

**Statement of
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**Before the Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives**

**Pathway to a Vaccine:
Efforts to Develop a Safe, Effective and Accessible COVID-19 Vaccine**

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Chairwoman DeGette, Ranking Member Guthrie, and Members of the Subcommittee, I am Dr. Menelas Pangalos, Executive Vice President, Biopharmaceuticals Research and Development (“R&D”) at AstraZeneca. I have been with AstraZeneca since 2010, and I am responsible for R&D activities from discovery through late-stage development for cardiovascular, renal and metabolism, respiratory, and immunology diseases. I am here today to convey to you AstraZeneca’s strong commitment to ongoing efforts to develop and manufacture vaccines and therapeutics for the prevention and treatment of COVID-19. We greatly appreciate the opportunity to engage with you today on this important topic, and I hope to emphasize our dedication to finding safe and effective solutions for the COVID-19 pandemic in the U.S. and across the world.

With respect to the COVID-19 vaccine, our strategic approach has focused on partnering with scientists, governments, international organizations, and manufacturers to establish agreements for the development, supply and distribution of the vaccine in an equitable manner across the world, should it prove effective and well-tolerated. *To support our goal of providing broad and equitable access as quickly as possible, we have entered into agreements with the United States and certain other governments and organizations, for supply of hundreds of millions of doses of our vaccine. The cost of the doses of the vaccine under those agreements will provide no profit for AstraZeneca.*

I would first like to provide some background on AstraZeneca. We are a global, science-led biopharmaceutical company that focuses on the discovery, development, manufacturing, and commercialization of innovative medicines, primarily for the treatment of diseases in the following therapeutic areas: Oncology, Cardiovascular, Renal & Metabolism, and Respiratory and Immunology. We are proud to call Wilmington, Delaware home to our North American Headquarters, and that one of our three global R&D headquarters is located in Gaithersburg, Maryland. Overall, we have approximately 13,000 employees in the United States, with operations in 12 different states and Puerto Rico (California, Delaware, Indiana, Kentucky, Maryland, Massachusetts, New Jersey, New York, North Carolina, Ohio, Pennsylvania, and Texas), including eight manufacturing sites. These sites account for nearly one-third of our total manufacturing footprint. In addition to our U.S. presence, we have an additional 18 manufacturing sites throughout the rest of the world. In total, AstraZeneca operates in over 100 countries, and we are leveraging our global workforce and resources to address this worldwide crisis.

Today I will focus on three core aspects of AstraZeneca's approach to advancing novel vaccines and therapeutics for COVID-19:

- *First*, AstraZeneca is seeking to develop a novel vaccine for the prevention of COVID-19. AstraZeneca has entered into an exclusive licensing arrangement with the University of Oxford for the global development, production, and supply of the University's potential COVID-19 vaccine candidate, AZD1222.

In the U.S., to avoid any delays that could result in the unnecessary loss of life, we are scaling up to manufacture up to 300 million doses of the vaccine so that they will be available immediately upon approval or emergency use authorization. Our agreements so far across the world amount to supply of approximately two billion doses, and we are building a number of parallel supply chains with partners around the world to support broad and equitable global access.

AstraZeneca's development and manufacturing programs are designed to satisfy all applicable regulatory approval and emergency use authorization standards. We fully support the mission of regulatory agencies, such as the U.S. Food and Drug Administration ("FDA"), to ensure that vaccines and other medical products are determined to be safe and effective based on sound science and data before receiving approval or emergency use authorization. *Sound science and patient safety and health are, and will continue to remain, our top priorities in this effort.*

We are proud to confirm that our novel vaccine candidate has begun late-stage clinical trials based on data from pre-clinical studies and Phase I/II clinical trials in over 1,000 healthy volunteers. We are rapidly progressing these clinical programs with the hope that results from our late-stage trials, which are currently planned to involve close to 50,000 volunteers collectively, will be available this fall.

- *Second*, through our scientific expertise in infectious disease and proprietary antibody discovery technology, we have rapidly mobilized our research efforts toward discovering novel coronavirus-neutralizing antibodies as a prophylactic and possible treatment approach against COVID-19 disease.

