DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Vaccines: Saving Lives, Ensuring Confidence, and Protecting Public Health

Witness appearing before the
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Chairman Alexander, Ranking Member Murray and distinguished members of this committee thank you for inviting me to discuss the Department of Health and Human Services' (HHS) Operation Warp Speed (OWS) efforts and the importance of vaccination. I am grateful for this opportunity to address how the National Institutes of Health (NIH) is working tirelessly with other parts of the government, and with industry partners, to prevent, diagnose, and treat the novel coronavirus SARS-CoV-2. We thank Congress for your continual partnership in response to COVID-19.

I am also pleased to be here today to reinforce the importance vaccines play in protecting public health from childhood immunizations to the annual flu and pneumonia vaccines in keeping Americans safe and healthy. While our immediate focus has been on the development of a COVID-19 vaccine, we can't lose sight of the need to encourage the continued uptake of all vaccines by the American people.

To accelerate the development and subsequent production of a vaccine for COVID-19, in mid-May, President Trump announced Operation Warp Speed (OWS). OWS aims to deliver up to 300 million doses of a safe and effective vaccine for COVID-19 in early 2021, as part of a broader strategy to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics (collectively known as medical countermeasures). OWS is a partnership among components of HHS, including NIH, Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), and Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense (DoD), with the aim of a unified government approach to respond to the pandemic. OWS engages with private firms and other federal agencies, including the Department of Agriculture, the Department of Energy, and the Department of Veterans Affairs. OWS coordinates with existing

HHS-wide efforts, including the NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership, NIH's Rapid Acceleration of Diagnostics (RADx) initiative, and research activities by the National Institute of Allergy and Infectious Diseases (NIAID).

NIH is the HHS agency leading the biomedical research response to COVID-19 and the novel coronavirus that causes the disease, SARS-CoV-2. We have done everything possible to unleash the most rapid and innovative approaches to address this global pandemic. The importance of studying the safety and efficacy of vaccine and therapeutic candidates during the critical clinical trial phases is now NIH's top priority. OWS has been selecting the most promising countermeasure candidates and providing coordinated government support. Protocols for the demonstration of safety and efficacy are being aligned, which allows the trials to proceed more quickly. The protocols for the trials are being overseen by the Federal Government, in contrast to traditional public-private partnerships, in which pharmaceutical companies are solely responsible for design and implementation of their own protocols. Rather than eliminating steps from traditional development timelines, steps are proceeding simultaneously. That includes starting manufacturing of a vaccine candidate at industrial scale well before the demonstration of vaccine efficacy and safety, as happens normally. This increases the financial risk in the event of non-optimal product performance, but not the product risk.

It is important to highlight that none of the safety and efficacy assessments will be skipped or abbreviated. Efforts to shorten the timeline from bench to bedside, but still achieve a safe and effective vaccine, have been accomplished by eliminating down times and assuming the costs of at-risk manufacturing. Throughout the clinical trials, an independent data and safety monitoring board (DSMB) continues to monitor ongoing results to ensure study participant well-being and safety as well as study integrity. The critical final steps in clinical trials will be well-

coordinated and done in parallel with manufacturing, but with NIH and industry providing the FDA with all of the critical safety and efficacy data necessary for sound scientific decision-making.

NIH is deeply engaged in the vaccine trial program. NIAID recently established the COVID-19 Prevention Network (CoVPN) by leveraging four existing NIAID-funded clinical trials networks: the HIV Vaccine Trials Network (HVTN), the HIV Prevention Trials Network (HPTN), the Infectious Diseases Clinical Research Consortium (IDCRC), and the AIDS Clinical Trials Group (ACTG), in partnership with the DoD. The CoVPN is engaged in assisting enrollment of tens of thousands of volunteers in large-scale clinical trials testing a variety of investigational vaccines, monoclonal antibodies (mAb), and drugs intended to treat and protect people from COVID-19. The CoVPN is a functional unit of the OWS partnership led by HHS to invest in and coordinate the development, manufacture, and distribution of COVID-19 vaccines, therapeutics, and diagnostics. The CoVPN is participating in harmonized protocols, developed in collaboration with the ACTIV public-private partnership, vaccine manufacturers, and BARDA. The network will participate in numerous trials at more than 100 clinical trial sites across the United States and internationally. The CoVPN has developed an extensive community engagement framework to reach out to the diverse communities most affected by COVID-19; understand interest in, and concerns about, research participation; and partner with them to ensure their input is reflected in study implementation. The CoVPN plans to evaluate both therapeutic and vaccine candidates. While the long-term goal is to have a safe and effective vaccine, NIH is continuing its vital work on researching and evaluating all potential therapeutic approached against SARS-CoV-2.

