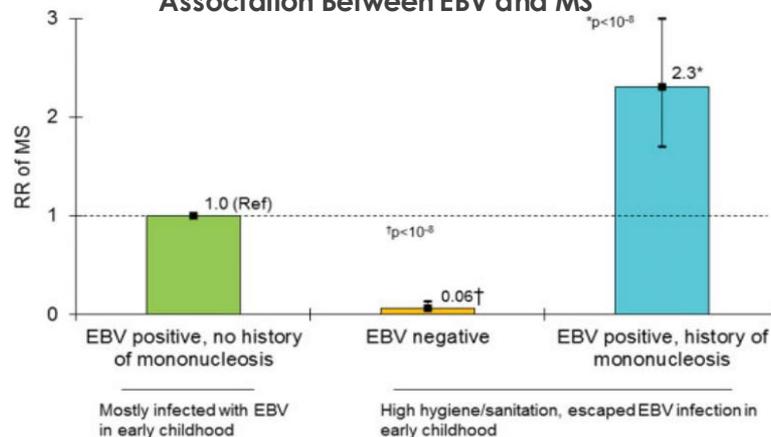
# EBV vaccine (mRNA-1189) opportunity

- We estimate worldwide direct costs of EBV-linked IM to reach \$500 million annually and indirect costs to exceed \$1 billion
- Vaccine that prevents IM in seronegative adolescents could be a significant commercial opportunity, analogous to meningitis vaccines
  - Bexsero (Meningitis B vaccine) has forecasted revenue of ~\$970 million in 2020<sup>1</sup>
- Prevention of EBV infection – in addition to prevention of IM – could encourage broader adoption and upside<sup>2</sup>
- Impact on EBV-associated diseases, such as increased risk of some cancers and multiple sclerosis, would be a long-term potential upside but are not part of the current clinical development plan<sup>3</sup>

## Market potential



## Association Between EBV and MS



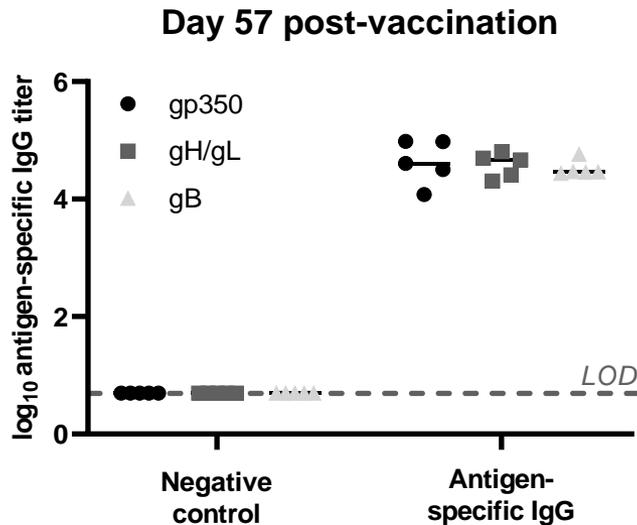
<sup>1</sup>EvaluatePharma

<sup>2</sup>Nielsen. *Arch Neurol.* 2007; 64:72; Ascherio. *Semin Neurol.* 2016; 36:103

<sup>3</sup>Semin Neurol 2016; 36(02): 103-114

# EBV vaccine (mRNA-1189)

Preclinical data demonstrates the ability to induce antibodies against EBV antigens



Antibody titers against glycoproteins involved in epithelial and B cell entry were observed in preclinical studies

Results shown here represent five animals per group and demonstrate high levels of antigen-specific immunoglobulin G ("IgG") as compared to negative controls.

Naïve Balb/c mice were given two doses of a vaccine against EBV antigens in combination approximately four weeks apart. Antibody titers against viral proteins involved in epithelial cell entry (gH/gL and gB) or B cell entry (gp350, gH/gL and gB) were measured in peripheral blood at day 57.

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