



Moderna COVID-19 Vaccine Retains Neutralizing Activity Against Emerging Variants First Identified in the U.K. and the Republic of South Africa

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Out of an abundance of caution, Moderna launches clinical program to boost immunity to emerging variants

Manuscript posted to preprint server; company to host conference call once manuscript is available

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 25, 2021-- [Moderna Inc.](#) (Nasdaq: MRNA), a biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines, today announced results from in vitro neutralization studies of sera from individuals vaccinated with Moderna COVID-19 Vaccine showing activity against emerging strains of SARS-CoV-2. Vaccination with the Moderna COVID-19 Vaccine produced neutralizing titers against all key emerging variants tested, including B.1.1.7 and B.1.351, first identified in the UK and Republic of South Africa, respectively. The study showed no significant impact on neutralizing titers against the B.1.1.7 variant relative to prior variants. A six-fold reduction in neutralizing titers was observed with the B.1.351 variant relative to prior variants. Despite this reduction, neutralizing titer levels with B.1.351 remain above levels that are expected to be protective. This study was conducted in collaboration with the Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). The manuscript has been submitted as a preprint to *bioRxiv* and will be submitted for peer-reviewed publication.

The two-dose regimen of the Moderna COVID-19 Vaccine at the 100 µg dose is expected to be protective against emerging strains detected to date. Nonetheless, Moderna today announced its clinical strategy to proactively address the pandemic as the virus continues to evolve. First, the Company will test an additional booster dose of its COVID-19 Vaccine (mRNA-1273) to study the ability to further increase neutralizing titers against emerging strains beyond the existing primary vaccination series. Second, the Company is advancing an emerging variant booster candidate (mRNA-1273.351) against the B.1.351 variant first identified in the Republic of South Africa. The Company is advancing mRNA-1273.351 into preclinical studies and a Phase 1 study in the U.S. to evaluate the immunological benefit of boosting with strain-specific spike proteins. Moderna expects that its mRNA-based booster vaccine (whether mRNA-1273 or mRNA-1273.351) will be able to further boost neutralizing titers in combination with all of the leading vaccine candidates.

"As we seek to defeat the COVID-19 virus, which has created a worldwide pandemic, we believe it is imperative to be proactive as the virus evolves. We are encouraged by these new data, which reinforce our confidence that the Moderna COVID-19 Vaccine should be protective against these newly detected variants," said Stéphane Bancel, Chief Executive Officer of Moderna. "Out of an abundance of caution and leveraging the flexibility of our mRNA platform, we are advancing an emerging variant booster candidate against the variant first identified in the Republic of South Africa into the clinic to determine if it will be more effective to boost titers against this and potentially future variants."

First detected in September 2020 in the United Kingdom, the SARS-CoV-2 B.1.1.7 variant has seventeen mutations in the viral genome with eight mutations located in the spike (S) protein. The B.1.351 variant, first detected in South Africa, has ten mutations located in the spike (S) protein. Both variants have spread at a rapid rate and are associated with increased transmission and a higher viral burden after infection^{1,2}.

The in vitro study assessed the ability of mRNA-1273 to elicit potently neutralizing antibodies against the new SARS-CoV-2 variants, using sera from eight Phase 1 clinical trial participants (aged 18-55 years) who received two 100 µg doses of mRNA-1273, and separately using sera from non-human primates (NHPs) immunized with two doses of 30 µg or 100 µg of mRNA-1273.

For the B.1.1.7 variant, neutralizing antibody titers remained high and were generally consistent with neutralizing titers relative to prior variants. No significant impact on neutralization was observed from either the full set of mutations found in the B.1.1.7 variant or from specific key mutations of concern. Although these mutations have been reported to lessen neutralization from convalescent sera and to increase infectivity, sera from the Phase 1 participants and NHPs immunized with mRNA-1273 were able to neutralize the B.1.1.7 variant to the same level as prior variants.

For the B.1.351 variant, vaccination with the Moderna COVID-19 Vaccine produces neutralizing antibody titers that remain above the neutralizing titers that were shown to protect NHPs against wildtype viral challenge. While the Company expects these levels of neutralizing antibodies to be protective, pseudovirus neutralizing antibody titers were approximately 6-fold lower relative to prior variants. These lower titers may suggest a potential risk of earlier waning of immunity to the new B.1.351 strains.

Conference Call and Webcast

Moderna will host a live conference call and webcast once the manuscript has posted on the *bioRxiv* preprint site. Conference call details will be announced separately.

About the Moderna COVID-19 Vaccine

The Moderna COVID-19 Vaccine (also referred to as 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 NIAID's 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 NIH on February 24, 2020, 42 days from sequence selection. The first participant in the NIAID-led Phase 1 study of the vaccine was dosed on March 16, 63 days from sequence selection to Phase 1 study dosing. On May 12, the FDA granted the Moderna COVID-19 Vaccine Fast Track designation. On May 29, the first participants in each age cohort: 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.

