Research provides framework for developing Ebola virus therapeutic under animal rule

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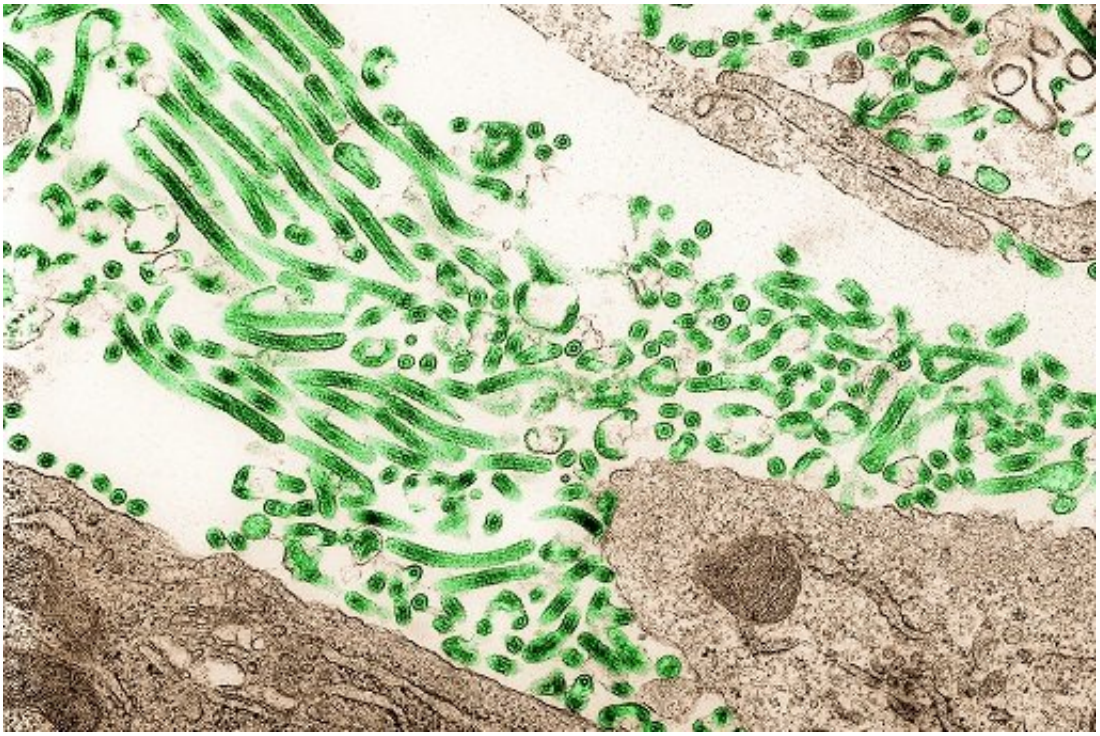

Ebola virus. Credit: NIAID

The U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) today announced that, for the first time, the U.S. Food and Drug Administration (FDA) has provided formal regulatory agreement for use of an animal model to support development of a drug candidate, remdesivir, for treating deadly Ebola virus (EBOV) infections. This agreement was made possible through a 2018 Natural

History Study (NHS) of Ebola virus conducted by USAMRIID in close collaboration with Gilead Sciences, Inc., the sponsor of remdesivir development, and The Geneva Foundation (Geneva), and funded by the Joint Project Manager for Medical Countermeasure Systems (JPM-MCS), a component of the U.S. Department of Defense's Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense.

Specifically, FDA agreed that the rhesus macaque, infected by intramuscular (IM) injection, is a relevant and adequately characterized model of Ebola virus disease to support filing under the FDA Animal Rule. In addition, the agency agreed that the rhesus IM/EBOV disease model is sufficient as a single animal model for therapeutic product development. Notably, FDA also agreed that a specific delayed time-to-treat approach is appropriate for future nonclinical studies aimed at characterizing the efficacy of remdesivir.

Sponsors must demonstrate efficacy before a medical product can be approved by the FDA; however, for certain products, when obtaining efficacy data from human patients is not ethical or feasible, the FDA may grant approval under the Animal Rule. Such approval would be based on efficacy data from well-controlled studies in adequately characterized animal model(s), when the results of those studies establish that the drug candidate is reasonably likely to produce clinical benefit in humans. The sponsor must still demonstrate the product's safety in humans.

"For years, development of Ebola virus medical countermeasures has been subject to regulatory uncertainties regarding which models, if any, would be acceptable to the FDA as a foundation for evaluating efficacy under the Animal Rule," said COL Gary Wheeler, USAMRIID commander. "The study design and data-quality posture USAMRIID adopted for the Ebola virus NHS sets a precedent that has the potential

to be useful for medical countermeasure development efforts targeting other similar human pathogens, such as Marburg or Sudan viruses."

USAMRIID and Gilead Sciences, Inc. worked in close partnership to develop the study plan for conducting the IM/EBOV NHS in rhesus monkeys, analyze the study outcome and submit data to the FDA. A team of over 100 USAMRIID and Geneva personnel, representing the divisions of Molecular and Translational Sciences, Virology, Telemetry, Pathology, Veterinary Medicine, Advanced Research Studies and Quality Assurance participated in the study, which was conducted in a Biosafety Level 4 (BSL-4) laboratory under maximum containment conditions. Importantly, this project was the first-ever study to be completed in compliance with Good Laboratory Practice (GLP) standards in a BSL-4 laboratory. In January 2019, FDA auditors visited USAMRIID to conduct a data quality and integrity inspection of USAMRIID's GLP facilities and processes. The results of the audit were reported as "No Action Indicated," a classification that occurs when no objectionable conditions or practices were found during the inspection.

"To date, there are no FDA-approved therapeutics for treatment of Ebola virus disease. Both the current outbreak in the Democratic Republic of Congo and the 2014-2016 West Africa outbreak, the largest in history, highlight the urgent need for antiviral therapy to combat this deadly disease. We are committed to developing our investigational antiviral agent, remdesivir, for the treatment of Ebola virus infection using the Animal Rule or other appropriate regulatory pathway based on feedback from FDA," said John McHutchison, AO, MD, Chief Scientific Officer and Head of Research and Development, Gilead Sciences, Inc. Remdesivir is an investigational agent and is not approved by any regulatory agency globally. Its safety and efficacy have not been established.

"This project is a testament to the efficiency of public-private

partnership to accelerate the development of critically needed medical countermeasures," said COL David Hammer, Joint Project Manager for Medical Countermeasure Systems. "We can advance products more quickly when we work together to leverage the skills of multiple organizations."

The NHS was conducted as part of the overall remdesivir development plan, and product-independent qualification of the rhesus IM/EBOV model through the FDA Animal Model Qualification Program has not been sought or obtained.

Provided by US Army Medical Research Institute of Infectious Diseases