RAHUL PRASAD: Thank you Kathleen.

Our final speaker today, Lexi Walls, is a scientist at the University of Washington's Veesler Lab. She has co-authored 28 scientific publications, contributed to four US patents, been featured on numerous podcasts, and her work has led to two clinical trials currently being evaluated in humans. Lexi will share how her work contributes to our understanding of the coronavirus pandemic and how she and her team are continuing to innovate and respond to the ongoing challenges we face as a society today. Please welcome Lexi Walls.

'THE FUTURE OF PANDEMIC PREPAREDNESS' – LEXI WALLS

LEXI WALLS: December. I think of snow. Holidays and cookies. A new year on the horizon. Resolutions with the hope of completion.

Like many of you, I make those yearly resolutions in December and had exciting ones for 2020. Do you remember yours? I planned to cook for my friends rather than meet at a bustling restaurant like we often did to catch up from the work week. I was looking forward to a cross country trip to have a college reunion in my friend's new home city. I also wanted to put more time into my hobbies and a little bit less of my time into work.

Well. You can guess how those resolutions panned out.

In December of 2019 I heard rumblings that at the time seemed inconsequential outside of my professional life. They were even, dare I say it, exciting. A novel virus? That doesn't happen often.

But I still went about my daily life. I traveled. I hugged the people I care about. I complained about the weather.

But even I had no sense of all that would follow the moment after I first read the press release, "it's a novel coronavirus."

My name is Dr. Lexi Walls, I'm a scientist at the University of Washington, and I study coronaviruses. I spent my PhD learning about what coronaviruses looked like, how they functioned, and what we could do to stop them.

I've studied coronaviruses so long that people used to ask me, "Wait… what's the name of the virus you work on, again?" or, "that virus you study, what does it do anyways?" I always had my elevator pitch ready to go- sharing why I

thought these viruses were worth studying, explaining that there had been two novel human coronavirus outbreaks in the past 20 years alone, more than most other emerging viruses like Zika or influenza, and that we had no vaccine or therapeutics for any human infecting coronavirus.

Let me tell you, people no longer ask me to repeat the name of the virus I work on anymore. What does still happen is I'm working as hard as ever to answer many questions that still plague us about coronaviruses, therapies, and vaccines.

In December of 2019 I knew that coronaviruses had pandemic potential, but it hadn't sunk in yet.

I was out of town the moment the novel coronavirus was identified. Remember my resolution to work less? Even though I knew I should be enjoying my vacation I was glued to my computer frantically searching for any information I could
find.

What I could find was scattered- I was clicking on twitter threads and one-off news articles…and frantically emailing my boss David to plan out what we would do next. This was early January 2020, and we knew we had to make decisions quickly and all we had to go off of was our previous research experience and the newly released genetic code of the novel virus.

But at this point in early January, it was still just a work thing.

By the end of January 2020, I called into a CDC meeting to listen to experts answering reporter's questions and discussing the situation. The first novel coronavirus case was in Washington state, my home. I called in on my way to the airport, not realizing that I would be getting on my last pre-pandemic flight before the race against the virus and for knowledge began.

As soon as the scientific ingredients I needed arrived, I started sprinting and working full throttle. My experiments were planned down to the hour because time was of the essence. The pace was grueling, but it was made a little bit easier knowing that my work was directly applicable to the patients and doctors in the hospital down the hall.

While this was motivating, it was also necessary to forget the larger implications of my day-to-day job when so much was riding on my shoulders. When the world is waiting for your answers, you have to quiet those thoughts and break it

down to the small daily tasks and to-do lists. On more than one occasion I had to stop and remind myself that every day I worked late I was learning the answers to questions that no one else in the world knew, but that the rest of the world needed to know, and that could change the course of the pandemic. I really never expected to be a world expert on a pathogen causing a global pandemic. I was thrown into it, just like the rest of you.

I've been part of that global team of scientists that started a mad dash of work in January of 2020 that hasn't let up since. The world generated so much knowledge and understanding about this new virus, not to mention multiple successful vaccines combatting the COVID-19 pandemic. All. In. One. Year. These vaccines are based on work that scientists like myself have been doing on coronaviruses since before they were well known.

