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Pathway to Protection: Expanding Availability of COVID-19 Vaccines

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Chairwoman DeGette, Ranking Member Griffith, and Members of the Subcommittee, thank you for the opportunity to appear before you today. I am John Trizzino, and I am executive vice president, chief business officer and chief commercial officer at Novavax. I have been with Novavax for a total of 10 years and have held a number of leadership roles that have given me a deep understanding of the company. I also have more than 25 years of direct vaccine industry experience in pediatric and adult immunizations as well as influenza pandemic preparedness, all of which is directly related to the COVID-19 pandemic response.

I. Novavax

Novavax is a biotechnology company focused on the development of next-generation vaccines for serious infectious diseases. The company is headquartered in Gaithersburg, Maryland. We are proud to be at the forefront of the fight against COVID-19. While we initiated development of our SARS-CoV-2 vaccine candidate in January 2020, our company has been developing vaccines for almost two decades and for the past ten years we have focused on using our recombinant nanoparticle platform technology. This includes the production of vaccines for two coronaviruses, Middle East Respiratory Syndrome (MERS) in 2012 and severe acute respiratory syndrome (SARS) in 2003. We also have a late-stage respiratory syncytial virus (RSV) vaccine candidate and an influenza vaccine candidate, NanoFlu™, for which we concluded

a successful Phase 3 clinical trial in 2020. This extensive experience with our platform technology positioned Novavax to quickly initiate development of a SARS-CoV-2 vaccine candidate shortly after the virus was isolated. This testimony will walk you through our recombinant nanoparticle platform technology, development of our COVID-19 vaccine candidate, NVX-CoV2373, and our US manufacturing operations and supply chain.

II. Our Science

A. *Recombinant Nanoparticle Technology*

The two key features of our vaccine platform include a recombinant protein nanoparticle engineered from the genetic sequence of the target pathogen and our Matrix-M™ adjuvant. Together, they trigger protective immune responses needed to prevent disease. Our recombinant vaccine engineering takes a new approach to provide robust and functional immunity, which may be more efficacious than traditional vaccines. Using this technology, we are able to produce vaccine candidates to efficiently and effectively respond to both known and emerging disease threats.

Vaccines typically take years, or even decades to develop. In addition, many pathogens have evolved to avoid the immunity induced by recurring infections. Because of this, there are several advantages to using our recombinant nanoparticles in place of the old technology. First, our technology platform gives us the ability to tailor our vaccines to key components of pathogens to enhance functional immunity and lead to better protection against infection and disease. Our insect cell platform efficiently expresses native-conformation antigens, and these protein antigens are then processed into nanoparticles. Taken together, these features of our technology allow us to produce highly immunogenic vaccines in a scalable, efficient recombinant vaccine production system.

B. *Our Adjuvant*

Novavax's proprietary Matrix-M™ adjuvant improves immune responses and enables vaccine dose-sparing. Combined with the nanoparticle antigen we produce, our Matrix-M adjuvant means that our vaccines can use lower doses of antigen to achieve the desired immune response, which results in increased supply and manufacturing capacity. This means

that our technology platform could give us the ability to vaccinate more people in the US and worldwide.

Matrix-M is derived from saponin, which is found in the inner bark of the Chilean soapbark tree, *Quillaja saponaria*. After purification and processing, it is a critical component of our vaccine candidates, and increases the breadth and height of the immune response. Saponins have a multi-decade track record of use in experimental and licensed vaccines. Overall, this extensive clinical experience has demonstrated this class of adjuvants to be well-tolerated.

We learned from our experience with NanoFlu, our quadrivalent seasonal influenza candidate, that the Matrix-M adjuvant is a powerful tool in the fight against antigenic drift during the flu season. In a pivotal Phase 3 clinical trial, NanoFlu met or exceeded the primary and secondary endpoints, demonstrating safety and non-inferior immunogenicity for all four strains included in the vaccine compared to a U.S.-licensed quadrivalent influenza vaccine.

