## Cytomegalovirus (CMV) vaccine (mRNA-1647)

**Last program update: May 6, 2021**

<table>
<thead>
<tr>
<th>Program</th>
<th>ID #</th>
<th>Preclinical development</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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**Program Update:** May 6, 2021
Cytomegalovirus (CMV) Overview

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

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

Most common cause of congenital infection worldwide

>$1B in annual healthcare costs

1 in 5

will have severe, life-altering health problems
Modernà’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) clinical development

Phase 3 pivotal efficacy trial expected to start in 2021

**Phase 1**
- **Phase 1 Start**: Dec. 2017
- **Positive Data**: Sept. 2019
- **3-month interim analysis**
- **Positive Data**: Jan. 2020
- **7-month interim analysis**
- **Positive Data**: Aug. 2020
- **12-month interim analysis**

**Phase 2**
- **Phase 2 Start**: Jan. 2020
- **Positive Data**: Sept. 2020
- **3-month interim analysis**
- **Positive Data**: Apr. 2021
- **7-month interim analysis**
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

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

Lyophilized, Single-Dose (0.5mL), 5°C storage ≥18months 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

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose (µg)</th>
<th>Vaccine Type</th>
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</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td>50</td>
<td>mRNA-1647 or placebo</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>100</td>
<td>mRNA-1647 or placebo</td>
</tr>
<tr>
<td>Cohort 3</td>
<td>150</td>
<td>mRNA-1647 or placebo</td>
</tr>
<tr>
<td>Cohort 4</td>
<td>50</td>
<td>mRNA-1647 or placebo</td>
</tr>
<tr>
<td>Cohort 5</td>
<td>100</td>
<td>mRNA-1647 or placebo</td>
</tr>
<tr>
<td>Cohort 6</td>
<td>150</td>
<td>mRNA-1647 or placebo</td>
</tr>
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</table>
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

1ST VACCINATION

2ND VACCINATION

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>
<tr>
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<tr>
<td>FEVER</td>
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<tr>
<td>HEADACHE</td>
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<tr>
<td>FATIGUE</td>
<td></td>
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<tr>
<td>MYALGIA</td>
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<tr>
<td>ARTHRALGIA</td>
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<tr>
<td>CHILLS</td>
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</tbody>
</table>
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
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
Pivotal Phase 3 CMV trial to start in 2021

Based on the Phase 2 interim analysis, the Phase 3 pivotal trial will test the 100 μg dose level

**Primary endpoint:** prevention of primary CMV infection in seronegative females 16-40 years old
Phase 3 CMV trial expects to enroll ~8,000 participants

- ~150 sites across the U.S., Europe and APAC
- Pivotal Phase 3 trial will test the 100 μg dose level
- Expected enrollment of ~8000 participants
- Expected to start in 2021

CMV Trial Participants – US Demographic Composition

<table>
<thead>
<tr>
<th>Demographic Composition</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, non-Hispanic</td>
<td>58%</td>
</tr>
<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>
</tr>
<tr>
<td>Others</td>
<td>3%</td>
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<tr>
<td>White</td>
<td>58%</td>
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<td>Persons of Color</td>
<td>42%</td>
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