Identifying Therapeutics to Treat COVID-19

NIH, in collaboration with the Foundation for the NIH, launched an innovative public-private partnership to speed up the development of COVID-19 therapeutics and vaccines. The ACTIV public-private partnership brings together stakeholders from across the U.S. government, industry, and the European Medicines Agency to develop an international strategy for a coordinated research response to the COVID-19 pandemic. The ACTIV public-private partnership is led by an Executive Committee co-chaired by me and Dr. Paul Stoffels of Johnson & Johnson, and has engaged more than 100 experts from both sectors in a 24/7 effort to prioritize therapeutic options. ACTIV has designed five adaptive master protocols for ACTIV clinical trials. These master protocols provide an efficient and coordinated evaluation of multiple investigational agents as they become available within the same clinical trial structure and across multiple study sites. Adaptive master protocols reduce administrative burden and cost, provide a flexible framework to identify rapidly drug candidates that work, and quickly move additional experimental agents into the trial.

Effective therapeutics for COVID-19 are critically needed to treat patients who have been infected with SARS-CoV-2. NIH was engaged in this effort from the very beginning of the pandemic. On February 21, 2020, NIAID launched a multicenter, randomized placebo-controlled clinical trial, the Adaptive COVID-19 Treatment Trial (ACTT), to evaluate the safety and efficacy of therapeutics for COVID-19, initially examining the antiviral drug remdesivir for treatment of severe COVID-19 in hospitalized adults (ACTT-1). An analysis of preliminary data from ACTT-1 indicated that those who received remdesivir had a 32 percent faster time to recovery, a median of 11 days compared with 15 days for those who received placebo. These initial findings were published on May 22, 2020, in the *New England Journal of Medicine*. The

adaptive design of this trial will enable the evaluation over time of additional promising therapies, such as the anti-inflammatory drug baricitinib. This drug was added to the second iteration of the study (ACTT-2); enrollment for ACTT-2 is now complete. The third iteration of the study (ACTT-3), announced by NIH on August 6, 2020, is a randomized, controlled clinical trial to study the use of interferon beta-1a, which is typically used to treat individuals with multiple sclerosis.

Monoclonal antibodies (mAbs) are another promising approach for the treatment of COVID-19. At least 21 companies are developing mAbs that target SARS-CoV-2 and several of them are already being studied in clinical trials. On August 4, 2020, NIH launched two clinical trials under the ACTIV-2 and ACTIV-3 master protocols. ACTIV-2, a Phase 2/3 clinical trial, will evaluate potential therapeutics in study participants with mild to moderate COVID-19 who *do not* require hospitalization. The first stage of ACTIV-2 is looking at the potential of synthetic mAbs to treat the disease. The trial may also investigate other experimental therapeutics later under the same trial protocol. Another Phase 2/3 randomized, controlled trial known as ACTIV-3 will test mAb treatments in *hospitalized* patients. The initial stage of the ACTIV-3 clinical trial plans to enroll approximately 300 volunteers who have been hospitalized with mild to moderate COVID-19. ACTIV-3 will initially study the investigational mAb from Lilly, LY-CoV555, discovered by Abcellera Biologics in collaboration with NIAID's Vaccine Research Center (VRC).

Developing Vaccines to Prevent SARS-CoV-2 Infection and/or COVID-19 Disease

A safe and effective vaccine for SARS-CoV-2 will be essential to stopping the spread of infection, reducing rates of morbidity and mortality, and preventing future outbreaks. It is among our best hopes for getting our country back to normal.

NIAID has been supporting development of several SARS-CoV-2 vaccine candidates, including vaccines based on platform technologies that have shown promise against coronaviruses that cause SARS and MERS. As part of a longstanding collaboration, the NIAID VRC worked with biotechnology company Moderna, Inc., to develop a vaccine candidate using a messenger RNA (mRNA) vaccine platform expressing the SARS-CoV-2 spike protein. On July 14, 2020, encouraging interim findings from the Phase 1 clinical trial were published in the *New England Journal of Medicine*. The investigational mRNA-1273 vaccine was generally well tolerated and induced robust neutralizing antibody responses in healthy adults in this interim analysis of data from the ongoing trial. On May 29, 2020, a Phase 2 clinical trial, sponsored by Moderna, was initiated to further study the safety and immune response to the experimental mRNA vaccine. The Phase 2 study closed to enrollment on July 30, 2020, and is now in follow up – no safety concerns have been identified. The Coalition for Epidemic Preparedness Innovations (CEPI) funded the manufacture of the vaccine candidate for the Phase 1 trial, and BARDA is supporting advanced development of the candidate.