Vaccines are the best option we have to combat disease, whether against novel pathogens like coronavirus, or well-known ones like seasonal influenza. Vaccines are like training wheels for the immune system, allowing our bodies to practice and strengthen against a pathogen without ever encountering it. Do you know anyone who has been infected with smallpox? What about polio? The answer, 'yes' has become more and more rare since the near eradication of these devastating diseases with global vaccination campaigns.

What I'm going to tell you about today is how myself and a team at the University of Washington are working to prevent this current pandemic and hopefully future ones as well. And we're going to do this with next generation vaccines.

The first question was, what part of the coronavirus should we focus on for a vaccine? We wanted to train the immune system to dismantle the virus before it ever has a chance to infect and spread. When you look at the virus- there is one component on the exterior that is responsible for getting the virus into your body, then into your cells and ready to infect you. That piece is a protein called the Spike and these spikes protrude and form a crown around the surface of the virus. That crown, or corona, is responsible for the coronavirus name.

The spike is currently what all coronavirus vaccines are based on! But I wanted to find the weak point of the spike and focus our efforts there. The portion we honed in on is responsible for 90% of the neutralizing immune response against coronaviruses and is called the receptor binding domain. This is the Achilles heel of the virus- we wanted to highlight the receptor binding domain to train the immune system to target the virus at it's weakest point. The goal was to find the

best coronavirus target for our vaccine, and the receptor binding domain was our plan to achieve this.

The next question was, we've picked our vaccine target, now how do we display and deliver this target to maximize efficiency?

Imagine legos. They are building blocks that can make different shapes and sizes and be stuck together. Those different shapes may give rise to different types of buildings or different functions. Well- the vaccine we've designed is just that- made out of two distinct lego-like building blocks that stick together when mixed like velcro. The building blocks are made out of designed proteins- tweaked to function exactly how we want them to. Once these protein lego components are assembled, they are called nanocages and form a beautiful 3-D structure.

These nanoparticles can further be fused to components of the coronavirus, like the kryptonite receptor binding domain, and display multiple copies to the immune system for effective and efficient training.

We successfully produced and characterized this vaccine early last year and tested it first in the laboratory and then in two animal models. We showed that the nanoparticle produces a strong and potent immune response and protects from coronavirus infection. This vaccine is stable at ambient temperature, is effective at low doses, and is scalable for large production. This vaccine worked better than we could have imagined when we designed it. This vaccine, our vaccine, is currently in clinical trials and is the first of its kind! And some days I still can't believe it.

The sleepless nights, the stress, all of my graduate thesis work feel so worth it in these moments- because it all led to a vaccine that is in the clinic and has the chance to help change the world. This is an incredible first step of a vaccine against a devastating disease and has got me thinking about the future of vaccines and immunity.

What if I told you, we're not fully satisfied just having a vaccine for this coronavirus pandemic? We are dreaming bigger.

Part of the benefit of the fully designed nanoparticle system is just that: we can design and change any component with ease. We can put not just the kryptonite receptor binding domain but other domains or proteins as well. What if we put the receptor binding domain not just from this coronavirus, but from all the different strains worldwide on the same nanoparticle. We can even go boarder- including all the more distantly related coronaviruses that infect humans. We're

also working on viruses other than coronaviruses- like influenza- and seeing that this platform is robust and works with many different pathogens. How big can we go? Can we build a vaccine that responds to all current human infecting coronaviruses? We think we can. And what's even more- we think this vaccine can even bring about protection for the next pandemic- one we haven't even predicted yet- due to the strong responses induced by these extraordinary vaccines.

So, even though we have a nanoparticle vaccine in clinical trials the work isn't over yet, it's only just beginning. I'm dreaming of all the possibilities these vaccines and others like it can bring, and I welcome you to join me in conjuring ideas of your dream vaccines.

Imagining a world without a pandemic, due to vaccines that can prevent current and future, unknown diseases, is truly a welcome thought today. Join me in entertaining that enticing thought. And now know that we're working hard towards that goal and are excited to show it may be possible sooner than we think.

Thank you all so much for listening and dreaming with me!