



## Moderna Announces Publication in The New England Journal of Medicine of Interim Results From Older Adult Age Cohorts in Phase 1 Study of its mRNA Vaccine Against COVID-19 (mRNA-1273)

September 29, 2020

*mRNA-1273 induced consistently high levels of pseudovirus neutralization antibody titers in all participants in the 56-70 (n=10) and 71+ (n=10) age cohorts*

*Potent neutralization responses were confirmed by 3 different live virus assays*

*mRNA-1273 elicited Th1-biased CD4 T cell responses in the 56-70 and 71+ age cohorts*

*Neutralizing antibody titers and T cell responses in the 56-70 and 71+ age cohorts were consistent with those reported in younger adults*

*At the 25 µg and 100 µg dose levels, mRNA-1273 was generally well-tolerated in all age cohorts*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 29, 2020-- Moderna, Inc., (Nasdaq: MRNA) a biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced the publication of the second interim analysis of the open-label Phase 1 study of mRNA-1273, its vaccine candidate against COVID-19, in [The New England Journal of Medicine](#). This interim analysis evaluated a two-dose vaccination schedule of mRNA-1273 given 28 days apart in 40 healthy adult participants across two dose levels (25 and 100 µg) in two age cohorts (ages 56-70 and ages 71+), and reports results through Day 57 (1 month after the second dose). This analysis found that both the 25 µg and 100 µg dose levels were generally well-tolerated in both age cohorts. Immune responses were dose-dependent with the 100 µg dose eliciting higher binding and neutralizing antibody titers, supporting the selection of the 100 µg dose for further study in the Phase 3 trial. The study was led by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH).

"These interim Phase 1 data suggests that mRNA-1273, our vaccine candidate for the prevention of COVID-19, can generate neutralizing antibodies in older and elderly adults at levels comparable to those in younger adults," said Tal Zaks, M.D., Ph.D., Chief Medical Officer of Moderna. "Given the increased morbidity and mortality of COVID-19 in older and elderly adults, these data give us optimism in demonstrating mRNA-1273's protection in this population, which is being evaluated in the Phase 3 COVE study."

Both the 25 µg and 100 µg dose levels of mRNA-1273 were generally well-tolerated, with no serious adverse events reported through Day 57. The most common solicited adverse events were headache, fatigue, myalgia, chills, and pain at the injection site, the majority of which were mild-to-moderate in severity and of self-limited duration. Local and systemic reactogenicity were more common and more frequently moderate in severity after the second dose. Two severe solicited systemic adverse events occurred following the second vaccination: fever in one participant in the ages 56-70 cohort who received the 25 µg dose and fatigue in one participant in the ages 71+ cohort who received the 100 µg dose. Clinical laboratory values of Grade 2 or higher revealed no pattern of concern. Participants will continue to be followed through 13-months to allow for a longer assessment of vaccine-related adverse events.

At both the 25 µg and 100 µg dose levels, after two vaccinations, mRNA-1273 induced dose-dependent binding antibody responses reaching the upper quartile of the distribution of convalescent sera. At Day 57 (1 month post-dose 2), geometric mean titers (GMT) exceeded the median of those seen in convalescent sera from 41 individuals with confirmed COVID-19 diagnosis.

Neutralizing activity was assessed with multiple assays, including a pseudovirus neutralization assay (pseudotyped lentivirus reporter single-round-of-infection neutralization assay [PsvNA]) against the two most common SARS-CoV-2 variants (614D and 614G) and three live-virus neutralization assays (SARS-CoV-2 nanoluciferase high-throughput neutralization assay [nLUC HTNA], focus reduction neutralization test mNeonGreen [FRNT-mNG] and classical plaque-reduction neutralization test [PRNT]). No participants had detectable neutralizing responses by any assay prior to vaccination, and robust neutralizing activity was observed in all participants 14 days after the second vaccination.

Pseudovirus neutralization responses were observed as early as seven days after the second vaccination and were dose-dependent across all age groups (18-55, 56-70 and 71+). At Day 43 at the 100 µg dose level, PsvNA ID<sub>50</sub> titers in the older adult cohorts ages 56-70 (GMT 402) and 71+ (GMT 317) were comparable to those seen in the age 18-55 cohort (GMT 360), and 3- to 4-fold higher than those seen in convalescent sera (GMT 106). Titers remained high through four weeks after the second dose in all age cohorts. Neutralizing activity against the 614G variant was also observed at the 100 µg dose in all age cohorts.

Results were consistent using 3 live virus assays. Neutralizing antibody titers as measured by nLUC HTNA and FRNT-mNG were similar across all age groups (18-55, 56-70 and 71+). At Day 43, PRNT<sub>80</sub> GMT in the 100 µg dose groups was 878 in the 56-70 and 317 in the 71+ age cohort, representing 5.5 and 2.0-fold above convalescent sera respectively, and 4.1-fold above convalescent sera in the 18-55 age group (GMT 654).

The 25 µg dose in the 56-70 age cohort and the 100 µg dose level across all age groups (18-55, 56-70 and 71+) elicited a strong Th1-biased CD4 T cell response.

The U.S. government has agreed to purchase 100 million doses of mRNA-1273, with an option to purchase an additional 400 million doses.

