Moderna Announces Positive Interim Phase 1 Clinical Data Demonstrating First mRNA Vaccine Candidate, mRNA-1440, Induces High Levels of Immunogenicity

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100% of subjects in 100 µg intramuscular (IM) cohort achieved HAI titers that are accepted correlate of seroprotection against seasonal flu

mRNA-1440 safe and well tolerated; tolerability consistent with approved vaccines

Data published in the journal Molecular Therapy; First human proof-of-concept data from Moderna's novel mRNA platform

CAMBRIDGE, Mass., April 27, 2017 — Moderna Therapeutics, a clinical stage biotechnology company that is pioneering messenger RNA (mRNA) Therapeutics™ to create a new generation of transformative medicines for patients, todayannouncedpositive interim data from an ongoing Phase 1 study of mRNA-1440, an mRNA infectious disease vaccine against avian H10N8 influenza, demonstrating mRNA-1440 induced high levels of immunogenicity, and was safe and well tolerated. The findings were published online today in the journal *Molecular Therapy*.

Moderna is conducting a Phase 1 randomized, double-blind, placebo-controlled, dose-escalating study to evaluate the safety and immunogenicity of mRNA-1440 against H10N8 influenza in healthy adult subjects. H10N8 is a subtype of the influenza A virus, for which there are no approved vaccines.

In a 100 µg intramuscular (IM) cohort of 31 subjects (23 of whom received mRNA-1440 and eight of whom received placebo), mRNA-1440 demonstrated strong efficacy based on Hemagglutination Inhibition Assay (HAI) and Microneutralization Assay (MN) titers, two measures of immunogenicity in response to vaccination. 100% (n = 23) and 87% (n = 20) achieved titers consistent with protection at day 43 as measured by HAI titers and MN titers, respectively, compared to 0% in the placebo arm. The majority of adverse events were mild to moderate; three subjects who received mRNA-1440 (13%) experienced severe adverse events, which included injection-site reactions and common cold-like symptoms. These events were considered expected, and were manageable and reversible. There were no serious adverse events. Overall, mRNA-1440 was safe and well tolerated, and demonstrated a safety profile consistent with that of approved vaccines.

"We're highly encouraged by these data; they provide early evidence that our mRNA vaccine technology is safely and effectively directing the body's cells to produce and express viral antigenic proteins and elicit high levels of immunity that are expected to protect against viral infection," said Tal Zaks, M.D., Ph.D., Chief Medical Officer of Moderna. "Furthermore, they provide important validation of our core mRNA platform, as we continue to advance our development pipeline, tackling more complex vaccines including personalized cancer vaccines, and moving our mRNA therapeutics into clinical development."

These are the first human proof-of-concept data from Moderna's mRNA technology platform. In addition, they are the first-ever published data demonstrating a prophylactic mRNA vaccine's ability to elicit robust immunity in humans. The publication also included preclinical data demonstrating that mRNA-1440 and Moderna's second mRNA vaccine program, mRNA-1851 against avian H7N9 influenza, both generated strong protective immunity in mice, ferrets and non-human primates, demonstrating that Moderna's platform technology translated across species from small animals to large animals to humans.

"These human proof-of-concept data mark a crucial milestone for Moderna as we work to advance the potential of mRNA vaccines and therapeutics to translate into clinical benefit across a breadth of diseases and unmet needs. Importantly, these published data also represent continued progress for the emerging field of mRNA science as a whole, as we explore the viability and expansive promise of this entirely new class of medicines," said Stéphane Bancel, Chief Executive Officer of Moderna. "We look forward to completing this study and sharing the full data results in 2018, and to reporting other preclinical and clinical milestones related to our development pipeline this year."

About the Study Design

Moderna is conducting a Phase 1 randomized, double-blind, placebo-controlled, dose-escalating study to evaluate the safety and immunogenicity of mRNA-1440 against H10N8 influenza in healthy adult subjects. H10N8 is a subtype of the Influenza A virus, for which there are no approved vaccines. The primary endpoint of the study was safety and tolerability, with immunogenicity measured by Hemagglutination Inhibition Assay (HAI) and Microneutralization Assay (MN), as additional exploratory endpoints. The Phase 1 study was designed to evaluate two doses of mRNA (prime + boost) at Day 1 and Day 22 in healthy volunteers. HAI titers and MN titers were measured at Day 43.