We are advancing a combination of monoclonal antibodies against the SARS-CoV-2 spike protein through pre-clinical development following a collaboration agreement with Vanderbilt University. This came at the same time that we signed an interagency agreement with the U.S. Biomedical Advanced Research and Development Authority ("BARDA") and the U.S. Defense Advanced Research Projects Agency ("DARPA") to support the Phase I clinical trial and the manufacturing of the investigational product for testing in Phase I.

The team is currently designing an accelerated development program, working with scientists, governments, multilateral organizations, and manufacturers around the world, with the aim of reaching clinical trials within a matter of weeks.

- *Third*, we have initiated new clinical trials to investigate our new and existing medicines to see how they could protect organs from damage or suppress the body's overactive immune response in severely ill patients. As the SARS-CoV-2 virus is new, the scientific community is constantly learning about the virus and advancing our understanding on how best to tackle and treat this disease.

For example, a new global clinical trial for our Bruton's tyrosine kinase ("BTK") inhibitor, Calquence[®], will assess the potential of the treatment in the exaggerated immune response, or cytokine storm, associated with COVID-19 infection in severely ill patients. Our sodium-glucose cotransporter 2 ("SGLT2") inhibitor, Farxiga[®], is being explored as a potential medicine to protect against organ damage in patients hospitalized with COVID-19 and at risk of developing serious complications.

In addition to these efforts on a vaccine and therapeutics, we have donated three million face masks to be distributed to healthcare workers across the United States to aid these brave and dedicated individuals in battling COVID-19.

Addressing the COVID-19 pandemic is an urgent priority for our company. We come to work every day focusing on the goal that our efforts will save lives and alleviate the devastating humanitarian, social, and economic consequences of the ongoing pandemic throughout the world. We thank the support of members of this Subcommittee in our efforts to achieve these goals, and we appreciate the opportunity to testify today.

I. AstraZeneca is Committed to Ending the COVID-19 Pandemic and Saving Lives

AstraZeneca is collaborating with scientists, governments, multilateral organizations and manufacturers around the world to advance a novel vaccine and monoclonal antibody therapy for the prevention and treatment of COVID-19. In addition to our commitment to enable broad and equitable access across the world to approximately two billion doses of AZD1222, the vaccine candidate licensed from the University of Oxford Jenner Institute, we are also planning to advance a monoclonal antibody combination into clinical development. These monoclonal antibodies will be used in combination with each other both to prevent and treat COVID-19. We believe it is imperative to employ a multi-pronged approach -- both with a prophylactic vaccine and with therapeutics -- in tackling COVID-19.

Our immediate goal is to help prevent further loss of life and to put an end to the unprecedented devastation that the COVID-19 pandemic has caused throughout the U.S. and the world. To support our goal of providing broad and equitable access as quickly as possible, we have entered into agreements with the U.S., and certain other governments and organizations, for supply of hundreds of millions of doses of our vaccine. The cost of the doses of the vaccine under those agreements will provide no profit for AstraZeneca. We are extraordinarily grateful for the support we have received, which has helped make this commitment possible.

Right now, we are intensely focused on helping to overcome the global public health emergency through the development of our candidates. We recognize that we are only one of many companies working on potential vaccines and therapeutics for COVID-19. We hope that

the other companies testifying today are also successful in their pursuits, as their achievements would offer patients and governments more options, which we believe are necessary to effectively combat this pandemic. I know that none of the companies involved in this project view this as a competition against each other -- our sole adversary is COVID-19.

As noted, although we have yet to determine whether the vaccine will satisfy the rigorous safety and efficacy standards necessary for approval, even prior to any approval or emergency use authorization, we are proceeding to manufacture the vaccine with the support of the U.S. and other governments. We made this decision so that, if the vaccine is approved or authorized under an emergency use authorization, it will be ready for immediate distribution and administration. The alternative of waiting until we have greater certainty that the vaccine works -- which would delay the manufacture of the vaccine by several months or years -- was simply not an option.