### About mRNA-1273

mRNA-1273 is an mRNA vaccine against COVID-19 encoding for a [prefusion stabilized](#) form of the Spike (S) protein, which was co-developed by Moderna and investigators from the National Institute of Allergy and Infectious Disease's (NIAID) Vaccine Research Center. The first clinical batch, which was funded by the Coalition for Epidemic Preparedness Innovations, was completed on February 7, 2020 and underwent analytical testing; it was shipped to the National Institutes of Health (NIH) on February 24, 42 days from sequence selection. The first participant in the NIAID-led Phase 1 study of mRNA-1273 was dosed on March 16, 63 days from sequence selection to Phase 1 study dosing. On May 12, the FDA granted mRNA-1273

Fast Track designation. On May 29, the first participants in each age cohort: healthy adults ages 18-55 years (n=300) and older adults ages 55 years and above (n=300) were dosed in the Phase 2 study of mRNA-1273. On July 8, the [Phase 2 study](#) completed enrollment.

The [Phase 3 COVE study](#) of mRNA-1273, being conducted in collaboration with the NIH and BARDA, began on July 27. Results from a non-human primate preclinical viral challenge study evaluating mRNA-1273 were recently [published](#) in *The New England Journal of Medicine*. On July 14, an interim analysis of the original cohorts in the NIH-led Phase 1 study of mRNA-1273 was [published](#) in *The New England Journal of Medicine*. A summary of the company's work to date on COVID-19 can be found [here](#).

The Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS), is supporting the continued research and development of mRNA-1273 with \$955 million in federal funding under Contract no. 75A50120C00034. BARDA is reimbursing Moderna for 100 percent of the allowable costs incurred by the company for conducting the program described in the BARDA contract. The U.S. government has committed up to \$1.525 billion to purchase supply of mRNA-1273 under U.S. Department of Defense Contract No. W911QY-20-C-0100.

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

Moderna scientists designed the company's prophylactic vaccines modality to prevent infectious diseases. More than 1,900 participants, prior to enrolling the Phase 3 study of mRNA-1273, have been enrolled in Moderna's infectious disease vaccine clinical studies under health authorities in the U.S., Europe and Australia. Clinical data demonstrate that Moderna's proprietary vaccine technology has been generally well-tolerated and can elicit durable immune responses to viral antigens. Based on clinical experience across Phase 1 studies, the company designated prophylactic vaccines a core modality and is working to accelerate the development of its vaccine pipeline.

The potential advantages of an mRNA approach to prophylactic vaccines include the ability to combine 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 has built a fully integrated manufacturing plant which enables the promise of the technology platform.

Moderna currently has [nine development candidates](#) in its prophylactic vaccines modality, including:

#### *Vaccines against respiratory infections*

- Respiratory syncytial virus (RSV) vaccine for older adults (mRNA-1777 and mRNA-1172 or V172 with Merck)
- RSV vaccine for young children (mRNA-1345)
- Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) vaccine (mRNA-1653)
- COVID-19 vaccine (mRNA-1273)
- Influenza H7N9 vaccine (mRNA-1851)

#### *Vaccines against infections transmitted from mother to baby*

- Cytomegalovirus (CMV) vaccine (mRNA-1647)
- Zika vaccine (mRNA-1893 with BARDA)

#### *Vaccines against highly prevalent viral infections*

- Epstein-Barr virus (EBV) vaccine (mRNA-1189)

To date, Moderna has demonstrated positive Phase 1 data readouts for eight prophylactic vaccines (H10N8, H7N9, RSV, chikungunya virus, hMPV/PIV3, CMV, Zika and COVID-19). Moderna's CMV vaccine is currently in a Phase 2 dose-confirmation study. Moderna's investigational Zika vaccine (mRNA-1893), currently in a Phase 1 study, was granted FDA Fast Track designation in August 2019.

### **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, cardiovascular diseases, and autoimmune and inflammatory diseases, independently and with strategic collaborators.

Headquartered in Cambridge, Mass., Moderna currently has strategic alliances for development programs with AstraZeneca PLC and Merck & Co., 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) and the Coalition for Epidemic Preparedness Innovations (CEPI). 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).

### **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 the potential for mRNA-1273 to generate binding and neutralizing antibodies in older adults, the potential for adverse side effects from mRNA-1273, the U.S. government's potential purchases of mRNA-1273, the acceleration of the Company's development of its vaccine pipeline, and the potential benefits of mRNA-based prophylactic vaccine development. 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: preclinical and clinical development is lengthy and uncertain, especially for a new class of medicines such as mRNA, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance to or in the clinic; no commercial product using mRNA technology has been approved, 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; despite having ongoing interactions with the FDA or other regulatory agencies, the FDA or such other regulatory agencies may not agree with the Company's regulatory approval strategies, components of our filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted; the fact that the rapid response technology in use by Moderna is still being developed and implemented; the fact that the safety and efficacy of mRNA-1273 has not yet been established; potential adverse impacts due to the global COVID-19 pandemic such as delays in clinical trials, preclinical work, overall operations, regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy; and those risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Quarterly Report on Form 10-Q 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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