



## Moderna Announces Positive Interim Results from Phase 1 Cytomegalovirus (CMV) Vaccine (mRNA-1647) Study and Progress Toward Phase 2 and Pivotal Trials

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*Vaccination immunized seronegative participants to levels consistent with or above seropositive titers and boosted baseline titers in seropositive participants*

*Vaccine was generally well-tolerated*

*Phase 2 study to confirm dose to be initiated in near term, with planned interim analysis through 3 months; Phase 3 study planning is underway*

*CMV is the most common infectious cause of birth defects in the U.S.; there is no approved vaccine to prevent CMV*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 12, 2019-- Moderna, Inc., (Nasdaq: MRNA) a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced positive data from the three-month interim analysis of safety and immunogenicity of the Phase 1 study of its investigational cytomegalovirus (CMV) vaccine (mRNA-1647). mRNA-1647 is a wholly owned program in Moderna's prophylactic vaccine portfolio.

Based on these data, Moderna is advancing mRNA-1647 to a dose-confirmation Phase 2 study in the near term. Preparation has also begun for a pivotal Phase 3 study designed to evaluate the efficacy of mRNA-1647 against primary CMV infection. The Phase 2 study will test the intended Phase 3 formulation, which contains the same proprietary lipid nanoparticle (LNP) used in this Phase 1 study.

mRNA-1647 is a vaccine combining six mRNAs in a single vial, which encode for two antigens on the surface of CMV: five mRNAs encoding the subunits that form the membrane-bound pentamer complex and one mRNA encoding the full-length membrane-bound glycoprotein B (gB). Both the pentamer and gB are essential for CMV to infect barrier epithelial surfaces and gain access to the body. mRNA-1647 is designed to produce an immune response against both the pentamer and gB for the prevention of CMV infection.

"I am very encouraged by the ability of mRNA-1647 to induce high levels of durable immune responses that can reach or exceed the levels generated by natural CMV infection," said Tal Zaks, M.D., Ph.D., chief medical officer at Moderna. "We recognize there is an urgent need for a preventative vaccine against congenital CMV and will be advancing mRNA-1647 into a Phase 2 study in the near term to confirm the appropriate dose, while we plan for a pivotal Phase 3 study."

"Cytomegalovirus is the leading infectious cause of birth defects, and there is a great need for a vaccine that blocks transmission of the virus from the mother to the fetus," said Sallie Permar, M.D., Ph.D., associate dean of physician scientist development and professor of pediatrics, immunology, and molecular genetics and microbiology at Duke Medical School. "These interim data are exciting because mRNA-1647 has shown the ability to induce immune responses in seronegative individuals that are greater than what is seen in those naturally infected with CMV, which is important in that natural immunity is not completely protective against congenital CMV transmission."

The Phase 1 study, which has completed enrollment, is evaluating the safety and immunogenicity of mRNA-1647 in 169 healthy adult volunteers. The study population includes those who were naïve to CMV infection (CMV-seronegative) and those who had previously been infected by CMV (CMV-seropositive). Participants were randomized to receive either placebo, or 30, 90, 180 or 300 µg of mRNA-1647 on a dosing schedule of 0, 2 and 6 months. This first planned interim analysis assessed safety and immunogenicity of the first three dose levels (30, 90, and 180 µg) at three months, one month after the second vaccination and before the third vaccination. Neutralizing antibody titers (levels of circulating antibodies that block infection<sup>1</sup>) were assessed in two assays utilizing epithelial cells and fibroblasts, which measure immune response to the pentamer and gB vaccine antigens, respectively. Seropositive baseline titers are associated with lower rates of congenital CMV transmission.

