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USAMRIID Research Provides Regulatory Framework for Developing Ebola Virus Therapeutic under FDA “Animal Rule”

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.

About USAMRIID

USAMRIID is celebrating its 50th year of providing leading edge medical capabilities to deter and defend against current and emerging biological threat agents. The Institute is the only laboratory in the Department of Defense equipped to safely study highly hazardous viruses requiring maximum containment at Biosafety Level 4. Research conducted at USAMRIID leads to vaccines, drugs, diagnostics, and training programs that protect both warfighters and civilians. Established in 1969, the Institute plays a key role as the lead military medical research laboratory for the Defense Threat Reduction Agency's Joint Science and Technology Office for Chemical and Biological Defense. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command. For more information, visit www.usamriid.army.mil

About 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, aims to provide U.S. military forces and the nation with safe, effective and innovative medical solutions to counter chemical, biological, radiological and nuclear threats. JPM-MCS facilitates the advanced development and acquisition of medical countermeasures and systems to enhance the nation's biodefense response capability.

About Gilead Sciences, Inc.

Gilead Sciences, Inc. is a research-based biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet medical need. The company strives to transform and simplify care for people with life-threatening illnesses around the world. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California. For more information on Gilead Sciences, please visit the company's website at www.gilead.com

About The Geneva Foundation

The Geneva Foundation is a 501(c) 3 non-profit organization that advances military medicine through innovative scientific research, exceptional program management, and a dedication to U.S. service members and veterans, their families, and the global community. Geneva is proud to have over 25 years of experience in delivering full spectrum scientific, technical, and program management expertise in the areas of federal grants, federal contracts, industry sponsored clinical trials, and educational services. www.genevaUSA.org

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