



## Moderna Announces Positive Phase 1 Results for the First Systemic Messenger RNA Therapeutic Encoding a Secreted Protein (mRNA-1944)

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*mRNA-1944 successfully encoded for functional antibody (CHKV-24) in humans at all dose levels tested (0.1, 0.3 and 0.6 mg/kg)*

*Antibody level predicted to protect against chikungunya infection achieved within hours; projected to be maintained for at least 16 weeks at the middle and high doses*

*No significant adverse events were observed at the low and middle doses; infusion-related adverse events were observed at the high dose, which resolved spontaneously without treatment*

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 in the first analysis of safety and activity in its Phase 1 study evaluating escalating doses of mRNA-1944 administered via intravenous infusion in healthy adults. mRNA-1944 encodes for an antibody (CHKV-24) with activity against chikungunya virus. At all three dose levels, the administration of mRNA-1944 led to detectable levels of CHKV-24 antibody in all participants, ranging from 1 µg/mL to 14 µg/mL. These results mark the first systemic mRNA therapeutic to show production of a secreted protein in humans.

mRNA-1944 is being developed with financial support from the Defense Advanced Research Projects Agency (DARPA), an agency of the U.S. Department of Defense. mRNA-1944 is the first development candidate from the Company's systemic therapeutics modality to start clinical testing and utilizes the same lipid nanoparticle (LNP) formulation as the Company's rare disease program for methylmalonic acidemia (mRNA-3704).

A total of 22 healthy adults have been enrolled in the study to date. The initial analysis evaluated the safety and pharmacology of intravenous administration of mRNA-1944 at three dose levels of 0.1 mg/kg (n=6), 0.3 mg/kg (n=6) and 0.6 mg/kg (n=4); six participants received placebo.

Administration of mRNA-1944 resulted in dose-related increases in CHKV-24 antibody levels, with average C<sub>max</sub> antibody levels of 2.0, 7.9 and 10.2 µg/mL at the low, middle and high doses, respectively. At all doses, all participants exceeded the levels of antibody expected to be protective against chikungunya infection (> 1 µg/mL) following a single dose, with the middle and high doses projected to maintain antibody levels above protective levels for at least 16 weeks. All participants also showed circulating neutralizing antibody activity against chikungunya virus replication in an NT50 assay, demonstrating that mRNA-1944 resulted in the production of fully functional protein *in vivo*.

All participants in the study received antihistamine premedication. No participants received corticosteroids either as premedication or treatment.

None of the participants treated with mRNA-1944 at the low (0.1 mg/kg) or middle (0.3 mg/kg) doses experienced significant adverse events (AEs). Three of the four participants at the high (0.6 mg/kg) dose had infusion-related AEs, with the highest grade by subject being Grade 1 (n=1), Grade 2 (n=1) and Grade 3 (n=1). The Grade 3 AEs were tachycardia and an elevated white blood cell count. The same participant experienced Grade 2 AEs of nausea, emesis, fever and inverted T waves on a routine EKG (without associated cardiac symptoms and which later resolved). The fourth participant at the high dose had no related adverse events. There were no meaningful changes in liver or kidney laboratory results. There have been no serious AEs in the study. All AEs were transient and resolved spontaneously without treatment.

"These Phase 1 data represent a significant scientific breakthrough: this study shows for the first time the ability to generate therapeutic levels of a complex protein in humans through systemic administration of an mRNA, essentially instructing the body to make its own medicines," said Tal Zaks, M.D., Ph.D., chief medical officer at Moderna. "The findings not only show the potential of mRNA-1944 to protect against chikungunya infection at a well-tolerated dose, but also the ability of our platform to translate therapeutically relevant pharmacology from preclinical species to humans."

This is an interim analysis of an ongoing study. At this time, the Company has not enrolled the last two participants at the 0.6 mg/kg dose. The Company is evaluating further exploration of the safety and pharmacology of mRNA-1944, which may include repeat dosing or dosing in combination with commonly used steroid premedications to prevent infusion-related reactions.

CHKV-24, the antibody encoded by mRNA-1944, was isolated from B cells of a patient with potent immunity against chikungunya infection by scientists at Vanderbilt University Medical Center. mRNA-1944 is composed of two mRNAs that encode respectively for the heavy and light chains of CHKV-24 that are formulated within Moderna's proprietary LNP technology for systemic intravenous injection.

"Protection against infectious diseases like chikungunya is urgently needed around the world. While we are often able to identify protective antibodies to emerging infections, a major challenge is the ability to rapidly scale such discoveries into humans," said James Crowe Jr., M.D., director of the Vanderbilt Vaccine Center. "These exciting data demonstrate a new way to address infectious diseases that uses mRNA to make antibodies in humans, establishing a powerful technology that could be deployable in a pandemic setting."