On July 14, an interim analysis of the original cohorts in the NIH-led Phase 1 study of the vaccine was [published](#) in *The New England Journal of Medicine*. On July 28, results from a non-human primate preclinical viral challenge study evaluating the vaccine were [published](#) in *The New England Journal of Medicine*. Results from the second interim analysis of the NIH-led Phase 1 study of the Moderna COVID-19 Vaccine in the 56-70 and 71+

age groups were [published](#) on September 29 in *The New England Journal of Medicine*. On November 30, Moderna [announced](#) the primary efficacy analysis of the Phase 3 study of the vaccine conducted on 196 cases. On November 30, the Company also announced that it filed for Emergency Use Authorization with the U.S. FDA and a Conditional Marketing Authorization (CMA) with the European Medicines Agency. On November 30, the Company [announced](#) new data showing that mRNA-1273, its COVID-19 vaccine candidate, remains stable at 2° to 8°C (36° to 46°F), the temperature of a standard home or medical refrigerator, for 30 days. On December 3, a [letter to the editor](#) was published in *The New England Journal of Medicine* reporting that participants in the Phase 1 study of the Moderna COVID-19 Vaccine retained high levels of neutralizing antibodies through 119 days following first vaccination (90 days following second vaccination). On December 18, 2020, the FDA authorized the emergency use of the Moderna COVID-19 Vaccine in individuals 18 years of age or older.

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 the Moderna COVID-19 Vaccine 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 agreed to purchase supply of the Moderna COVID-19 Vaccine under U.S. Department of Defense contract no. W911QY-20-C-0100.

Moderna has also received authorization for its COVID-19 vaccine from regulatory authorities in the United States, Canada, Israel, the European Union, the United Kingdom and Switzerland. Additional authorizations are currently under review in other countries and by the World Health Organization. A summary of the Company's work to date on COVID-19 can be found [here](#).

AUTHORIZED USE IN THE UNITED STATES:

The Moderna COVID-19 Vaccine has been [authorized](#) for emergency use by the U.S. Food and Drug Administration (FDA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

IMPORTANT SAFETY INFORMATION

- Do not administer the Moderna COVID-19 Vaccine to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of the Moderna COVID-19 Vaccine.
- Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Moderna COVID-19 Vaccine. Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (<https://www.cdc.gov/vaccines/covid-19/>).
- Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished response to the Moderna COVID-19 Vaccine.
- The Moderna COVID-19 Vaccine may not protect all vaccine recipients.
- Adverse reactions reported in a clinical trial following administration of the Moderna COVID-19 Vaccine include pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, axillary swelling/tenderness, fever, swelling at the injection site, and erythema at the injection site.
- Available data on Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion.
- There are no data available on the interchangeability of the Moderna COVID-19 Vaccine with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Moderna COVID-19 Vaccine should receive a second dose of Moderna COVID-19 Vaccine to complete the vaccination series.
- Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Moderna COVID-19 Vaccine.
- Vaccination providers must complete and submit reports to VAERS online at <https://vaers.hhs.gov/reportevent.html>. For further assistance with reporting to VAERS, call 1-800-822-7967. The reports should include the words " Moderna COVID-19 Vaccine EUA " in the description section of the report.

About Moderna

In 10 years since its inception, Moderna has transformed from a science research-stage company advancing programs in the promising-but-still-unproven field of messenger RNA (mRNA), to an enterprise with its first medicine having treated millions of people, a diverse clinical portfolio of vaccines and therapeutics across six modalities, a broad intellectual property portfolio in areas including mRNA and lipid nanoparticle formulation, and an integrated manufacturing plant that allows for both clinical and commercial production at scale and at unprecedented speed. Moderna maintains alliances with a broad range of domestic and overseas government and commercial collaborators, which has allowed for the pursuit of both groundbreaking science and rapid scaling of manufacturing. Most recently, Moderna's capabilities have come together to allow the authorized use of one of the earliest and most-effective vaccines against the COVID-19 pandemic.

Moderna's mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases and auto-immune diseases. Today, 24 development programs are underway across these therapeutic areas, with 13 programs having entered the clinic. Moderna has been named a top biopharmaceutical employer by *Science* for the past six years. To learn more, visit 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 statements regarding: the Company's development of a vaccine against the novel coronavirus (SARS-CoV-2); the potential for the Moderna COVID-19 Vaccine to prevent COVID-19 disease and slow the spread of SARS-CoV-2 by producing neutralizing titers against new, emerging strains of SARS-CoV-2, including the B.1.1.7 and B.1.351 variants; plans to test additional booster doses of the Moderna COVID-19 Vaccine against emerging strains of SARS-CoV-2; the Company's development of a new, strain-specific booster candidate (mRNA-1273.351) against SARS-CoV-2; the speed and flexibility with which the Company's mRNA technology can develop vaccines against new strains of the coronavirus; and the necessity of additional booster doses to address waning immunity to, and new variants of, the coronavirus. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "could," "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 fact that there has never been a commercial product utilizing mRNA technology approved for use; the fact that the rapid response technology in use by Moderna is still being developed and implemented; the safety, tolerability and efficacy profile of the Moderna COVID-19 Vaccine observed to date may change adversely in ongoing analyses of trial data or subsequent to commercialization; 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; Moderna may encounter delays in meeting manufacturing or supply timelines or disruptions in its distribution plans for the Moderna COVID-19 Vaccine; whether and when any biologics license applications and/or additional emergency use authorization applications may be filed in various jurisdictions and ultimately approved by regulatory authorities; potential adverse impacts due to the global COVID-19 pandemic such as delays in regulatory review, manufacturing and clinical trials, supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy; and those other 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. 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.

¹ Rambaut et al., 2020

² Tegally et al., 2020

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