In seronegative participants:

- A dose-related increase in neutralizing antibody titers was observed in both epithelial cell and fibroblast assays.
- In epithelial cells, after the second vaccination, neutralizing antibody titers were 3 to 5 times higher than CMV-seropositive baseline titers at the 90 and 180 µg dose levels.
- In fibroblasts, after the second vaccination, neutralizing antibody titers were equivalent to CMV-seropositive baseline titers at the 90 and 180 µg dose levels.
- For the 12 sentinel participants who received mRNA-1647 under an earlier arm of the protocol (Phase A) and who received three doses (at 0, 2 and 6 months), neutralizing antibody titers were further boosted at 7 months and were sustained at or above CMV-seropositive baseline levels for at least 12 months.

In seropositive participants:

- A dose-related increase in neutralizing antibody titers was observed in both epithelial cell and fibroblast assays.
- In epithelial cells, the second vaccination boosted neutralizing antibody titers to a level of 10-fold to 19-fold baseline titers in all dose groups.
- In fibroblasts, the second vaccination boosted neutralizing antibody titers to a level of 2-fold to 4-fold baseline titers in all dose groups.

A safety analysis indicated that the vaccine was generally well-tolerated. There were no vaccine-related serious adverse events (SAEs). The most

common solicited local adverse event (AE) was injection site pain. The most common solicited systemic AEs were headache, fatigue, myalgia, chills and fever. In general, solicited systemic AEs occurred more frequently after the second dose compared to the first, and were more common in the seropositive cohorts compared to the seronegative cohorts. The most common Grade 3 solicited AEs in seropositive participants were myalgia (9-33% of a given dose cohort), chills and fatigue (9-27% of a given dose cohort) and fever (0-27% of a given dose cohort). There was a single Grade 4 AE of an isolated lab finding of elevated partial thromboplastin time (PTT), which was elevated at baseline (Grade 1) and self-resolved on the next lab test with no associated clinical findings.

A similar overall safety and tolerability profile was observed in an earlier arm of the protocol (Phase A), for which data are available out to 12 months. Additionally, the 300 µg cohort has completed the second vaccination without study pause; interim analysis of safety and immunogenicity is pending.

“We are very pleased with these strong interim results and the immunogenicity demonstrated by our CMV vaccine. The Moderna research, development and manufacturing teams have been working to ensure this program can transition in the near term to a dose-confirmation Phase 2 study, while also preparing for a pivotal Phase 3 study with the goal of ensuring commercial readiness,” said Stéphane Bancel, Moderna’s chief executive officer. “Given the urgent need for CMV prevention around the world, we believe mRNA-1647 has the potential to be a blockbuster commercial opportunity for Moderna. This is the sixth positive Phase 1 readout for a Moderna investigational prophylactic vaccine, and underscores why I believe our vaccine platform will be an important pillar of our future growth.”

### **About mRNA-1647**

mRNA-1647 is a two-antigen vaccine designed to protect against CMV infection. It combines six mRNAs in a proprietary LNP in a single vial and encodes for two immuno-dominant proteins of CMV. mRNA-1647 comprises five mRNAs encoding the subunits of the pentamer complex and one mRNA encoding the glycoprotein B (gB) target antigen. The pentamer is important for CMV entry into a variety of cells, including epithelial and endothelial cells, while gB is important for entry into all susceptible cells including fibroblasts.<sup>2</sup> A vaccine that produces an immune response against both the pentamer and gB has the potential to prevent CMV entry into cells and thus prevent congenital infections. Unlike a protein-based vaccine, mRNA-1647 instructs cells to specifically make the pentamer and gB antigens with a structure that mimics the ones presented to the immune system by the virus during a natural infection.

Preclinical data previously published in [Vaccine](#) showed that vaccination with mRNA-1647 in animal models elicited potent and durable neutralizing antibody titers.

### **About the Phase 1 Study**

This randomized, observer-blind, placebo-controlled, dose-ranging study is designed to evaluate the safety and immunogenicity of mRNA-1647 in healthy adults. The study is investigating a three-dose vaccination schedule (0, 2 and 6 months) of mRNA-1647 at four dose levels (30, 90, 180 and 300 µg) in both CMV-seronegative and CMV-seropositive participants. Primary outcome measures include solicited AEs. Secondary outcome measures include anti-CMV neutralizing antibody titers against epithelial cell infection and fibroblast cell infection.

