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

Dr. Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, AstraZeneca

The Honorable Brett Guthrie (R-KY):

- **Experts from across AstraZeneca have joined forces with our industry colleagues, as well as international health authorities, governments, and academia to accelerate the development of medicines to prevent or treat COVID-19. We do not consider this a competition, but rather a collaboration to release the grip this virus has on the world. Scientists around the world, including ours, are sharing data and research findings in unprecedented ways.**

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?

   We are collaborating with the FDA and NIH on key aspects of our protocol and development program, including study design, study population, endpoints, and requirements for licensure. In addition to the FDA and NIH, AstraZeneca is working closely with other U.S. government agencies as part of Operation Warp Speed, including the CDC and BARDA at HHS.

   While we are working on expedited timeframes, we are conducting our development and manufacturing programs in accordance with all applicable regulatory requirements. Similar to other vaccine developers, we are accelerating our global clinical development program by compressing the timelines, working in partnership with University of Oxford and regulators and sharing data on a real-time basis.

   The process has helped us see where improvements could be made in order to continue to foster and grow innovation. For example, manufacturers could have improved access to FDA. This current process has demonstrated that having open and transparent discussions, and decision making by all parties is critical. Additionally, coordination between health authorities could be of tremendous help to vaccine developers. The FDA, in coordination with other U.S. agencies, could also create guidance for the industry for rapid development of a vaccine in a pandemic setting. This could help speed up development in the future.

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

The ChAdOx1 vector system, developed by Oxford University, is an AstraZeneca licensed vaccine platform. This platform utilizes disposable manufacturing systems, transferable analytical tools and a manufacturing process that enables us to rapidly scale up and supply global COVID-19 vaccination programs. In the future, these technologies and principles can be applied to address new pandemics and investments in these platform technologies can help with rapid manufacturing and development, should the need arise.

We have also made investments in developing our manufacturing platforms that have been essential in our rapid vaccine development. For example, our investment internally in end-to-end manufacturing capability has been essential to move product from a cell bank vial to drug product in timelines never seen before.

Digital and technology solutions have played a pivotal role in our response to the COVID-19 pandemic, helping us accelerate the evaluation of potential COVID-19 treatments while maintaining delivery of our innovative pipeline.

At AstraZeneca, we have been investing in digital technologies over the past few years, and this has enabled us to quickly adapt during the pandemic to deliver our clinical trials and maintain a smooth trial experience for patients. This has also been important for vaccine development. Upgrading to a cloud-based system has enabled vaccine supply to sites and monitoring of global stocks in days versus months. In addition, by using data and analytics to model rate of infection across the globe, we have been able to select sites where the rates of infection remain high. We have also expedited the launch of eConsent, a new digital tool that enables remote sharing and review capabilities of the informed consent with patients. This has helped get new trials underway safely and at speed. Finally, through the use of new digital and technology solutions, we are using remote data collection from home wherever possible to safeguard the wellbeing of patients.

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

The COVID-19 pandemic has challenged the way that the healthcare industry, including the pharmaceutical industry, delivers care to patients. Traditional methods for conducting clinical trials have been disrupted in unprecedented ways. This disruption has forced regulators and industry to think progressively about how to enable and execute new methods for delivering care to patients. Innovative thinking and modified regulatory policy have allowed for the implementation of continuity solutions to accommodate the ongoing conduct of clinical trials, while maintaining patient safety and data integrity.

The use of digital and technology solutions are key to furthering innovative clinical trials. This includes developing digital solutions to enhance the delivery of medicines, reduce inefficiencies, and support patients in engaging with their own health; redefining the clinical trial experience through the use of digital tools and technologies to improve patient safety and outcomes; and harnessing data science and artificial intelligence to transform the way we discover and develop new medicines. Our drive towards integrated care is dependent on building interoperable and trusted health data frameworks to unlock the full potential of scientific data for patients and healthcare systems.