The study, which began dosing healthy volunteers in December 2015, and is being run by PAREXEL (NASDAQ: PRXL) at its Berlin, Germany site, has completed enrollment, with 201 healthy volunteers enrolled. The study remains active, with subjects continuing to be followed. Upon study completion and data analysis in 2018, Moderna plans to publish full study findings.

About the Interim Results

The interim results announced and published today were obtained 43 days post-vaccination of 31 subjects, 23 of whom received mRNA-1440 at 100 µg intramuscularly and 8 of whom received placebo.

Immunogenicity Findings

- 100% of subjects who received mRNA-1440 (n = 23) achieved a 1:40 HAI titer, compared to 0% of placebo subjects.
- 78% (n = 23) had a 4x HAI increase from baseline, compared to 0% of placebo subjects.
    - HAI titers of 1:40 or an HAI increase of 4x from baseline are expected to be protective in seasonal flu vaccines.
- 87% of subjects who received mRNA-1440 (n = 20) achieved a 1:20 MN titer, compared to 0% of placebo subjects.

- 87% (n = 20) achieved a 4x MN increase from baseline, compared to 0% of placebo subjects.
    - MN titers of 1:20 or an MN increase of 4x from baseline are expected to be protective.

Safety Findings

- The vaccine was safe and well tolerated, with tolerability consistent with other approved vaccines.
- The majority of adverse events (AEs) were mild (107/163 events; 66%) or moderate (52/163 events; 32%), using the FDA Center for Biologics Evaluation and Research (CBER) AE severity scale. [1]
- The majority of AEs included injection-site pain, myalgia, headache, fatigue and chills/common cold-like symptoms.
- Four events (accounting for 2.5% of all events) that occurred in 3 subjects (13% of subjects) were categorized as severe and included injection-site erythema (redness of the skin, 1.2%), injection-site induration (hardening, 0.6%), and chills/common cold-like symptoms (0.6%). These were expected and reversible.
- No serious adverse events were observed.

Currently there are four Phase 1 mRNA vaccine studies and one Phase 1 mRNA therapeutic study underway utilizing Moderna's mRNA platform technology. To date, more than 450 healthy volunteers have been dosed across these initial five clinical programs. Seven additional development candidates, including mRNA vaccines and mRNA therapeutics, are advancing toward clinical development. Moderna is advancing its development pipeline and research programs through proprietary development and collaborations with strategic partners, including AstraZeneca (NYSE: AZN), Merck (NYSE: MRK), Alexion Pharmaceuticals (NASDAQ: ALXN) and Vertex Pharmaceuticals (NASDAQ: VRTX).

ADDITIONAL DETAILS

About the Hemagglutination Inhibition Assay (HAI) and Microneutralization Assay (MN)

HAI measures the amount of antibodies specific for hemagglutinin (HA) that are generated by a subject in response to receiving a vaccine. HA is a viral antigenic protein. By binding to HA, antibodies inhibit HA binding to erythrocytes (red blood cells) and, thus, inhibit the formation of an insoluble red aggregate at the bottom of a test vessel. An HAI titer measures the maximum dilution in which binding is inhibited. HAI titers of at least 40 (1:40 diluted) are associated with at least a 50% reduction in risk for seasonal influenza; 1:40 is used by the U.S. Food and Drug Administration (FDA) as the approval endpoint for seasonal flu vaccines.

MN is a functional assay that measures whether a subject's serum prevents viral infection *in vitro*. MN titers measure the maximum dilution in which viral infection is inhibited. An MN titer of at least 20 (1:20 dilution) is thought to be clinically meaningful.

mRNA-1440 and mRNA-1851 – Enabling Rapid Assessment of Platform Safety and Efficacy

Moderna selected mRNA vaccines against H10N8 (mRNA-1440) and H7N9 (mRNA-1851), two Influenza A strains with pandemic potential, as its first development candidates (DCs) in order to rapidly assess the safety and efficacy of its mRNA platform in humans.