### **About mRNA-1647 Development**

The first planned interim analysis of the Phase 1 study includes data from one month after the second vaccination with mRNA-1647 at 30, 90 and 180 µg dose levels. Forthcoming data from the Phase 1 study will include safety and immunogenicity analyses of the 300 µg dose group as well as data from the third vaccination of all participants at the 30, 90 and 180 µg dose levels. Full Phase 1 data will be presented at a future medical meeting.

Based on these Phase 1 interim data, Moderna is advancing mRNA-1647 into a Phase 2 dose-confirming study in the near term, where the first interim safety and immunogenicity analysis is planned at 0, 2 and 6 months. This Phase 2 study will test the intended Phase 3 formulation, which contains the same proprietary lipid nanoparticle (LNP) used in this Phase 1 study. In parallel, preparation is underway for the pivotal Phase 3 study designed to evaluate mRNA-1647 for the prevention of primary CMV infection in a population that includes women of childbearing age. The design of this Phase 3 study is subject to FDA and global regulatory feedback.

### **About Cytomegalovirus (CMV)**

CMV is a common pathogen and member of the herpesvirus family. Congenital (present at or before birth) CMV infection results when infected mothers transmit the virus to their unborn child, and it is the leading infectious cause of birth defects in the United States with approximately 25,000 newborns in the U.S. infected every year.<sup>3,4</sup> Birth defects occur in approximately 20 percent of infected babies and include neurodevelopmental disabilities such as hearing loss, vision impairment, varying degrees of learning disability and decreased muscle strength and coordination.<sup>5</sup> There is currently no approved vaccine for the prevention of CMV infection.

CMV is spread through saliva, mucus and urine and is common in healthy babies and toddlers; as a result, young children can be a major source of infection for pregnant women, particularly mothers, daycare workers, preschool teachers, therapists and nurses. Efforts to create a vaccine began in the 1970s, and in 1999 the Institute of Medicine (now National Academy of Medicine) [designated](#) CMV as a “highest priority” category for vaccine development. Prior studies of investigational vaccines that did not protect against the CMV pentamer antigen demonstrated limited efficacy against CMV infection and limited durability of immune response.

### **About Moderna’s Prophylactic Vaccines Modality**

Moderna scientists designed the Company’s prophylactic vaccines modality to prevent or control infectious diseases. This modality now includes eight development candidates, all of which are vaccines against viruses. The potential advantages of an mRNA approach to prophylactic vaccines include the ability to mimic natural infection to stimulate a more potent immune response, combining multiple mRNAs into a single vaccine, rapid discovery to respond to emerging pandemic threats and manufacturing agility derived from the platform nature of mRNA vaccine design and production.

Moderna currently has five development candidates for potential commercial uses in this modality, including: respiratory syncytial virus (RSV) vaccine (mRNA-1777 and mRNA-1172 or V172 with Merck), cytomegalovirus (CMV) vaccine (mRNA-1647), human metapneumovirus and parainfluenza virus type 3 (hMPV+PIV3) vaccine (mRNA-1653) and Zika vaccine (mRNA-1893) with the Biomedical Advanced Research and Development Authority (BARDA). Three development candidates in this modality are being explored for potential global health uses including: influenza H10N8 vaccine (mRNA-1440), influenza H7N9 vaccine (mRNA-1851) and chikungunya vaccine (mRNA-1388) with the Defense Advanced Research Projects Agency

(DARPA).

To date, Moderna has demonstrated positive Phase 1 data readouts for six prophylactic vaccines (H10N8, H7N9, RSV, chikungunya virus, hMPV+PIV3 and CMV). Moderna's investigational Zika vaccine (mRNA-1893), currently in a Phase 1 study, was [recently granted FDA Fast Track designation](#).