Scientists at NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Montana, are collaborating with University of Oxford researchers to develop the SARS-CoV-2 chimpanzee adenovirus-vectored vaccine candidate AZD1222, formerly known as ChAdOx1. The University of Oxford has partnered with the pharmaceutical company AstraZeneca on this vaccine candidate, now in a Phase 3 clinical trial in the U.S. supported by NIAID and BARDA. BARDA has announced plans to support advanced development and production of AZD1222.

In July, OWS committed to working with Novavax on their new COVID-19 vaccine candidate after Phase 1 trials of this vaccine were done in Australia with promising results. A Phase 3 trial is expected to begin in the U.S. by the end of September. Janssen Pharmaceutical Companies of Johnson & Johnson have a viral vector COVID-19 vaccine candidate that has demonstrated protection in nonhuman primate models. OWS is working with this company and Phase 1 trials began on July 27, 2020, in the U.S. Depending on results from the early trials, a Phase 3 clinical trial is expected to begin this month. Additionally, Sanofi working with GSK developed a protein-based vaccine candidate that is currently in preclinical development. A Phase 1 trial is expected to begin this month with a goal of entering Phase 3 by the end of 2020.

Lastly, Pfizer working with BioNTech developed an RNA vaccine candidate for COVID-19. Phase 3 trials for this vaccine began on July 27, 2020. The RNA vaccines, developed by Pfizer in partnership with BioNTech, and by Moderna in partnership with NIAID, have already begun large scale manufacturing in order to be ready to distribute if the Phase 3 trials show promising results on the safety and efficacy of the vaccine candidates. OWS is working to refurbish manufacturing sites to scale up manufacturing for the other COVID-19 vaccine candidates in testing. The CoVPN at NIH is currently working to enroll thousands of volunteers in the clinical trials for vaccine candidates and preventive interventions. We continue to prioritize enrollment of racial and ethnic populations impacted disproportionately by this disease. It is critical that we continue to engage all communities in this effort with transparency and the highest standards of safety and ethics.

The CoVPN developed a community engagement framework to assist researchers in reaching out to communities, and potential research volunteers. In order to have the trust of the community, NIH has prioritized open and transparent communication with participants, sharing

the specific details involved in participating in the clinical trials for COVID-19 vaccine candidates or therapeutics and using their feedback to improve the trial designs. To facilitate outreach to key communities, the CoVPN established expert panels of 10-15 scientific experts from within those respective communities. NIH believes that by engaging communities early we can address any concerns about the treatments and vaccines in advance of potential distribution of FDA-approved/licensed vaccines.

COVID-19 and Seasonal Influenza

The fight against the COVID-19 pandemic may become more difficult as we enter the fall and winter "flu season". Each year influenza causes a surge in hospitalizations. This expected surge, in combination with COVID-19, is a serious concern for healthcare systems across the U.S. In addition to the expected surge in patient numbers, the clinical symptoms for influenza and SARS-CoV-2 can overlap, and an increase in influenza infections will require testing for SARS-CoV-2 in order to determine if the patient has COVID-19 or influenza. NIAID is currently supporting studies investigating the impact of seasonal influenza co-circulation with SARS-CoV-2, and coinfections have already been observed in the Southern hemisphere. An increase in the vaccination rate for influenza will help to safeguard our healthcare systems against this surge, by reducing flu morbidity, to allow for COVID-19 surge capacity in hospitals and reducing the number of sick individuals presenting to outpatient clinics. During the 2018-2019 fall and winter, the influenza vaccination rate for adults was 45.3 percent. It is imperative that we increase this vaccination rate to protect our healthcare systems. Lastly, it is important to remind the public that childhood vaccinations are another way we can protect our communities and healthcare systems from avoidable illnesses and deaths.

Conclusion

The rigorous clinical testing required to establish vaccine safety and efficacy means that it may take some time for a licensed SARS-CoV-2 vaccine to be available to the general public, but there is growing optimism that one or more of these vaccine candidates will prove safe and effective by late 2020 or early 2021.

The NIH is the world's largest biomedical research funder, but we are also America's research engine. Right now, our funded scientists are working around the clock to find the best ways to diagnose, prevent, and treat COVID-19. We won't rest until this job is done.