Because the H10N8 and H7N9 strains are not circulating in the general population where the trials are taking place (the U.S. and Germany), Moderna is able to study the efficacy of its vaccine technology in naïve patient populations. Therefore, the protective antibodies present in subjects' blood after treatment with mRNA-1440 and mRNA-1851 are likely attributed to Moderna's vaccines and not to active immunity as a result of previous exposure to the virus.

In addition, studying these influenza strains is allowing Moderna to measure vaccine efficacy against a well-understood endpoint, HAI titers. HAI is used by the FDA and the World Health Organization (WHO) to measure how well antibodies are predicted to inactivate an influenza virus. Vaccines demonstrating titers of 1:40 are considered effective in reducing the risk for influenza infection and are, thus, approved as seasonal flu vaccines.

About mRNA-1440 – Influenza A Virus Subtype H10N8 Vaccine

Influenza A subtype H10N8 has infected three people in China in 2013, resulting in two deaths. If H10N8 were to become a pandemic, there is no approved vaccine. A Phase 1 study of healthy volunteers conducted in Europe has completed enrollment, with a total of 201 subjects enrolled. The study remains active, with subjects continuing to be followed. Moderna plans to publish complete findings in 2018 upon completion of the study and full data analysis.

About mRNA-1851 – Influenza A Virus Subtype H7N9 Vaccine

Influenza A subtype H7N9 has a high potential of becoming a pandemic. As of April 12, 2017, nearly 1,440 cases have been confirmed and 545 deaths since February 2013.[2] There is no approved vaccine against this strain. A Phase 1 study of healthy volunteers is underway in the U.S. with 156 healthy volunteers dosed.

How mRNA-1440 and mRNA-1851 Work

Each day, trillions of mRNA deliver the genetic code the body's cells need to produce proteins. When used as a drug, mRNA can direct cells to produce therapeutic proteins (mRNA therapeutics) to fight disease or antigenic proteins (mRNA vaccines) to prevent disease.

mRNA-1440 and mRNA-1851 are mRNA vaccines that encode for the viral protein hemagglutinin as the antigen. The vaccines deliver mRNA encoding for hemagglutinin to the body's cells, directing them to produce and express this viral antigenic protein transiently on the cell's surface, much like a native infection would do, but without the ability to cause disease. This is because no other viral proteins are present to enable the production of an infectious virus.

As a result, the immune system recognizes the hemagglutinin as foreign to the body and produces antibodies that have the potential to neutralize the

H10N8 or H7N9 virus, and prevent infections in the event the vaccinated person is exposed to the actual virus in the future.

Moderna's mRNA vaccines are delivered via intramuscular (IM) injection, similar to traditional vaccines. Unlike DNA vaccines, mRNA vaccines do not require electroporation or other delivery devices, which can be painful.

[1] https://www.fda.gov/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm074775.htm
[2] *Source:* http://www.fao.org/ag/againfo/programmes/en/empres/h7n9/situation_update.html

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About Moderna Therapeutics

Moderna is a clinical stage pioneer of messenger RNA (mRNA) Therapeutics™, an entirely new drug technology that directs the body's cells to produce intracellular or secreted proteins. With its breakthrough platform, Moderna is developing mRNA vaccines and therapeutics as a new class of medicines for a wide range of diseases and conditions, in many cases by addressing currently undruggable targets. Moderna is developing its innovative mRNA medicines for infectious diseases, cancer (immuno-oncology), rare diseases, cardiovascular disease and pulmonary disease, through proprietary development and collaborations with strategic partners.

Headquartered in Cambridge, Mass., privately held Moderna currently has strategic agreements with AstraZeneca, Merck, Alexion Pharmaceuticals and Vertex Pharmaceuticals, 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 Bill & Melinda Gates Foundation. To learn more, visit www.modernatx.com.

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