Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

Hearing on
"Pathway to a Vaccine: Efforts to Develop a Safe, Effective and Accessible COVID-19 Vaccine"

July 21, 2020

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The Honorable Frank Pallone, Jr. (D-NJ):

1. **During the hearing, you indicated that Pfizer was putting together its clinical trial protocol for its Phase III study and would follow the U.S. Food and Drug Administration's (FDA) guidelines that suggest enrollment of up to 30,000 patients.**

    a. **What is the minimum number of patients Pfizer will seek to enroll in its Phase III trial, and how did the company arrive at this range?**

    Response: The Phase 2/3 part of the study initially seeks to enroll approximately 29,300 participants. This number was based upon the FDA Guidance for Industry on Development and Licensure of Vaccines to Prevent COVID-19.

    b. **What makes your company confident this will be a large enough pool of participants to adequately assess the safety and efficacy of any of its vaccine candidates?**

    Response: The number of participants in the study was determined on the basis of the FDA Guidance for Industry on Development and Licensure of Vaccines to Prevent COVID-19. Per the guidance, we currently project that the planned number will allow for adequate assessment of both safety and efficacy, however we will continue to monitor this closely.

2. **As we heard at the hearing, there are many companies racing to begin and complete the Phase III clinical trials that will be necessary to support an authorization or approval by FDA. What steps is Pfizer taking to ensure the company is able to recruit the tens of thousands of healthy participants needed for a Phase III clinical trial?**

    Response: The more than 120 investigative sites across the U.S. are raising awareness of the trial and recruiting individuals based on their own practices to meet the unique needs of their respective communities. In addition, we are complementing this effort with additional awareness building efforts and referrals to sites, including: a study website, social media and local newspaper and radio communications. We are also partnering with community, government and local advocacy groups to raise awareness of the importance of participation

with their constituents from racial and ethnically diverse communities that have been disproportionately impacted by COVID-19.

3. **Ensuring quality manufacturing of a future vaccine is critical to ensuring rapid access for patients, as well as preventing any potential disruptions that could limit such access. At the hearing you noted that Pfizer's previous manufacturing quality issues associated with sterile injectables were attributable to facilities associated with Hospira that was acquired by the company in 2017. You noted that your remediation for those sites was to be completed by 2020 and that those sites "were on track." While I understand you intend to manufacture a future COVID-19 vaccine candidate in your legacy Pfizer network, what are the lessons learned for Pfizer in the remediation of the sterile injectable facilities you acquired, and what steps is the company taking now to mitigate against any potential quality or compliance issues in your legacy facilities to ensure uninterrupted access to a future vaccine?**

   Response: Pfizer has effectively integrated sterile injectable manufacturing facilities acquired over the years and ensured improvements were made through application of Pfizer's quality standards and necessary capital investments. Pfizer is committed to the delivery of safe and effective products to patients. Pfizer operates a Quality Management System (QMS) within and across relevant functions and departments, and maintains a quality-focused culture to ensure the highest priority is placed on the safety, efficacy and quality of our products, the safety of our patients, and the quality of data supporting regulatory submissions. Pfizer has established a Corporate Quality Policy that describes overall intentions and direction of the company related to quality including key quality expectations and responsibilities for all Pfizer colleagues and contingent workers. The potential COVID-19 vaccine is being developed within the Pfizer QMS in an accelerated fashion taking appropriate steps to identify and mitigate any potential risks. The vaccine supply chain includes Pfizer manufacturing sites operating in accordance with current Good Manufacturing Practices under Pfizer's QMS following our well-established quality standards.

The Honorable Brett Guthrie (R-KY):

1. **Through Operation Warp Speed and the efforts of your companies and many more, we are seeing an unprecedented effort to quickly develop a safe and effective vaccine. What lessons or changes from this process should we consider making permanent in an effort to fundamentally change the traditional, years-long process for vaccine development going forward?**

   Response: The development of a novel vaccine is a complex and lengthy process that generally takes 10 to 15 years. Given the current global scale of the COVID-19 pandemic, Pfizer is working at an unprecedented speed to develop a potential vaccine in a safe and responsible way, collaborating closely with regulatory and health authorities around the world – compressing stages that have taken years into months, and those that have taken months into weeks. We are doing so with an unwavering commitment to scientific rigor, clinical trial quality, and participant safety.