III. Development of NVX-CoV2373

NVX-CoV2373 is a protein-based vaccine candidate engineered from the genetic sequence of the Wuhan SARS-CoV-2 strain, the virus that causes COVID-19 disease. NVX-CoV2373 was created using our recombinant nanoparticle technology as I described to generate antigen derived from the coronavirus spike (S) protein and is adjuvanted with Matrix-M to enhance the immune response and stimulate high levels of neutralizing antibodies. NVX-CoV2373 contains purified protein antigen and can neither replicate, nor can it cause COVID-19.

In early clinical testing of multiple candidates, two doses of NVX-CoV2373 administered 21 days apart evoked the strongest immune system response. Our vaccine candidate is stored at 2-8°C in a refrigerator-stable, liquid formulation, allowing for successful cold chain management with existing infrastructure. It is presented in ten-dose vials, is preservative-free, and is ready for use as an intramuscular injection using standard needles and syringes. Because our vaccine can be distributed through existing vaccine supply chain channels, it offers specific benefit to rural and underserved populations, which can be harder to reach.

Giving you a preview of what I will detail further, we recently announced that NVX-CoV2373 demonstrated high clinical efficacy against the original virus strain, and it was the first vaccine to demonstrate clinical efficacy against both of the rapidly emerging variants that are circulating in the United Kingdom and South Africa, and now known to be present in the US.

A. *Our Partners*

Novavax is working closely with US government partners as well as non-governmental organizations and industry partners to advance development of NVX-CoV2373. Our exceptional partnerships have enabled the progress we have made to date. In May 2020, we announced that based on our strong preclinical data, the Coalition for Epidemic Preparedness Innovations (CEPI) would invest up to $399 million to support our Phase 1 and 2 clinical trials and dramatically increase large-scale manufacturing capacity for antigen and adjuvant production in multiple locations outside of the USA.

In June 2020, Novavax was awarded a contract by the US Department of Defense for up to $60 million to support Novavax in its production of several components of the vaccine that are being manufactured in the US, and the delivery of 10 million doses of NVX-CoV2373 for the DoD.

In July 2020, Novavax was selected to participate in Operation Warp Speed (OWS) and was awarded up to $1.6 billion (recently increased to $1.75 billion) by the federal government to complete late-stage clinical development in the US, including a pivotal 30,000 subject Phase 3 clinical trial; establish large-scale US-based manufacturing; and deliver 100 million doses of NVX-CoV2373. This essential funding, together with the dedicated partnership of the US government, has provided Novavax the ability to conduct a timely and robust clinical development program while simultaneously establishing a dedicated US manufacturing and supply chain for this pandemic.

B. *Phase 1 / Phase 2*

Turning to our clinical program, the NVX-CoV2373 development plan combined a Phase 1/2 approach to allow rapid advancement during the current coronavirus pandemic. In early August, Novavax announced positive results from the Phase 1 portion of the Phase 1/2 clinical

trial of NVX-CoV2373, and within a month, the data were published in *The New England Journal of Medicine*. The trial was randomized, observer-blinded, and placebo-controlled, and we enrolled 131 healthy adults 18-59 years of age. NVX-CoV2373 was generally well-tolerated and elicited robust antibody responses numerically superior to that seen in human convalescent sera. The Phase 2 portion of the Phase 1/2 clinical trial is ongoing and is being conducted in Australia and the United States to expand the evaluation of immunogenicity and safety of NVX-CoV2373 in a broader age range, including adults 60-84 years of age. We have reported that the vaccine was well tolerated by older adults and maintained its favorable safety profile.

In addition, we conducted and recently announced the successful results from a Phase 2b clinical trial to assess safety and efficacy in South Africa. The Phase 2b study enrolled over 4,400 volunteers beginning in August 2020, with COVID-19 cases counted from November through mid-January. During this time, the new South Africa variant was widely circulating in South Africa. Based upon preliminary results, of the COVID-19 cases with available genetic sequence data, 92.6% matched the South Africa variant. Overall, we observed 60% efficacy for the prevention of mild, moderate, and severe COVID-19 disease in the 94% of the study population that was HIV-negative. Importantly, the data from this trial suggests that prior infection with COVID-19 may not protect against subsequent infection by the South Africa variant, however, vaccination with NVX-CoV2373 provided significant protection.

C. *Phase 3*

NVX-CoV2373 is currently being evaluated in two pivotal Phase 3 trials: a trial in the United Kingdom (UK) that completed enrollment in November and for which we reported preliminary results in January, and the PREVENT-19 trial taking place in the US and Mexico that began in December and has completed enrollment of over 30,000 participants.

