BioSpectrum
the business of Bio & Health Sciences
ASIA EDITION

Moderna Advances in Platform Science and Innovative Vaccine Research

June 2, 2020 | News

The research includes innovations in mRNA and protein engineering and delivery science to improve therapeutic properties



Moderna, Inc., a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, 2 June 2020 announced new research to be highlighted at the Company's third annual Science Day, held virtually this year. The program is designed to provide insight into the continued diverse efforts underway at Moderna and with collaborators to better understand how to use mRNA as a medicine, and underscores the Company's continued commitment to basic science and innovation.

"Science Day is an opportunity for us to provide insights into the advancements in our platform science and our further understanding of how to use mRNA as a medicine. Our substantial investments in basic science to date have resulted in major steps forward in our platform's capabilities, and these have allowed us to open new therapeutic areas and new scientific directions," said Stephen Hoge, M.D., President of Moderna. "Today, we're excited to highlight novel approaches to our lipid nanoparticle technology, which will be used with mRNA-3745, our GSD1a candidate in preclinical development. We are also pleased to provide an update on our collaboration with IAVI, NIAID and Bill & Melinda Gates Foundation toward the development of an HIV vaccine using Moderna's mRNA platform. We remain firmly committed to further advancing our mRNA science to create a new generation of transformative medicines for patients."

At this year's Science Day, Moderna will present new platform science and preclinical research, including:

Engineering mRNA and Proteins to Improve Therapeutic Properties

An advantage of mRNA medicines over small molecule drugs is the ease of engineering their properties to achieve desired pharmacology. New research will be presented on efforts to engineer both mRNAs and encoded proteins to improve and extend therapeutic effect.

These efforts include modifications to mRNA and proteins to prevent degradation and lengthen half-life. Presentations will include data on the addition of an inverted deoxythymidine (idT) to the 3'-end of mRNA, which is designed to stabilize mRNA

by blocking its degradation through deadenylation. Preclinical data show that 3'-idT-stabilized mRNA encoding phenylalanine hydroxylase (PAH), the enzyme missing or dysfunctional in the metabolic disorder phenylketonuria (PKU), supports sustained reduction of serum phenylalanine levels in a PKU mouse model. Data will also be presented on removal of ubiquitination sites from PAH, designed to prevent ubiquitin-mediated protein degradation. Results show that combining mRNA stabilization along with PAH stabilization maintained low serum phenylalanine levels even further, suggesting an additive effect.

One challenge for the production of mRNA therapeutics is to minimize or eliminate double-stranded RNA (dsRNA) impurities produced during the synthesis process, as this can trigger undesirable innate immune responses*in vivo*. At Science Day, Moderna will present a protein engineering workflow by which it has engineered a Moderna T7 RNA polymerase (MT7) that does not produce dsRNA impurities.

Optimizing Lipid Nanoparticle Technology

The Company will present new research in delivery science to optimize its lipid nanoparticles (LNPs). The presentations will highlight a novel squaramide-based ionizable lipid designed to enhance the interactions between the lipid and mRNA. Preclinical data from new LNPs incorporating this novel ionizable lipid show improved protein expression after IV administration, including repeat dosing, and efficient delivery to the liver, as compared to current state-of-the-art Moderna proprietary LNPs.

This squaramide-based LNP represents a new delivery system and will be used with the Company's glycogen storage disease type 1a (GSD1a) candidate (mRNA-3745), which is in preclinical development. Preclinical studies with this new LNP containing mRNA encoding for G6Pase, the missing or dysfunctional enzyme in GSD1a, show sustained improvements in fasting blood glucose in a mouse model of GSD1a, achieving the target product profile.

Collaborating on an HIV Vaccine

Science Day will also include presentations from William Schief, Ph.D., Professor, Immunology and Microbiology, Scripps Research Institute and Executive Director, Vaccine Design, International Aids Vaccine Initiative (IAVI) and Paolo Lusso, M.D., Ph.D., Chief, Viral Pathogenesis, Laboratory of Immmunoregulation, National Institute of Allergy and Infectious Diseases (NIAID) showcasing research conducted through Moderna's ongoing collaborations with IAVI, NIAID and the Bill & Melinda Gates Foundation. This research seeks to deliver an engineered HIV immunogen using Moderna's mRNA platform that allows for a faster, more flexible approach to rapid iterative vaccine design and clinical testing. This approach could significantly accelerate early clinical trials and transform HIV vaccine science and development efforts. The data presented today will highlight progress toward creating a protective HIV-1 vaccine designed to elicit broadly neutralizing antibodies to prevent HIV-1 infection.

Moderna currently has 23 mRNA development candidates in its portfolio with 13 in clinical studies. Across Moderna's pipeline, more than 1,900 participants have been enrolled in clinical studies. The Company's updated pipeline can be found at www.modernatx.com/pipeline. Moderna and collaborators have published more than 45 peer-reviewed papers.