We normally do all vaccine development and manufacturing work sequentially. In light of the urgency of the pandemic, we are now doing the development and manufacturing processes in parallel and we're investing significant capital at risk to help compress the timelines to meet this global challenge. With our partner BioNTech, we selected the most promising version and dose among four potential vaccine candidates, based on Phase 1 clinical studies conducted in the U.S. and Germany. These data and our recommendation for our final vaccine candidate were shared with the FDA and other global regulators who approved our planned Phase 3 study in only a few days. We then rapidly moved into large-scale, randomized testing in 30,000 volunteers that will tell us if the vaccine is both safe and effective.

We've seen the benefit of embracing novel clinical trial designs including seamless adaptive trial designs and platform approaches to test multiple assets in the clinic simultaneously. These mechanisms are not new and should be leveraged routinely, particularly for other serious and life-threatening diseases where similar benefit/ risk considerations apply.

2. How did investments into platform technology help speed up the vaccine development process?

Response: Fortunately, we have been able to leverage several years of ongoing research on the mRNA platform for potential influenza vaccines with our partner BioNTech, dating back to 2018. This is an important foundation for the work in our COVID-19 vaccine program, including preclinical and manufacturing data to support the safety of the underlying mRNA technology. This early work allowed Pfizer and BioNTech to accelerate entry into clinical testing, while preserving high standards for safety and not cutting any corners.

Additionally, the mRNA vaccine platform allows for precise genetic profiling of the viral protein and rapid manufacturing scale-up (millions of doses by the end of 2020 and hundreds of millions in 2021). These unique platform attributes could also be deployed to address future pandemics and pathogens.

From a policy perspective, there is tremendous potential to further leverage a wide variety of genomic platform technologies, for example in vaccines, gene therapies, and small-molecule targeted therapies in the future by leveraging prior knowledge of the platform performance characteristics. The Committee set the stage for this approach through passage of the 21st Century Cures Act, which established a program - Targeted Therapies for Rare Diseases (§3012) - to help streamline the life-cycle submission and review of genetically targeted drugs and variant protein targeted drugs. We encourage the Committee to consider further expanding this program to promote broader FDA utilization of the program across additional genomic platform technologies and therapeutic areas.

3. Do any of your companies have recommendations about how to further innovate clinical trials?

Response: The COVID-19 pandemic has pressure tested regulatory systems as never before. And most will agree that the biomedical research ecosystem will never be quite the same again. The durable lessons learned can help prepare us for future pandemics and accelerate the development of therapies for other debilitating and life-threatening conditions. We see the opportunity in several areas:

First is building a digitally resilient clinical trials system. We learned that digital tools could be used to great effect to ensure that patients can continue to safely participate in research during the pandemic. Decentralized trials, adaptive designs, master protocols, and real-world evidence are not new, but the mutual experience gained during the pandemic can help ensure that they become routine elements of a modern regulatory toolkit.

Second, is the value of robust, interactive scientific dialogue between FDA and sponsors during development and throughout the review process. In the usual drug development journey, the process of preparing regulatory data packages to submit to the FDA and then waiting to hear back is typically iterative and time consuming, often taking months. With all hands-on-deck in the fight against COVID-19 across the globe, regulators are responding to data very quickly, often in real time, to help keep trials running as quickly as possible. Additional FDA resourcing may be required to help sustain this type of interaction for COVID-19 and other areas of unmet medical need.

Finally, the breadth and depth of the collaboration needed between regulators, researchers, and industry in the global pandemic has highlighted the need for enhanced secure data platforms for information exchange. This helps to facilitate real-time or rolling review for COVID-19 vaccines and therapeutics and accommodate large data sets and new tools, including computational models, real-world evidence, and "big data."