The UK Phase 3 study enrolled more than 15,000 volunteers between 18-84 years of age, including 27% over the age of 65. The first interim analysis was based on 62 cases, of which 56 cases of COVID-19 were observed in the placebo group versus 6 cases observed in the NVX-CoV2373 group, resulting in a point estimate of vaccine efficacy of 89.3%. Preliminary analysis indicates that the UK variant strain that was increasingly prevalent was detected in more than

50% of the PCR-confirmed symptomatic cases. Based on PCR performed on strains from 56 of the 62 cases, efficacy by strain was calculated to be 95.6% against the original COVID-19 strain and 85.6% against the UK variant strain. The interim analysis included a preliminary review of the safety database, which was reassuring and showed that severe, serious, and medically attended adverse events occurred at low levels and were balanced between vaccine and placebo groups.

PREVENT-19 (the **PRE**-fusion protein subunit **V**accine **E**fficacy **N**ovavax **T**rial | COVID-**19**) is a Phase 3, randomized, placebo-controlled, observer-blinded study in the US and Mexico to evaluate the efficacy, safety, and immunogenicity of NVX-CoV2373 in up to 30,000 subjects 18 years of age and older compared with placebo. The trial was designed to ensure diverse representation of vulnerable populations and of ethnic and racial minorities and enrolled approximately 13% African American, 20% LatinX, 5% Asian American, and 6 % Native America, as well as 13% 65 years-of-age and over. The trial design has been harmonized to align with other Phase 3 trials conducted under the auspices of Operation Warp Speed, including the use of a single external independent Data and Safety Monitoring Board (DSMB) to evaluate safety and conduct an unblinded review when predetermined interim analysis events are reached. The trial's primary endpoint is the prevention of PCR-confirmed, symptomatic COVID-19. The key secondary endpoint is the prevention of PCR-confirmed, symptomatic moderate or severe COVID-19. Both endpoints will be assessed at least seven days after the second study vaccination in volunteers who have not been previously infected with SARS-CoV-2.

We have recently submitted a protocol amendment to the FDA to include a blinded crossover. This will allow all trial participants to decide to return to their trial site for a second set of injections; if the participant received placebo the first time, they will receive active vaccine in the second set and those that received vaccine will receive placebo. This protocol allows us to ensure that our trial participants are ultimately vaccinated, while also allowing us to continue to follow participants for safety. Participants will be eligible for the blinded crossover once the primary efficacy endpoint is met, and sufficient safety data has been collected.

D. *Taking on the Variants*

The emergence and circulation of COVID-19 variants poses challenges to vaccine delivery in the pandemic environment. Soon, subsequent vaccination boosters or new multivalent formulations may be needed. We commend the FDA for its commitment to publish guidance establishing a clear and efficient path for manufacturers to address these new variants, similar to the current regulatory approach for seasonal influenza vaccines.

Novavax is already aggressively working on a strategy to provide the broadest coverage. We initiated development of new constructs against the emerging strains in early January of this year and are already testing them in preclinical animal models. A hallmark of our technology platform is that our manufacturing processes are easily adaptable to producing other versions of the coronavirus spike protein that match the new strains. The company plans to begin clinical testing of these new vaccine candidates in the first half of this year.

A primary benefit of our platform is that it uses a very small amount of antigen, which provides the ability to create a bi- or multivalent vaccine and also the rapid creation and large-scale production of vaccine candidates that could potentially address multiple circulating strains of COVID-19. Combined with the reassuring safety profile that has been observed in our studies to-date with our COVID-19 vaccine in more than 30,000 participants, as well as prior studies in influenza, we are confident in our ability to rapidly adapt to evolving conditions.

IV. US Supply

A. *Dedicated US Manufacturing and Supply Chain*

Six months ago, we began to build out a global manufacturing operation to produce NVX-CoV2373 at commercial scale worldwide. This complex network includes a dedicated US supply chain, meaning vaccines we deliver to the US government are manufactured here in the US. We have a separate supply chain for foreign demand. Over the summer, we announced an agreement to manufacturer bulk drug substance with FUJIFILM Diosynth Biotechnologies. The antigen produced at the Fuji sites in North Carolina and Texas are a critical component of our US supply chain. Our adjuvant is manufactured through our partnership with AGC Biologics in

Seattle, Washington, and final drug product fill and finish is completed by Par Pharmaceuticals in Michigan and Jubilant HollisterStier in Washington State.