### R&D Day Webcast Today

The Company also [announced](#) positive Phase 1 data for mRNA-1944 (mRNA encoding for antibody against chikungunya virus) today. A summary of data from both of these Phase 1 trials will be presented at the Company's annual R&D Day, being held today in New York City beginning at 8:30 a.m. ET. A live webcast will be available under "Events & Presentations" in the Investors section of the Moderna website at <https://investors.modernatx.com>. A replay of the webcast will be archived on Moderna's website for 30 days following the presentation.

### About Moderna

Moderna is advancing messenger RNA (mRNA) science to create a new class of transformative medicines for patients. mRNA medicines are designed to direct the body's cells to produce intracellular, membrane or secreted proteins that can have a therapeutic or preventive benefit and have the potential to address a broad spectrum of diseases. Moderna's platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, providing the Company the capability to pursue in parallel a robust pipeline of new development candidates. Moderna is developing therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases and cardiovascular diseases, independently and with strategic collaborators.

Headquartered in Cambridge, Mass., Moderna currently has strategic alliances for development programs with AstraZeneca, Plc. and Merck, Inc., as well as the Defense Advanced Research Projects Agency (DARPA), an agency of the U.S. Department of Defense; the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS). Moderna has been ranked in the top ten of *Science's* list of top biopharma industry employers for the past four years. To learn more, visit [www.modernatx.com](http://www.modernatx.com).

### Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended including, but not limited to, statements concerning: advancing mRNA-1647 into a dose-confirmation Phase 2 study; preparation for a pivotal Phase 3 study of mRNA-1647 against primary CMV infection; the potential blockbuster commercial opportunity for mRNA-1647; the potential for Moderna's vaccine platform to support its future growth; and mRNA-1647's potential to protect against CMV infection and prevent congenital CMV infection. In some cases, forward-looking statements can be identified by terminology such as "will," "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 press release 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, among others: whether the interim results for mRNA-1647 will be predictive of the final results for the ongoing study or any future clinical studies; whether mRNA-1647 will be unsafe or intolerable during further clinical studies; the fact that clinical development is lengthy and uncertain, especially for a new class of medicines such as mRNA, and therefore our clinical programs or development candidates may be delayed, terminated, or may never advance; no mRNA drug has been approved in this new potential class of medicines, and may never be approved; mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new class of medicines; and those risks and uncertainties described under the heading "Risk Factors" 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 the SEC, which are available on the SEC's website [www.sec.gov](http://www.sec.gov). Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements in this press release 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 hereof.

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<sup>1</sup>Centers for Disease Control and Prevention.

<sup>2</sup> McVoy, Michael A. Cytomegalovirus vaccines. *Clinical Infectious Diseases*. 2013; 57(Suppl 4): S196-S199.

<sup>3</sup> Congenital CMV and Hearing Loss. Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/cmV/hearing-loss.html>.

<sup>4</sup> Schleiss et al. Progress toward development of a vaccine against congenital cytomegalovirus infection. *Clinical and Vaccine Immunology*. 2017; 24(12): e00268-17.

<sup>5</sup> Congenital CMV and Birth Defects. American Pregnancy Association. Available at: <https://americanpregnancy.org/birth-defects/congenital-cmv-birth-defects/>.

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Source: Moderna, Inc.

Moderna Contacts:

#### Media:

Colleen Hussey  
Senior Manager, Corporate Communications  
203-470-5620  
[Colleen.Hussey@modernatx.com](mailto:Colleen.Hussey@modernatx.com)

Dan Budwick

1AB  
973-271-6085  
[dan@1abmedia.com](mailto:dan@1abmedia.com)

Investors:  
Lavina Talukdar  
Head of Investor Relations  
617-209-5834  
[Lavina.Talukdar@modernatx.com](mailto:Lavina.Talukdar@modernatx.com)