We have also initiated new clinical trials to investigate our new and existing medicines to see how they could address serious and life-threatening complications from COVID-19 in severely ill patients. We have commenced our CALAVI-US study, a multicenter, randomized, open-label, Phase II clinical trial to evaluate the efficacy and safety of adding Calquence[®], our BTK inhibitor, to best supportive care to reduce the need for assisted ventilation or death in patients with life-threatening COVID-19 symptoms. We are conducting this trial in the U.S. and began enrolling patients in May 2020. The trial design for CALAVI-US is based on strong scientific evidence supporting the role of the BTK pathway in the production of inflammatory cytokines derived from a NIH study. The NIH study was led by researchers in the Center for Cancer Research at the National Cancer Institute (“NCI”), in collaboration with researchers from the National Institute of Allergy and Infectious Diseases (“NIAID”), as well as the U.S. Department of Defense’s Walter Reed National Military Medical Center and four other hospitals.

In addition, Saint Luke’s Mid-America Heart Institution, in collaboration with AstraZeneca, initiated the DARE-19 study, a Phase III, international, multicenter, parallel-group, randomized, double-blind, placebo-controlled, investigator-sponsored trial evaluating the effect of our SGLT2 inhibitor, Farxiga[®], in addition to background local standard of care therapy, on the risk of all-cause death or disease progression and clinical complications. This study began enrolling patients in April 2020 and will be conducted in approximately 50 centers in the U.S. and in other countries with a high COVID-19 burden. We are hopeful that these clinical programs will help improve patient outcomes and provide important data for the scientific community to better understand the SARS-CoV-2 virus.

II. AstraZeneca is Collaborating with Academia and Governments to Advance its Vaccine and Monoclonal Antibody Candidates for the Treatment and Prevention of COVID-19

The progress that AstraZeneca has made in identifying and developing the vaccine would not have been possible without significant contributions from academia and government agencies. We have taken a truly global approach to this project. Our collaborations with institutions and government agencies have been essential in expediting the R&D programs for our candidates, and

in ensuring that the cost of the doses of the vaccine to be supplied under our agreements with the U.S., and certain other governments and organizations, will provide no profit for AstraZeneca, if the vaccine is ultimately approved or authorized under an emergency use authorization.

In May 2020, AstraZeneca entered into an exclusive global development and distribution agreement with the Jenner Institute at the University of Oxford and the Oxford Vaccine Group. This agreement gave AstraZeneca a license to develop and potentially to distribute the University's novel recombinant adenovirus vaccine candidate AZD1222, formerly known as ChAdOx1 nCoV-19. We did so because we recognized the extraordinary potential of the ChAdOx1 vaccine platform and the groundbreaking research conducted by Oxford. And, while I cannot speak for Oxford, I believe the team recognized that a partnership with AstraZeneca would facilitate accelerated global clinical development, would allow scaled-up manufacturing to the unprecedented levels required to mitigate the impacts of a global pandemic, and would promote broad and equitable access to the vaccine around the world, assuming it is approved or authorized under an emergency use authorization.

We are also finalizing an agreement for more than \$1 billion with BARDA for the development, production, and delivery of 300 million doses of AZD1222 to the U.S. Under this agreement, AstraZeneca's goal is to supply the initial doses beginning in October 2020 and the remaining doses in 2021. The U.S. government will then own the doses of vaccine that we produce and determine how the doses are distributed. The development program under this agreement includes a Phase III clinical trial with 30,000 participants and a pediatric trial. We are very pleased that the government has moved with speed to advance this critically important agreement with AstraZeneca, and I would like to take this opportunity to thank the Administration and Congress for their unwavering commitment and the funding needed to advance this effort.

We are also extremely proud that the vaccines covered by this agreement will be manufactured in the United States. We are now moving forward with activities at our West Chester, Ohio site, related to the formulation, filling, and packaging of the vaccine for the U.S. market. The West Chester site is one of our key U.S. operations centers, and we selected this site for this important initiative because it is an aseptic sterile filling and packaging facility that has the capability to manufacture the vaccine to scale. We have also partnered with other U.S. pharmaceutical manufacturers to manufacture the vaccine at additional domestic sites.

