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Testimony to the Subcommittee on Investigations & Oversight of the House Committee on Science, Space and Technology.

Hearing: ***Repurposing Therapeutic Drugs for COVID-19: Research Challenges and Opportunities***

I thank the members of the sub-committee for inviting me to speak on my experiences as a clinical investigator during the COVID19 pandemic.

I am a pulmonary and critical care physician at National Jewish Health in Denver, Colorado where I see patients in our outpatient clinic and intensive care units. I have close to two decades of basic, translational and clinical research experience, and currently help lead our COVID19 clinical research program.

National Jewish Health is the leading respiratory hospital in the nation. Founded 121 years ago as a nonprofit, free hospital, National Jewish Health today is the only academic hospital system in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders for children and adults. National Jewish Health is a world leader in research on all facets of the lung, in both disease and health, as well as inflammation and immune function. Patients and their families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. We practice at over 20 locations in Colorado and work with several other hospital systems in Colorado, including our flagship National Jewish Health-Saint Joseph Hospital, to provide pulmonary and critical care medicine (our critical care physicians managing patients in 800 ICU beds each night at 3 hospitals in Colorado and 5 Western States), and we have established Respiratory Institutes in New York in partnership with Mount Sinai Health System and in Philadelphia with Jefferson Health.

COVID19 is the disease caused by infection with the SARS-CoV-2 virus. Most cases are mild but roughly 20% of patients develop pneumonia and at least 5% will develop respiratory failure, multi-system organ dysfunction and shock. The case fatality rate is roughly 2% though a range from less than 1% to over 7% has been reported. This is in comparison to seasonal flu which has a fatality rate of about 0.1%. Over 115,000 Americans have died of COVID19 in the past five months.

Responding to this pandemic has required a complete re-orientation and adaptation of our clinical and research programs at National Jewish Health. Clinically, we reorganized our workforce and physical plant to diagnose and treat COVID19 patients while simultaneously planning for the worst-case scenario. For our research operations, it meant halting existing clinical studies and starting up new studies related to COVID-19 as quickly as possible, all with much of our staff working remotely. For testing, we redirected our high complexity, referral laboratory Advanced Diagnostics to introduce SARS-CoV-2 molecular testing for detection of the virus in acutely infected individuals as well as specific antibody testing and have been providing that service for patients in Denver and beyond.

At National Jewish Health, we've launched new avenues of investigation in basic, translational and clinical realms. On the basic and translational side, we've worked to delineate the structure of SARS-CoV-2 proteins and have developed monoclonal antibodies to block viral entry into the cell as a possible COVID19 treatment or prophylaxis. We've launched animal models test therapeutic response for drug repurposing. Clinically, we have collaborations to study infection and transmission rates in children, adults, and front-

line health care workers as well as timing of the antibody response and the degree of protective immunity post-infection.

Regarding treatment, we've gone from zero COVID19 studies to more than 10 therapeutic trials in various stages of development over the last twelve weeks. Prior to embarking on any specific research study, each trial requires a number of time-consuming steps including: formal protocol review, assessment of our ability to perform the trial as designed, determination of any conflicts with other ongoing trials, budget negotiation, Institutional Review Board review, response and approval, and agreement on contracting terms. This process ordinarily takes three months or longer. During this crisis, we have been able to cut that time to a few weeks. For a pharmaceutical company or other study sponsor, this process must be repeated at every study site. As an example, the recently published Remdesivir study had sixty sites.

In reflecting on our experience at National Jewish Health during this pandemic, I would like to highlight three points to the subcommittee.

First, to rapidly deploy clinical trials of new or repurposed drugs, a pre-existing, organized national network of research sites is essential. The recently announced, NIH-led ACTIV Program is an example of this. ACTIV stands for "Accelerating COVID19 Therapeutic Interventions and Vaccines" and is a public-private partnership to create a collaborative framework for prioritizing vaccine and therapeutic candidates and streamlining clinical trials using existing clinical networks**.** Another example is the Prevention and Treatment of Acute Lung Injury, or "PETAL," Network. PETAL is an NIH-funded network of academic medical centers dedicated to studying Acute Lung Injury and the Acute Respiratory Distress Syndrome, the disease caused by SARS-CoV2. This network has been repurposed to study the clinical features and possible treatments of COVID19. In the past month, the PETAL Network developed and launched two research protocols and both studies will likely be completed in the coming weeks. Networks like these can be used in collaboration with industry as a platform to launch new studies on promising treatments.

Second, we need ongoing investigation of SARS-CoV-2 and COVID19 to understand the virus and mechanisms of this disease. Much of this research will be what we call pre-clinical studies; bench research in cells and animal models to expand our understanding of COVID19 pathophysiology. These are foundation studies where candidate drugs and non-pharmacologic therapies will be identified. However, this can only exist if we maintain a robust national medical research mission and infrastructure. Dividends from this kind of research are not always immediately apparent, however a basic understanding of the underlying science of disease drives development of new therapeutics. This is true for this pandemic and will prepare us better for the next one.

Third, another pandemic is likely in our future. What that will be, we don't know, but we should be planning now on how to incorporate a full research operation into in any future pandemic response. I have been impressed with the research community reaction to this crisis. However, even with this effort, an organized national response was not launched until several months into the pandemic. Coordination of what research will be performed and how it will be executed, the respective roles of organizations such as the FDA, NIH, CDC, as well as industry should be considered prospectively. Research will be as important to defeating this pandemic, and the next one, as personal protective equipment, intensive care units and ventilators.