We believe industry and regulators will emerge stronger than before by applying the lessons learned from this crisis to create a more efficient and patient-centric "new normal." We look forward to engaging with the committee on these concepts as it considers 21st Century Cures 2.0 and PDUFA 7 legislation.

We enclose for the committee's information a paper recently published in Nature that outlines areas that we believe lend themselves to continued innovation.

4. COVID-19 has been with us for about seven months. There is still much we don't know about the antibody response and how long it lasts. Is there anything from the last seven months that has been learned that provides any insights into immune responses, and why it might suggest that our vaccine enterprise is on the right track?

Response: Our studies to date have provided data that shows our investigational COVID-19 vaccine stimulates a strong response from both parts of the immune system, both antibodies and T cells. These are critical to providing protection against a virus such as SARS-CoV-2

and provide encouragement that the vaccine will be able to protect against COVID-19. That is what we now seek to demonstrate in the large-scale part of the study that is ongoing now.

5. **Do you have plans to have human challenge studies where you will take healthy individuals, immunize them with your vaccine candidate, and then challenge them with an infectious dose of COVID-19?**

    a. **If yes, how is this ethical, and will your human challenge studies include participants over 55 years of age?**

    b. **If nobody under 55 will be enrolled, will there be a gap in our knowledge about vaccine effectiveness in the 55 years and older age group?**

Response: We have no plans to perform human challenge studies. However we believe the placebo arm of our Phase 3 study may provide an indication of the degree of protection conferred by our vaccine.

6. **Could your vaccine candidate(s) be used with an adjuvant? If so, how many additional doses could be generated from the use of an adjuvant.**

Response: Because of the inherent immunogenicity of RNA-based vaccines, there is no need for an adjuvant for any specific populations.

    a. **If not, are there other ways your vaccine could be boosted to strengthen the immune response in patients?**

Response: Adjuvants are not necessarily the optimal approach for every type of vaccine. With our partner BioNTech we will continue to explore further opportunities for the mRNA vaccine platform.

The Honorable David B. McKinley (R-WV):

1. **When H.R. 3, the Lowering Drug Costs Now Act, was being considered in the House, members of this Committee raised concerns about what such legislation could do to innovation and drug development in the U.S., and Dr. Gerberding mentioned in her testimony how a robust biopharmaceutical research network has contributed to the accelerated development of a vaccine. H.R. 3 would undermine the important role of private-sector R&D in the U.S., as countries with price controls have suffered a decline in pharmaceutical R&D.**

Do you all have concerns about impacts on your research and development efforts, should such legislation become law in the U.S.? Why or why not?

Response: Many economists have raised concerns with referencing international prices to U.S. prices and the impact on incentives for innovation. We share those concerns. The Council of Economic Advisors warned in a 2018 report that lowering reimbursement for

medicines in the United States "makes better health costlier in the future by curtailing innovation." In fact, evidence shows that every $1-2 billion reduction in research and development investment leads to development of one fewer new medicine per year; an updated Council of Economic Advisors analysis specific to H.R. 3 forecasted as many as 100 fewer drugs entering the U.S. market over the next decade. The U.S. Department of Commerce found that international reference pricing and other price controls in foreign countries already suppress worldwide private research and development investment by 11-16 percent annually, and international reference pricing here in the U.S. would only compound that problem.

2. **Most of you have accepted awards from the U.S. Department of Health and Human Services (HHS) to assist with the development and manufacturing of a COVID-19 vaccine?**

    a. **Are each of you on schedule and on budget?**

    b. **If you are behind schedule, do you plan to invest your own capital if the government grant runs out before you are finished with development?**

    c. **If you are ahead of schedule and you have grant money left over, what are your plans for those funds?**

Response: To date, we (Pfizer and BioNTech) have not accepted any U.S. government funding for our COVID vaccine research and development efforts. We are on track with our progress at this time.