B. *Dose Capacity and Distribution*

Our initial delivery of doses is dependent upon an Emergency Use Authorization (EUA) from FDA. We will be ready to ship doses once we have this authorization. We are prepared to deliver the 110 million doses included in our current agreements with the US government by the 3rd quarter of this year. Once all of our capacity comes online globally, which we expect to happen in the mid-point of this year, we will have a global capacity to produce approximately 2 billion doses per year, roughly 150 million doses per month. This includes all of our partners, including Serum Institute of India. During the pandemic, we believe that the federal government and state and local jurisdictions are in the best position to determine how doses are distributed and allocated. We will work with government leaders to ensure that those who need a vaccine get it. We look forward to informing this process as appropriate.

C. *Timing*

PREVENT-19, our US Phase 3 trial, is fully enrolled, and we are collecting data. This is an event-driven trial, meaning that the timing of our interim and final analyses are based on disease incidence and rates of transmission in the areas where participants are enrolled as well as other epidemiological factors. Novavax has been submitting data to FDA on a rolling basis under our open IND and we expect to be able to complete our filing with FDA in the second quarter of this year.

V. Diversity and Inclusivity of Clinical Trials

As we are all aware, this virus has had a disproportionate impact on some of our most vulnerable communities. Novavax is committed to a representative population enrolled in our clinical trials that reflects our diverse world and prioritizes populations at high risk for COVID-19, including traditionally under-represented minority groups, those over the age of 65, and those with comorbidities. Novavax has worked with community leaders within minority populations, including partnering with historically black colleges and universities like Howard University here in Washington DC, to carry out our Phase 3 trials. We believe that with

knowledge comes confidence. We designed our clinical trials to ensure they are truly representative of the American public and we have provided regular enrollment updates on our company website, including providing detail on both total enrollment as well as on the diversity targets in our enrollment. We have provided transparency in not only our trial protocol, which we have posted on our company website, and also in our data. If people know that participants just like them volunteered and took part in our clinical trial, we believe they will be more confident in rolling up their sleeves and getting vaccinated.

VI. Vaccine Confidence and Access

We know that vaccines don't save lives, vaccinations do. We commend Congress for their attention to the critical issue of vaccine confidence, and Novavax stands ready to inform the US government as our nation's leaders work with state and local officials to ensure that providers, individuals, and community leaders have the most evidence-based information to bolster confidence that an approved COVID-19 vaccine is safe and effective. As part of this effort, Novavax is committed to transparency and accountability, which are critical to public confidence in COVID-19 vaccines. Novavax has been transparent around our clinical trial protocols, enrollment numbers, and scientific data, which we believe is one of the top ways to ensure public confidence in any vaccine that will ultimately be authorized for use.

We also know that pandemics don't observe country borders. Novavax is committed to reasonable pricing, equitable distribution and allocation, and expansive access worldwide, which is what will be required to fully control the pandemic. To that end, we have a built a strong partnership with Serum Institute of India, the world's largest producer of vaccines in terms of number of doses, whereby they will deliver significant numbers of doses of NVX-CoV2373 to low and middle-income countries throughout the world.

VII. Conclusion

Novavax is at the forefront of vaccine development and we are committed to producing a safe and effective vaccine to combat the COVID-19 pandemic, both today and as it evolves. We will continue to prioritize collaboration with the scientific community, partnership with the US government, and transparency in our contracts, our trial protocols, and our data.

Everyone on the Novavax team, with our partners, and in this room is interested in getting this vaccine in the arms of people and that is our priority and singular goal right now. Our team continues to work non-stop to get NVX-CoV2373 developed, authorized for use and ultimately delivered to vaccination clinics. I am proud of the progress that Novavax has made this year, and we at Novavax are proud of the advances the entire vaccine industry has made. We stand ready to work with Congress and the Administration to support the US supply chain of COVID-19 vaccines, which are essential to combat this urgent health threat.