



## Moderna Announces Additional Positive Phase 1 Data from Cytomegalovirus (CMV) Vaccine (mRNA-1647) and First Participant Dosed in Phase 2 Study

January 9, 2020

*New interim analysis after third and final vaccination shows continued boosting of neutralizing antibody titers in both seronegative participants (exceeding seropositive baseline levels 10-fold at 90 and 180 µg) and seropositive participants (exceeding baseline levels by 20- to 40-fold at 90 and 180 µg)*

*Phase 2 interim data at three months, expected in 2H 2020, intended to inform Phase 3 dose selection*

*Pivotal Phase 3 study manufacturing and planning already underway; study start expected in 2021*

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

*Conference call to be held at 8:00 a.m. ET on Friday, January 10, 2020*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 9, 2020-- 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 seven-month interim safety and immunogenicity data after the third and final vaccination in the Phase 1 study of its investigational cytomegalovirus (CMV) vaccine (mRNA-1647). The findings build on the previously reported three-month interim analysis, after two vaccinations, [announced](#) at the Company's R&D Day in September 2019. Additionally, the Company announced that the first participant was dosed in the Phase 2 dose-confirmation study. mRNA-1647 is a wholly owned program in Moderna's prophylactic vaccines portfolio.

"Prevention of CMV in women of childbearing age is an urgent unmet need, which we believe positions our wholly owned mRNA-1647 program as a potential blockbuster commercial opportunity. mRNA-1647 is the first mRNA vaccine for an infectious disease to enter a Phase 2 clinical trial," said Stéphane Bancel, Moderna's chief executive officer. "These new data, after the third vaccination, represent another critical clinical milestone in our CMV vaccine program and we are extremely pleased with this continued progress as we move into late-stage development, prepare for a pivotal Phase 3 study as quickly as possible and ensure commercial readiness."

mRNA-1647 comprises six mRNAs encoding two antigens in one vaccine, and is designed to protect against CMV infection. Of the six mRNAs, five encode the subunits of the CMV pentamer complex and one mRNA encodes the glycoprotein B (gB) protein, both of which are highly immunogenic. Both pentamer and gB proteins are essential for CMV to enter epithelial cells, which is the first step in CMV infection. mRNA-1647 is designed to produce an immune response to both pentamer and gB antigens to prevent CMV infection.

The second interim analysis of the Phase 1 trial reports safety and immunogenicity of the first three dose levels (30, 90 and 180 µg) through seven months (one month after the third vaccination) and the highest dose level (300 µg) through three months (one month after the second vaccination). Neutralizing antibody titers were assessed in two assays utilizing epithelial cells and fibroblasts, which measure immune response to pentamer and gB antigens, respectively.

Safety data were consistent with those reported at the three-month interim analysis. The vaccine was generally well-tolerated and there were no vaccine-related serious adverse events (SAEs). The most common solicited local adverse reaction (AR) across all vaccinations was injection site pain (54-100% of a given treatment group). The most common solicited systemic ARs reported overall were headache, fatigue, myalgia and chills. Fever was reported in 0-55% of CMV-seronegative treatment groups and in 8-67% of CMV-seropositive treatment groups. The most common Grade 3 solicited ARs were in CMV-seropositive participants, and were fatigue (0-27% of a given treatment group), chills (0-27% of a given treatment group) and fever (0-33% of a given treatment group). In general, the highest solicited systemic AR rates were reported after the second vaccination, were more frequent in the CMV-seropositive compared to the CMV-seronegative group, and tended to correlate to dose. As reported in the previous interim analysis, one related Grade 4 adverse event (AE) has been observed, which was 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.

In the CMV-seronegative group at seven months:

- Neutralizing antibody titers continued to increase after the third vaccination in both epithelial cell and fibroblast assays.
- Neutralizing antibody titers against epithelial cell infection were greater than 10-fold higher than CMV-seropositive baseline titers at the 90 and 180 µg dose levels after the third vaccination, compared to 3-fold to 5-fold higher after the second vaccination.
- Neutralizing antibody titers against fibroblast infection increased to 1.4-fold higher than CMV-seropositive baseline titers at the 90 and 180 µg dose levels after the third vaccination, compared to titers that were comparable to CMV-seropositive baseline titers after the second vaccination.

In the CMV-seropositive group at seven months:

- Neutralizing antibody titers continued to increase after the third vaccination in both epithelial cell and fibroblast assays.
- Third vaccination boosted neutralizing antibody titers against epithelial cell infection to levels of 22-fold to 40-fold over baseline across treatment groups, compared to 10-fold to 19-fold over baseline after the second vaccination.
- Third vaccination boosted neutralizing antibody titers against fibroblast infection to levels of 4-fold to 6-fold over baseline across treatment groups, compared to 2-fold to 4-fold over baseline after the second vaccination.

Samples from a subset of CMV-seronegative participants from the 30, 90 and 180 µg dose levels demonstrated T-cell reactivity against the gB antigen at all doses. Pentamer-based T-cell assays remain in development.

