Madam Chair, Ranking Member Burr, and Members of the Committee:

Thank you for the opportunity to discuss the role of the National Institute of Allergy and Infectious Diseases (NIAID) in the research response to the ongoing monkeypox public health emergency. Within the Department of Health and Human Services (HHS) and the National Institutes of Health (NIH), NIAID is responsible for conducting and supporting basic and clinical research on emerging and re-emerging infectious diseases, including monkeypox. As the Director of NIAID and the Chief Medical Advisor to the President, I am pleased to discuss NIAID research addressing the U.S. monkeypox outbreak. NIAID is committed to accelerating efforts to answer critical monkeypox research questions in alignment with the U.S. Monkeypox Research Priorities identified by the White House Office of Science and Technology Policy.

Pandemic Preparedness and Prototype Pathogen Approaches for Medical Countermeasures

The monkeypox virus is part of the *Orthopoxvirus* genus, which includes the variola virus that causes smallpox. Available medical countermeasures against monkeypox were made possible by decades of NIAID-supported research on orthopoxviruses. Our orthopoxvirus research is an example of the NIAID prototype pathogen approach to pandemic preparedness, in which basic research and countermeasures for a prototype pathogen within a given family of viruses can be used to help treat and prevent diseases caused by closely related pathogens within that family.

As part of its longstanding investment in biodefense research, NIAID supported early-stage development of the second-

monkeypox now known as J .

NIAID-supported research also facilitated the development of an antiviral for smallpox called tecovirimat (TPOXX). This drug is now being used to treat patients with monkeypox under an expanded-access investigational new drug protocol. NIAID is supporting new clinical trials of tecovirimat to gather additional safety and efficacy data to inform clinical and regulatory decision-making on the use of tecovirimat for the treatment of monkeypox. In addition, NIAID-supported scientists continue to conduct basic research to better understand monkeypox virus transmission and disease, and to identify additional antiviral candidates. NIAID researchers at the Vaccine Research Center (VRC) are isolating antibodies for evaluating vaccine-induced immune responses as well as the development of immune q0 nBT/F1 12 Tf1 0 0 1 Gf 0 0.00000912 0 612 792 reW*nBT/F1 12 Tf1 0 0

clinical evaluation.

In 2019, FDA approved JYNNEOS for individuals at high risk for smallpox or monkeypox virus infection. On August 9, 2022, FDA issued an emergency use authorization (EUA) for

patients with monkeypox under an expanded-access investigational new drug protocol. NIAID funded the discovery of tecovirimat as well as preclinical studies to determine its mechanism of action and its safety and efficacy in animals. NIAID and BARDA also have funded Phase 1 and Phase 2 clinical trials to test the safety and pharmacokinetics of an oral formulation of tecovirimat. The FDA approved the oral formulation of tecovirimat in 2018 for treating smallpox in adults and children and this formulation is part of the U.S. Strategic National Stockpile. An intravenous formulation of tecovirimat subsequently received FDA approval. Although this antiviral was approved for the treatment of smallpox, FDA approval was based on studies in animals infected with monkeypox virus. Clinical trials to evaluate tecovirimat in humans with monkeypox are needed to gather additional data about the safety and efficacy of the drug in the context of the current outbreak to aid clinical and regulatory decision-making.

In this regard, NIAID-supported investigators have launched a Phase 3, randomized, placebo-controlled, double-blind trial of tecovirimat for the treatment of monkeypox in outpatient settings in the United States through the AIDS Clinical Trials Group

NIAID preparedness efforts to study high-consequence pathogens in key international locations where they are endemic.

NIAID also supports early-stage research to help identify additional candidate antivirals for monkeypox. It is possible that monkeypox virus will develop resistance to tecovirimat. This is one of the reasons NIAID-supported scientists are screening novel compounds to help find new antiviral candidates to treat monkeypox.

Understanding Monkeypox Transmission and Reservoirs

Monkeypox is disproportionately affecting men who have sex with men in non-endemic countries. However, anyone exposed to the circulating virus can get monkeypox regardless of their age, gender identity, or sexual orientation. Of note, the previous outbreak of monkeypox in the United States in 2003 was driven by animal-to-person spread and involved domesticated prairie dogs that were infected by small mammals imported from West Africa. NIAID scientists are conducting animal studies to understand the human-animal interface with monkeypox virus and its suspected reservoir hosts, such as Gambian pouched rats, rope squirrels, and dormice. NIAID also is supporting the development of animal models to evaluate vaccine-induced immune responses to monkeypox virus.

In addition, NIAID-supported scientists are performing genomic sequencing to better understand the monkeypox virus and its various strains. Investigators with the NIAID-funded Centers for Research in Emerging Infectious Diseases (CREID) are supporting clinical surveillance in the DRC, Nigeria, and Sierra Leone. CREID investigators also are providing validated molecuh9l1 12 Tf1 0 0 1 4oW*nBT/F1 12 Tf1 0deW*nBT/F1 12 Tf199c.W*nBTim(a)4(s0 G[(n)-9(d45 obe)4(nt0

Cambodia.

NIAID scientists also are developing a high-throughput serologic assay that can distinguish between individuals infected with monkeypox virus and people