# Moderna’s other vaccines: CMV vaccine (mRNA-1647)

**Last program update: September 9, 2021**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Program</th>
<th>ID</th>
<th>Preclinical development</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Commercial</th>
<th>Moderna rights</th>
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<tr>
<td></td>
<td>CMV vaccine</td>
<td>mRNA-1647</td>
<td>Preclinical prep</td>
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<td></td>
<td>EBV prophylactic vaccine</td>
<td>mRNA-1189</td>
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<td>EBV therapeutic vaccine</td>
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<td>Zika vaccine</td>
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<td>HIV vaccine</td>
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<td></td>
<td>Nipah vaccine</td>
<td>mRNA-1215</td>
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<td>Worldwide NIH funded</td>
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**Prophylactic vaccines**
Cytomegalovirus (CMV) Overview

Sequelaes include:

• At birth: microcephaly, chorioretinitis, seizures, sensorineural hearing loss
• Long term: cognitive impairment, cerebral palsy, seizure disorder, sensorineural hearing loss

Most common cause of congenital infection worldwide

> $1B in annual healthcare costs

1 in 200 babies are born with a congenital CMV infection (CMV infection is present at birth)

1 in 5 will have severe, life-altering health problems
Moderna’s approach to a CMV Vaccine

• Comprises six mRNAs encoding the CMV pentamer complex and gB antigens together into one vaccine

• Phase 1 and 2 studies demonstrate functional antigen-specific responses that support the vaccine’s potential to prevent CMV infection

• We believe a vaccine that protects women from CMV infection should protect against congenital CMV infection

CMV vaccine (mRNA-1647) includes 6 mRNAs
5 encode the pentamer, 6th encodes gB antigen
CMV vaccine (mRNA-1647) clinical development

Phase 3 pivotal efficacy trial expected to start in 2021

Phase 1
- **Positive Data**
  - 3-month interim analysis: Sept. 2019
  - 7-month interim analysis: Jan. 2020
  - 12-month interim analysis: Aug. 2020

Phase 2
- **Positive Data**
  - 3-month interim analysis: Jan. 2020
  - 7-month interim analysis: Sept. 2020
- **Phase 2 Start**
- **Positive Data**
  - 7-month interim analysis: Apr. 2021
CMV vaccine (mRNA-1647) Phase 1 data summary (12-month IA)

• Generally well-tolerated, no vaccine-related serious adverse events (SAEs)
• Neutralizing antibody (nAb) response, CMV-seronegative group:
  – At 1 month after the 3rd vaccination, nAb geometric mean titers (GMTs) against epithelial cell infection (measuring pentamer response) ranged 2.8-fold to 17-fold higher than the CMV-seropositive baseline GMT benchmark, and nAb GMTs against fibroblast infection (measuring gB response) ranged 0.8-fold to 5.0-fold higher than the CMV-seropositive baseline GMT benchmark
• Neutralizing antibody titers in the CMV-positive group:
  – At 1 month after the 3rd vaccination, the ratio of nAb titers compared to baseline (geometric mean ratios, or GMRs) against epithelial cell infection ranged 13.4-40.8 and against fibroblast infection ranged 4.0-7.1
• Early evidence of immune persistence out to 12 months (6 months after the 3rd vaccination)
Key changes to mRNA-1647 in Phase 2 clinical trial

**Improved Potency**
- Improved ratio of mRNA components to increase potency

**Improved Tolerability**
- Optimized the manufacturing process to improve tolerability

**Lyophilization**
- Phase 2 utilizes the intended Phase 3 and commercial formulation

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**Liquid, Single-Dose Vial,**
-20°C storage ≥6 months shelf-life

**Lyophilized, Single-Dose (0.5mL),**
5°C storage ≥18 months shelf-life
CMV vaccine (mRNA-1647) Phase 2 trial overview

Key objective
- To assess the safety and immunogenicity of mRNA-1647 vaccine in its Phase 3 presentation-to select a dose level to progress into Phase 3 development

Primary endpoints
- Defined safety parameters
- Pentamer-specific and gB-specific neutralizing antibody responses as measured by epithelial cell and fibroblast assays

Secondary endpoints
- Pentamer-specific and gB-specific binding IgG responses as measured by ELISA

Participants enrolled in a 3:1 ratio of mRNA-1647: placebo

**Dosing schedule**

- **Month 0**
  - Cohort 1: 50 µg (n=60) mRNA-1647 or placebo
  - Cohort 2: 100 µg (n=60) mRNA-1647 or placebo
  - Cohort 3: 150 µg (n=60) mRNA-1647 or placebo

