GORDON DOUGLAS: I think 12 to 18 months is a very optimistic forecast for this incredible job of developing a COVID vaccine and making enough to ensure that the entire world can be immunized.

ANNOUNCER: Hello, and welcome to "We Roar." With coronavirus continuing to dominate our lives, we're getting in touch with students, faculty, staff and alumni all around the country to hear how Princetonians are living and working through the crisis, to hear how we're staying together from a distance, and how so many of us are working to serve the wider world. This episode features a former president of the vaccine division for the pharmaceutical company Merck.

### [ MUSIC ]

GORDON DOUGLAS: I'm Gordon Douglas. And I was the Class of 1955 at Princeton and 1959 at Cornell Medical School.

Getting a new vaccine licensed is a huge accomplishment. It really is not done anywhere near as frequently as you think. If you look back through vaccines that we've developed, like polio and measles and, uh, chickenpox, et cetera, most of them take around 10 to 15 years to develop. But there are two that we've done fairly rapidly. One is mumps and the other is Ebola. But they both took about four to five years.

There are two critical steps that could be taken to foreshorten that time frame. One is, you can actually improve the clinical development timeline by very careful, um, design of your clinical studies. But simultaneously, you have to develop a manufacturing process. How are you going to actually make this stuff, and how are you going to make it at massive scale? And you have to build the manufacturing plants. Those two processes have to be done together because you're trying to make, just for the United States, if it's a two-dose vaccine, 700 million doses of vaccine, which means — ideally you would put it in a pre-filled syringe, so the person administering the vaccine can just pick up the syringe and give it to the patient.

You have to fill 700 million syringes with identical material. And the syringes, by the way, all have to be perfect, and they all have to have a perfect needle on them, and the stuff you put in there has got to be perfect. And you have to do it 700 million times in a row without making a mistake. That's a huge bioengineering challenge.

But we can't just make 700 million doses for the United States. We have to make billions — not even millions, hundreds of millions of doses, but literally billions of doses, because we really should make enough vaccine for every person on this planet.

There's an organization called CEPI, which is the Center for Epidemic Preparedness Innovations. And they now estimate there are 137 candidate vaccines, uh, for COVID-19. And about a hundred of them are in, you know, active development. The wonderful thing about that is, different investigators have different ideas about what they think might work. And so each one of them is taking their shot at their best idea. There's a race to get there. There's a race -Imean, a lot of people really want to make this vaccine, and want to do it as rapidly as possible. And they want to be the ones who do it. And that's a great thing, because it means we've got people who really can probably get the job done.

Um, some of them are not going to be successful. If you think about it, in vaccine development,

about 90% of the products taken into phase one fail. So it's — you have to winnow out all of those vaccines that aren't going to work. And you have to select the ones that will work. And you need to build the manufacturing plant now, at the time of early clinical development, before you know exactly what the process is for making the vaccine and exactly which one is going to win. So I would say you have to build probably eight or ten different plants right now, today. And they cost about a billion dollars apiece. So there's a high cost to shorten the development timeline, but relative to the cost of the economic, um, damage that we have now because of the shutdown, it's trivial.

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I think, uh, 12 to 18 months is a very optimistic forecast for this, uh, incredible job of developing a COVID vaccine and making enough to ensure that the entire world can be immunized. The coronavirus epidemic began in January, so four months has gone by already. That's four out of the 12 to 18 months. And we have just in some — a few vaccine candidates in phase one trials. I think if you could do the clinical development in 18 months, that's gonna be — that's a miraculously fast development timeline. I think it can be done with some of the things I just suggested, but it — but's it's going to be a lot of work, and you gotta — and a little bit of luck.

### [ MUSIC ]

The year I graduated from Princeton, 1955, the Salk vaccine for polio was announced. And when I was growing up, polio was a terrible scourge. We had big epidemics in the '40s and early '50s. Obviously, we had a president who was severely afflicted with polio, and we had — all of us had friends who got polio. And so the — the fact that a vaccine was approved and licensed for this was an amazing thing to me, and I wanted to know: How are they made, what are they, how do they work? All the questions that you might ask about a vaccine. And that's what sort of drove me in that direction, and drove my career in that direction.

If I was in charge of this, I would immediately appoint a panel of what I thought were the six, eight, ten, maybe six or eight top vaccinologists. And I'd ask them to really look hard at these 130, 147 different vacc — candidate vaccines and select for me the top ten — or eight — ones that they think are going to be most likely to make it to the finish line.

I would review those clinical trial plans to make sure they're as foreshortened as they possibly can be, and I would simultaneously acquire funding from whatever government sources, NGOs, private companies to build the manufacturing plant for each of those ten products. And I'd do it today. And that's the way you would get a vaccine in 24 months, maybe. I've already added some time to the 18 months. I don't — I don't think we're going to do it in 18 months, but 24 is a target if you do everything the way I just described it.

### [ MUSIC ]

I spent 25 years in academic medicine and, and as a professor at medical schools, doing clinical infectious disease, but also doing research particularly on vaccines and antivirals.

We had a couple of vaccine, um, efforts at Merck when I first went there. And, um, none of them proved successful — as have — none — no vaccine effort has proved successful against HIV yet. We thought we had a pretty good idea, but it didn't pan out. A lot of other ideas have been

tried. We still don't have a vaccine. But what did work, and which did work pretty rapidly, was the development of antivirals.

With COVID-19, I think we'll get antivirals before we get a vaccine. They're just basically easier to develop. And there are a number of them in clinical trials now, as you know about. And I think, you know, most of those are products that were taken off the shelf because they were around for something else, and tried.

But as scientists understand how this virus replicates, how it — how it divides and makes daughter viruses in cells, and that process is known very well now, there are a number of places where an antiviral might work in that step of the way it replicates. So antivirals will come along. There will be antivirals, and I predict that there will be some pretty good antivirals for COVID-19. I can't tell you exactly when, but I would think soon, and I think sooner than a vaccine.

## [ MUSIC ]

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