CONVERSATIONS WITH MIKE MILKEN

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Mike Milken: I want to thank you for joining us. And we want to thank you for taking the job as the head of Operation Warp Speed. Tell us a little bit about why you took this assignment.

Moncef Slaoui: I spent all of my professional career at GlaxoSmithKline, and half of that I was a scientist and then the head of R&D for the vaccine division of the company, and had the fortunate privilege to discover and develop a large number of vaccines. Therefore I acquired very significant experience; when I became head of R&D for the corporation as a whole I remained chairman of the vaccine division It's what I love. And I have participated to the company's commitment to helping with pandemics in three successive events, unfortunately, which were the flu H1N1 pandemic in 2009, and then the Ebola outbreak where I let go

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This interview has been lightly edited for clarity and readability.

everything I was doing and put together a team of a hundred people and led them to make a vaccine in seven months to clinical trials, not to approval, and then Zika.

So I was always committed to public health and global health from a vaccine perspective. But I was also very frustrated with the fact that each time we were not prepared to tackle a pandemic. And in fact, I made a proposal to the U.S. government and others that they called the Bio-Preparedness Organization proposal to have a permanent organization dedicated to discovering, developing, and manufacturing small quantities of vaccine against known potential outbreak and pandemic agents. It was never funded, but this is something that was very high on my agenda, and many people knew this was very important to me.

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I got a call out of the blue late in April from Jim Greenwood, who used to be the CEO of the Biotechnology Innovation Organization and was a Congressman before, literally picking my brain about whether having something that looks like the Manhattan Project could make sense to have a vaccine very quickly against COVID-19. When I was called here to meet with the administration, I asked really for two things. One is full empowerment, and two is no political interference. And I was guaranteed that that would be the case. And that was it.

As you've responded to your fourth pandemic, we have moved technology along here. We have been monitoring 214 vaccines at our FasterCures center; 30 that have gone to humans, but the approval of the Pfizer vaccine and the approval we anticipate of the Moderna vaccine. As you've moved this organization in the world at quote warp speed, can the citizens depend on these vaccines being safe?

Yes, to the best of the wealth of information that we have on these vaccines. And I'll explain why we went so fast and why we haven't actually cut any specific corners that are relevant to either the effectiveness or the safety of the vaccine. We really went fast because we used what we call platform technologies. It's like taking a tape recorder, and each time you put a different tape in it, you listen to a different music. But it's the same tape recorder; 99% is the same thing. Only the tape is different. Platform technologies for vaccines are the same principle. If you take for instance, messenger RNA, whether you have a vaccine against polio virus or cytomegalovirus or COVID-19, 99% of the vaccine is the same thing. The sequence that defines the antigen against which you vaccinate is the only thing that's different. That allowed us to capitalize on more than 10

years of research and development done at companies like Moderna like CureVac, like BioNTech, which has the partnership with Pfizer, for the Pfizer vaccine to really work out how to design these vaccines, their toxicology and safety in animals, took them into the clinic with, in the case of Moderna – as you know, I was on the board of Moderna, and I'm very familiar with the work they've done in more than seven different diseases – to understand the kind of immune response it induces. So when COVID-19 came, the minute we had the sequence, the tape, we could plug it into the tape recorder or the messenger RNA platform and very quickly, within 60 days, be in clinical trials in humans. It wasn't short-cutting the process. It was actually the process had taken place for 10 years before that. And we understood exactly, and so did the FDA, what was being done.

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The second thing that we've done is in contrast to what happens normally, which is you go step by step in sequence in organizing your Phase One trials, and then Phase Two, and then Phase Three, and then you invest in your manufacturing. What we've done is that we planned the clinical trials in parallel. We didn't run them in parallel. What that allowed us is as soon as a Phase One was completed, we could start Phase Two the next day. Completed meant the FDA agreed this was safe. Likewise, with the Phase Three trial we run it much larger than what's needed. Usually the minimum requirement by the FDA for a new vaccine is 6,000 subjects. Our trials have between 30,000 and 60,000 subjects.

There were two reasons for that. One was it allows to accrue cases into the trial much faster than if you have a small number of people in the trial. So actually the trial is bigger. It's actually ended up faster in terms of achieving the endpoint for efficacy. And of course, the second point is we have experience on 15,000 or 30,000 subjects vaccinated over a period of, on average, four to five months, which is very important to describe at least the short- and mid-term safety of these vaccines.

The data are frankly compelling. I mean, the efficacy of these vaccines is spectacular. It's 95%. The efficacy is already achieved after one dose of the vaccine. The efficacy is 100% against severe disease. The efficacy is the same, whether you are an African-American or Hispanic or over 65 years old, which are people with co-morbidities. And remarkably, these two vaccines developed in different companies, two different continents, give

incredibly similar results, totally independent, which is also enhancing the likelihood that this data absolutely are real.