"DARPA has been advancing nucleic-acid-based technologies for infectious disease for several years, and the results of this clinical trial validate that approach," said Dr. Amy Jenkins, the DARPA program manager supporting the research. "The researchers have demonstrated that it is feasible to use mRNA sequences to produce and scale a highly potent antibody response against an infectious disease target. DARPA is encouraged by the prospects of creating a new, platform-based prophylactic and therapeutic approach that might better protect civilians and service members alike against the relentless threat of pandemic disease."

DARPA's financial support of mRNA-1944 is part the Agency's ADEPT: PROTECT (Autonomous Diagnostics to Enable Prevention and Therapeutics: Prophylactic Options to Environmental and Contagious Threats) initiative. The goal is to develop platform technologies that can be deployed safely and rapidly to provide the U.S. population with near-immediate protection against emerging infectious diseases and engineered biological weapons, even in cases when the pathogen or infectious agent is unknown. For more information about DARPA, visit <http://www.darpa.mil/about-us/about->

[darpa](#).

"These data represent another critical milestone for the validation of Moderna's mRNA platform in humans," said Stéphane Bancel, Moderna's chief executive officer. "This is the fifth modality for which we have shown translation from preclinical research to humans and the first demonstration of mRNA as a systemic therapeutic capable of creating high levels of protein at a well-tolerated dose. We believe these results further validate our approach, the scientific platform we have built and the potential of mRNA to become a new class of medicines. We look forward to learning from the ongoing Phase 1/2 study of mRNA-3704 for methylmalonic acidemia, the first of our rare disease programs to enter the clinic, as it utilizes the same technology demonstrated in this chikungunya study."

### **About the Study**

The randomized, placebo-controlled Phase 1 study is designed to evaluate the safety and tolerability of up to four escalating doses (0.1, 0.3, 0.6 and 1 mg/kg) of mRNA-1944 administered via intravenous infusion to healthy adults. Secondary objectives are to determine the pharmacology of mRNA-1944 and to evaluate whether the antibodies produced neutralize chikungunya virus *in vitro*, thereby confirming the potential for passive immunization of individuals via the production of functional circulating antibody. Passive immunity provides transient but rapid protection against an infectious disease and is particularly important when immediate protection is needed, such as in a pandemic setting.

More information about the study can be found at [ClinicalTrials.gov](#). Full Phase 1 data will be presented at a future medical meeting.

### **About mRNA-1944**

mRNA-1944 encodes a fully human IgG antibody originally isolated from B cells of a patient with a prior history of potent immunity against chikungunya infection. It is composed of two mRNAs that encode the heavy and light chains of this anti-chikungunya antibody within Moderna's proprietary lipid nanoparticle (LNP) technology. [Preclinical data](#) published in *Science Immunology* have shown mRNA-1944 was well-tolerated, resulted in linear dose-dependent protein expression and provided 100% protection in animal models.

### **About Chikungunya**

Chikungunya is a mosquito-borne virus that poses a significant public health problem in tropical and subtropical regions. The disease is characterized by an acute onset of fever, rash, muscle pain and sometimes debilitating pain in multiple joints. There are no vaccines approved to prevent chikungunya infection or disease, and effective mosquito control is challenging. Currently, people infected with chikungunya are treated with non-steroidal anti-inflammatory drugs to relieve some symptoms. In addition to a systemic secreted antibody that could provide passive immunity, Moderna is also exploring using mRNA to encode viral antigens as a prophylactic vaccine against the chikungunya virus (mRNA-1388).

### **R&D Day Webcast Today**

Moderna also [announced](#) positive interim Phase 1 data for mRNA-1647 (cytomegalovirus or CMV vaccine) today. A summary of data from both the antibody against chikungunya virus and CMV vaccine programs 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 have a therapeutic or preventive benefit with 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 and 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: predicted levels to protect against chikungunya infection; projected protection against chikungunya infection for at least sixteen weeks at the 0.3 and 0.6 mg/kg doses of mRNA-1944; Moderna's evaluation of whether to further explore the safety and pharmacology of mRNA-1944, which may include repeat dosing or dosing in combination with commonly used steroid pre-medications to prevent infusion reactions; the Phase 1 results for mRNA-1944 as an indicator of the potential of mRNA-1944 to protect against chikungunya virus infection and the ability of Moderna's platform to translate therapeutically relevant pharmacology from preclinical species to humans; and the potential of mRNA-based vaccines as powerful technology that could be deployable in a pandemic setting. 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: whether the Phase 1 results for mRNA-1944 will be predictive of any future clinical studies for mRNA-1944 or other development candidates with the same or similar LNP formulation, including mRNA-3704 for methylmalonic acidemia; whether mRNA-1944 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 Moderna's 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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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  
Founder, 1AB Media  
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)