This interim analysis also reports the first data from the 300 µg dose level through three months (one month after the second vaccination), which continued to show consistent dose-dependent increases in neutralizing antibodies against epithelial cell infection and against fibroblast infection in both CMV-seronegative and CMV-seropositive participants. Safety and tolerability at the 300 µg dose level was comparable to that observed at the 180 µg dose level.

“These data are significant because they show that after a third dose, mRNA-1647 continues to increase durable immune responses that exceed the levels of those with natural CMV infection,” said Tal Zaks, M.D., Ph.D., chief medical officer at Moderna. “There is no approved vaccine to prevent CMV infection despite repeated attempts over the last 50 years. With mRNA-1647, which encodes for both the pentamer and gB antigens, we believe we can significantly reduce the burden of CMV infection, including in women of childbearing age.”

The findings from this interim analysis build on the previously reported interim analysis of safety and immunogenicity through one month after the second vaccination in the three lower dose levels [announced](#) at the Company’s R&D Day in September 2019. A 12-month interim analysis is planned, which will report safety and immunogenicity through six months after the third vaccination.

### **First Participant Dosed in Phase 2 Study**

The first participant has been dosed in the randomized, observer-blind, placebo-controlled, dose-confirmation Phase 2 study, which will investigate the safety and immunogenicity of mRNA-1647 in approximately 252 healthy adults in the U.S. at three dose levels (50, 100 and 150 µg) in both CMV-seronegative and CMV-seropositive participants administered in a three-dose vaccination schedule (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 the Phase 1 study. The first interim analysis will evaluate safety and immunogenicity at three months (one month after the second vaccination) and is intended to inform Phase 3 dose selection. mRNA-1647 is the first mRNA vaccine for an infectious disease to enter a Phase 2 clinical trial.

### **About the Planned Phase 3 Study**

With the seven-month Phase 1 data and the launch of the Phase 2 study, the Company is actively preparing for a global randomized, observer-blind, placebo-controlled Phase 3 pivotal study to evaluate the efficacy of mRNA-1647 against primary CMV infection. Moderna has solicited and received Type C meeting feedback from the FDA on the preliminary design of the pivotal trial, which will evaluate prevention of primary CMV infection in a population that includes women of childbearing age. The Company believes this can be achieved with a trial with no more than 8,000 participants and feasibility assessments of study sites has already begun across North America and Europe. After the Phase 2 three-month data are analyzed, which is expected in the second half of 2020, these data will inform the dose selection for the Phase 3 pivotal study. The pivotal trial design will be finalized after discussion with the FDA and other global health authorities. Manufacturing and planning are already underway for the pivotal Phase 3 study, which is expected to start in 2021.

### **Conference Call**

Moderna will host a conference call and webcast on Friday, January 10, 2020 at 8:00 a.m. ET to discuss these new data. To access the call, please dial 866-922-5184 (domestic) or 409-937-8950 (international) and refer to conference ID 2684775. A live webcast of the call will also be available under “Events and Presentations” in the Investors section of the Moderna website at <https://investors.modernatx.com>. The archived webcast will be available on Moderna’s website approximately two hours after the conference call and will be available for 30 days following the call.

### **About mRNA-1647**

mRNA-1647 comprises six mRNAs encoding two antigens in one vaccine, and is designed to protect against CMV infection. Of the six mRNAs, five encode the subunits of the CMV pentamer complex and one mRNA encodes the glycoprotein B (gB) protein, both of which are highly immunogenic. The pentamer complex is important for CMV entry into a variety of cells, including epithelial cells, while gB is important for entry into all susceptible cells including fibroblasts. A vaccine that produces an immune response against both pentamer and gB has the potential to prevent CMV entry into a range of target cell types and thus prevent primary and congenital infections. Unlike a protein-based vaccine, mRNA-1647 instructs the body’s own cells to manufacture the antigens, resulting in functional antigens that mimic those presented to the immune system by CMV 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 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>1,2</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>3</sup> There is currently no approved vaccine for the prevention of CMV infection.

CMV is spread through saliva, breastmilk, 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 seven programs, 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 available 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](#). More than 1,000 participants have been enrolled in Moderna's infectious disease clinical studies.

## 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 named a top biopharmaceutical employer by *Science* for the past five 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, initiating clinical trial sites outside of the U.S. for mRNA-1647; planning for a pivotal Phase 3 study for mRNA-1647; exploration of three development candidates for potential global health; and the Company's belief that it can reduce the burden of CMV infection, including in women of childbearing age. 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: the results and timing of the Phase 2 study; the results of testing the Phase 3 formulation; the timing of the proposed Phase 3 study 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 at [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 contained 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> Congenital CMV and Hearing Loss. Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/cmV/hearing-loss.html>.

<sup>2</sup> Schleiss et al. Progress toward development of a vaccine against congenital cytomegalovirus infection. *Clinical and Vaccine Immunology*. 2017; 24(12): e00268-17.

<sup>3</sup> Congenital CMV and Birth Defects. American Pregnancy Association. Available at: <https://americanpregnancy.org/birth-defects/congenital-cmv-birth-defects/>.

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