- **Month 2**
  - Cohort 4: 50 µg (n=24) mRNA-1647 or placebo
  - Cohort 5: 100 µg (n=24) mRNA-1647 or placebo
  - Cohort 6: 150 µg (n=24) mRNA-1647 or placebo

- **Month 6**
  - Cohort 7: 50 µg (n=60) mRNA-1647 or placebo
  - Cohort 8: 100 µg (n=60) mRNA-1647 or placebo
  - Cohort 9: 150 µg (n=60) mRNA-1647 or placebo

CMV-seronegative Group

CMV-seropositive Group
Most Common Solicited Adverse Reactions (ARs) after Each Vaccination

CMV-seronegative group

- No treatment-related SAEs
- No study pause rules were met
- Injection site pain was the most commonly reported solicited local adverse reaction
- The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills
### Most Common Solicited Adverse Reactions (ARs) after Each Vaccination

#### CMV-seropositive group

- **No treatment-related SAEs**
- **No study pause rules were met**
- **Injection site pain was the most commonly reported solicited local adverse reaction**
- **The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills**

#### Graphs:

1. **1ST VACCINATION**
2. **2ND VACCINATION**
3. **3RD VACCINATION**

<table>
<thead>
<tr>
<th>% participants</th>
<th>PLACEBO</th>
<th>50 µg</th>
<th>100 µg</th>
<th>150 µg</th>
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<tbody>
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<td><strong>PAIN</strong></td>
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<td><strong>FEVER</strong></td>
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<td><strong>HEADACHE</strong></td>
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<td><strong>FATIGUE</strong></td>
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<td><strong>MYALGIA</strong></td>
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<tr>
<td><strong>ARTHRALGIA</strong></td>
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<td><strong>CHILLS</strong></td>
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Neutralizing antibody titers against epithelial cell infection through Month 7

Neutralizing antibodies against epithelial cell infection:

- Increased in a dose-related manner after the 1st vaccination in both seronegative and seropositive participants.
- Increased further after the 2nd vaccination and again after the 3rd vaccination to GMTs exceeding the seropositive benchmark GMTs in all treatment groups by over 20-fold.
Neutralizing antibodies against fibroblast infection:

- Increased after the 2nd vaccination to GMTs approaching or exceeding the seropositive benchmark GMT in all treatment groups.
- After the 3rd vaccination, GMTs in the 100 µg and 150 µg treatment groups were comparable to GMTs after the 2nd vaccination.
Phase 2 seven-month interim analysis conclusion

- mRNA-1647 CMV vaccine was generally well tolerated:
  - The most common solicited local AR was injection site pain
  - The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills.
  - In general, solicited AR frequency and severity after the 3rd vaccination were similar to or lower compared to the 2nd vaccination

- In CMV-seronegative participants in mRNA-1647 treatment groups after the 3rd vaccination:
  - Neutralizing antibody (nAb) GMTs against epithelial cell infection were at least 20-fold higher than the CMV-seropositive baseline GMT benchmark
  - nAb GMTs against fibroblast infection approximated the CMV-seropositive baseline GMT benchmark

- In CMV positive participants in mRNA-1647 treatment groups after the 3rd vaccination:
  - nAb GMRs against epithelial cell infection increased to at least 6.8-fold over baseline
  - nAb GMRs against fibroblast infection increased to approximately 2-fold over baseline
Phase 3 CMV trial to start in 2021

- Pivotal Phase 3 trial will test the 100 µg dose level
- Primary objective is demonstration of vaccine efficacy to prevent CMV infection
- Primary efficacy analysis will be triggered based on accrual of seroconversion cases; meeting the primary objective will be the basis for filing
- Seroconversion will be determined using an assay containing non-vaccine antigens
Phase 3 CMV trial expects to enroll ~8,000 participants

- ~150 sites across the U.S., Europe and APAC
- Expected enrollment of ~8000 participants

<table>
<thead>
<tr>
<th>CMV Trial Participants – US Demographic Composition</th>
<th>Target</th>
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<tbody>
<tr>
<td>White, non-Hispanic</td>
<td>58%</td>
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<tr>
<td>Hispanic or Latinx</td>
<td>23%</td>
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<tr>
<td>Black or African American</td>
<td>12%</td>
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<tr>
<td>Asian</td>
<td>4%</td>
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<tr>
<td>Others</td>
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<tr>
<td>White</td>
<td>58%</td>
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<td>Persons of Color</td>
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