The implementation of clinical trial continuity solutions has impacted all stakeholders (e.g., sponsors, investigators, patients) involved in clinical research. As a result, there is a rich opportunity to understand the numerous lessons learned from both challenges and successes. These learnings can inform future ways of working for industry as well future policy by regulators. The Modernizing Clinical Trial Conduct Initiative will use data and experience to develop practical guidance and solutions to further enable the successes implemented during COVID-19. This initiative, of which AstraZeneca is supportive, seeks to collaboratively engage other major stakeholders including regulators, patients, sites, and industry groups.

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?

As the SARS-CoV-2 virus is new, it is not known what kind and level of immune response is needed to prevent people from becoming ill with COVID-19. While high levels of neutralizing antibodies have been demonstrated in individuals who have recovered from SARS-CoV-2 infection, emerging data suggest that a T-cell response could play a role in mitigation of the disease. In some individuals who have been infected by the virus but remained asymptomatic, they have developed a robust T-cell response with the absence of antibodies. Rapid induction of antibodies and T-cells against SARS-CoV-2 may be important in protection against COVID-19.

We are conducting a comprehensive, global clinical trial development to assess safety, efficacy, and immune response of AZD1222. We have late-stage clinical trials ongoing in the US, UK, Brazil and South Africa, and trials are planned to start in Japan and Russia. These trials will enroll up to 50,000 participants globally (30,000 in the U.S), assessing at different dose levels and regimens, and will include diverse racial, ethnic and geographic groups who are healthy or have stable underlying medical conditions, including those living with HIV, and those at increased risk of infection from the SARS-CoV-2 virus e.g. frontline healthcare workers. Trial participants will also be followed over two years to study immune response in detail. Data from these trials will confirm if this approach provides the best potential to protect against COVID-19 disease. Results from the late-stage trials are anticipated later this year, depending on the rate of infection within the clinical trial communities.

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?

   To date, challenge trials have not been necessary. We believe it is too early to consider deliberately exposing trial participants to the pathogen, but it may become an option if found necessary to proceed with the research. Of course, we would work closely with FDA and other regulators and institutional review boards, to review and implement the protocols and subject protections in any such trials.

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

      N/A

   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?

      N/A

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.

   An adjuvant is not currently being considered for use with AZD1222.

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

      Based on accumulating preclinical and clinical data for AZD1222, we are proceeding with a two-dose strategy, which is being implemented in all ongoing clinical trials. Results will determine if this approach provides the best potential to protect against COVID-19 disease.

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?

We are concerned that H.R. 3 could limit or delay access to innovative medicines and reduce investment in future treatments. Research has shown that when countries intervene to set a cap on drug prices, research and innovation suffer and that it is "simply not true that government can impose significant price controls without damaging the chances for future cures[1]."

According to a PhRMA analysis, H.R. 3 could cost the biopharmaceutical industry as much as $1 trillion over 10 years – 4 times total annual U.S. net revenues earned by the industry. This drastic cut would jeopardize the almost $100 billion biopharmaceutical companies invest annually in R&D. This plan would erode incentives that are critical to support investment into the risky and uncertain R&D process for complex diseases.

We believe the current health care system needs to evolve, and we are committed to working with Congress and the Administration to address patient access and affordability while continuing to support scientific innovation.

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?

Phase 3 trials are underway and we are moving forward with manufacturing to meet our commitments under our initial agreement with the U.S. government. We continue to finalize our agreement with the U.S. government as negotiations continue to move ahead.

    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?

Funding under the terms of our agreement with the U.S. government is reimbursement for AstraZeneca's costs reasonably incurred in performing the contracted work. The provision does not put AstraZeneca in a position to profit from its work with the U.S. government.

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

We do not anticipate that the contract will reimburse us more dollars than we actually spend.

[1] Information Technology & Innovation Foundation. "The Link Between Drug Prices and Research on the Next Generation of Cures." September 2019. https://itif.org/sites/default/files/2019-drug-prices-cures.pdf