Additionally, in June 2020, we entered into an exclusive license agreement with Vanderbilt University for six of their most promising monoclonal antibodies, isolated from cells in patients who have recovered from COVID-19. We had evaluated more than 1,500 antibodies from different sources in our own laboratories. Our evaluation assessed their ability to bind to and neutralize the SARS-CoV-2 virus. We now plan to advance a combination of these antibodies into clinical development.

An antibody-based treatment could potentially be used both as a prophylactic approach for COVID-19 and as a complement to vaccines. For example, the antibody treatment could be used for patients who may not be eligible for vaccination or as additional protection for patients who are higher-risk. In addition, we plan to evaluate our monoclonal antibody combination candidate as another potential treatment for patients with COVID-19. Like our Oxford partnership, this

collaboration is intended to facilitate expedited development of this potential therapy. To support the monoclonal antibody development program, we entered into a \$25.1 million interagency agreement with BARDA and DARPA for a Phase I clinical trial and manufacture of investigational monoclonal antibodies for testing in this trial. We are in discussions with government agencies regarding Phase II/III clinical trials and manufacturing plans in the event that early clinical trials show that our monoclonal antibody combination candidate is effective and well-tolerated.

We have set an ambitious goal to supply the vaccine to as many countries around the world as possible. We are leveraging our own industrial capacity while also working with a number of partners to establish parallel supply chains in record time. In addition to our partnerships with the U.S., we have, or are in the process of negotiating, partnerships with the U.K., Europe's Inclusive Vaccines Alliance, the Coalition for Epidemic Preparedness Innovations, and Gavi.

III. AstraZeneca's Development and Manufacturing Programs Are Designed to Satisfy All Applicable Regulatory Approval and Emergency Use Authorization Standards

The development and full-scale manufacture of a novel vaccine or treatment often can take years. Given global public health imperatives, we are developing and manufacturing the vaccine and our monoclonal antibodies in a matter of months by compressing timelines and working in partnership with academia and regulators from around the world. However, we must also achieve all of this in a manner that complies with the applicable regulatory requirements. Our first priority is to demonstrate the safety and efficacy of the vaccine and monoclonal antibody candidates through sound science and clinical data derived from adequate and well-controlled studies. To that end, we maintain an open dialogue with regulators to obtain feedback and provide data and other updates in real-time, and we have sought input from FDA on key aspects of our protocol and development program.

Existing knowledge and data regarding the safety and effectiveness of the ChAdOx1 vaccine platform used for AZD1222 has also allowed studies to progress rapidly. Vaccines made from the ChAdOx1 platform had previously been administered safely. Specifically, the Jenner Institute at the University of Oxford had demonstrated the promise of this vaccine platform in prior early-stage clinical trials, including in one trial last year against an earlier coronavirus, Middle East Respiratory Syndrome ("MERS"). Because of that earlier work, we have been able to develop the potential COVID-19 vaccine more quickly.

Although we now have a preliminary understanding of the potential safety and effectiveness profile of AZD1222, protecting the safety of the participants in our clinical trials remains of highest importance. The U.K. has used an independent Data and Safety Monitoring Board ("DSMB") for this purpose, and we intend similarly to employ an independent DSMB for our planned Phase III study in the U.S. and our clinical programs for other treatment candidates. The DSMB will provide continuous oversight throughout the study and will monitor for safety and efficacy results, evaluate cumulative safety and other clinical study data at regular intervals, and make appropriate recommendations based on the available data. The DSMB safety analyses will also help to inform the vaccine's and monoclonal antibody combination's overall safety profiles and will provide valuable insights to regulators, such as FDA.

AstraZeneca is fully supportive of FDA's role in assessing vaccine and other treatment candidates against stringent safety, efficacy, and tolerability standards as part of the approval or emergency use authorization process. We were heartened by FDA Commissioner Dr. Stephen Hahn's recent testimony before the Senate Health, Education, Labor & Pensions Committee, in which he emphasized FDA's commitment to expedite this work without cutting corners in its regulatory decision making. We welcome FDA's recently issued guidance on the development and licensure of vaccines to prevent COVID-19, and we applaud FDA's commitment to maintain independence and ensure that decisions regarding COVID-19 vaccines and treatments are based on sound science and data. The American people must be able to trust in any approved or emergency use authorized vaccines and treatments.

IV. Vaccine Development Status

Clinical development of AZD1222 is progressing throughout the world. Pre-clinical data published in different animal models, such as mice, pigs and non-human primates, show that AZD1222 provokes an immune response against the SARS-CoV-2 virus, with increases in both antibodies and T-cells after a single dose. In the pig model, adding a second dose enhanced this immune response.

An ongoing Phase I/II clinical trial of AZD1222 commenced in April in the U.K. to evaluate the safety and immune response of AZD1222 in over 1,000 healthy adult volunteers. We hope to have the full data from this trial in the coming weeks. Review of initial safety and immune response data from this trial by the U.K. DSMB has allowed progression to late-stage trials, including in the U.K. with over 10,000 volunteers.

Late-stage Phase II/III trials are also progressing in Brazil and South Africa with approximately 5,000 volunteers and over 2,000 volunteers, respectively. We are planning a Phase III trial with approximately 30,000 volunteers and pediatric study in the U.S. and additional late-stage trials in other countries. Ensuring diversity in these trials, including in terms of race, ethnicity, gender, age, and other factors, is a priority in our efforts. These late-stage Phase II and III trials will determine how well the vaccine can protect patients from COVID-19 and will measure safety and immune responses in different age ranges and at various doses. We are evaluating one and two-dose strategies in order to maximize the prospects that the vaccine will protect against COVID-19.

We hope to have results from these larger trials in the fall, but the timing of those results will depend on the rate of infection within the clinical trial communities. AstraZeneca will continue to monitor infection rates and will adjust our global clinical trial program as appropriate. We will also continue to evaluate the number of doses of the vaccine that will be required, so that we can achieve the most optimal level of protection against COVID-19.

V. Monoclonal Antibody Development

We are currently in the pre-clinical evaluation stage for our monoclonal antibody combination candidate, and we hope to be in the clinic within weeks as we are making good progress. We plan to move this forward as quickly as possible. A possible future antibody-based

treatment could potentially be used as a prophylactic approach for COVID-19 and could be complementary to vaccines, *e.g.* for people who may not be able to have a vaccination or to provide added protection for high-risk populations. In addition, we plan to evaluate our monoclonal antibody combination candidate as a potential treatment for patients with COVID-19. AstraZeneca is committed to working with regulatory agencies to ensure rapid but safe access to the monoclonal antibody combination, should it prove effective in clinical trials. Based on current data, we are hopeful that an antibody combination approach will be able to neutralize the SARS-CoV-2 virus, to reduce the impact of any escape mutations, and to be prescribed as both a prophylactic and a treatment option for those exposed to the virus. We engineered the monoclonal antibody combination using our proprietary half-life extension technology, and prior experience with this technology suggests the combination could provide meaningful protection against the SARS-CoV-2 virus for as long as 150 days. The additional antibodies we licensed from Vanderbilt could also be important for future research efforts as we learn more about the virus and COVID-19, and we will continue to pursue such research in order to find an effective solution to the global pandemic.

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AstraZeneca is fully committed to fighting the COVID-19 pandemic and saving lives through the expedited, science-based development and manufacture of prophylactic and treatment options for COVID-19. Our team is continuing to make progress in our development programs, and we fully intend to provide broad access to therapeutics, if approved or authorized under an emergency use authorization, in the U.S. and across the world.

Chairwoman DeGette, Ranking Member Guthrie, and Members of the Subcommittee, on behalf of AstraZeneca, thank you for the opportunity to participate in today's hearing. We appreciate your keen interest in these important issues, and I look forward to answering your questions.