Likewise on the safety, there are side effects that are associated with the injection site, which is totally classic with many vaccines; some pain at the injection site, some redness, some chills, a little bit of fever. They lasted a day or 36 hours, and they are really noticeable, maybe in 10% or 15% of the subjects vaccinated.

In these trials, there were no serious adverse events of any specific nature. The trials were never put on hold. As you know, the Data Safety Monitoring Board which independently oversees the trials, has put on hold another vaccine trial by AstraZeneca using a different technology. These two trials were never put on hold. They never had any event of any specific nature. And therefore, we feel confident and comfortable that their short- and mid-term safety is very clear and very well understood.

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Now, there is one thing that's not described yet, which is their very long-term safety. We don't know whether these vaccines could have a side effect of some nature by definition, rare, in the very long-term. However, what we know is that in hundreds of thousands of subjects' data from people over the last 40 years that participated in clinical trials for vaccines in the FDA databases, 95% of all adverse events associated with vaccines, over all the follow-up time, on average two years in vaccine development, occur in the 40 days following completion of vaccination. So, we feel that we know those 95%, there is almost nothing serious at all in these trials. And therefore we can project that their long-term safety is very likely to be similar to that of all other approved vaccines. I will take the vaccine, and as soon as it will be approved for pediatric use, I'll give it even to my young child, of course.

Your young eight year old son.

My young eight-year-old, yes.

You've just spoken about the Pfizer vaccine and the Moderna vaccine. What about the other vaccines? Johnson & Johnson? AstraZeneca? The biotech company in China, Sinovac Biotech, that's been used in Indonesia, the UAE, and many other countries? What about the other vaccines? Where do you see them in the process?

Hundreds of millions of doses will be manufactured on a monthly basis between these two vaccines. Those processes are closer to a chemical synthesis process than to a pure biological process, which means they are more robust and predictable. The biggest challenge is access to certain raw materials, certain lipids that are very important in the formulation. And with the department of defense, we are working on ensuring appropriate access to those raw materials for both companies.

I would say in the strategy that we designed for Operation Warp Speed, we decided on day one that we were not going to bet on only one vaccine and not only one technology; we were going to take four different platform technologies. And for each one of them, we wanted to have two vaccines because we wanted to hedge the risk of failure, the risks of delay, the risk of poor execution. We are very pleased up to now that we have two vaccines from the fastest technology, which is the messenger RNA.

The next to use another platform technology, which is the non-replicating vectors vaccine, which are the AstraZeneca Oxford vaccine, and the J&J vaccine, are in Phase Three trials. The J&J vaccine here in the U.S. is being tested as a one-dose, one-shot or a two-shot vaccine in two different trials. And the one-shot vaccine has already more than 35,000 subjects recruited in it.

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The AstraZeneca vaccine trial in the U.S., which is different than the U.K. and Brazil trial that they have reported on with some potential mix-up, has also recruited more than 17,000 subjects and is likely to read somewhere late January or early February. These two technologies are actually easier to scale up in very high number of doses in terms of capacity than the messenger RNA technology. And as of the month of February or March, we will be producing between 150 and 200 million doses per month. Remember one of these two vaccines is a one-shot. So when you have 100 million doses that means 100 million people that get vaccinated.

And then we have two protein vaccines, one from Novavax, the biotech company here in the northeast and the one from the Sanofi and GlaxoSmithKline partnership, which are in Phase Two trials preparing to enter in Phase Three. They're likely to read out, I would say, in the early spring, most likely, and be available in April or May approved. And those can also produce hundreds of millions of those from each.

I feel confident that we can cover the U.S. population within the first half of 2021. I hope most people will accept to be vaccinated. I feel confident that these technologies, which are being tech transferred already into other manufacturing facilities that these companies have elsewhere, will be produced into several hundreds of millions, if not a billion doses already in the year 2021. If I sum them up all together, we probably will have two or three billion doses of vaccine.

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Morocco is starting a national vaccination program with 25 million doses of the inactivated virus vaccine in Indonesia you cited. I think that that technology is very likely to work. I would not give it to babies because of the historic observation in the early 1960s that the RSV vaccine, another respiratory virus that was inactivated with formaldehyde, has actually exacerbated disease in infants. So I wouldn't give it to young babies, but otherwise I think it's safe in broader populations.

They have a messenger RNA vaccine in China. I'm not familiar, frankly, with the technology. I haven't seen publications. And there is of course the norovirus-based vaccine from Russia, which is well-advanced. Again, I haven't seen any clinical trials. I'm very connected with CEPI, the Coalition for Epidemic Preparedness and Innovation. Some of the companies we're supporting are also supported by CEPI. We hope to find and identify immune correlates of protection that will help approve other vaccines that cannot be tested for efficacy, because it would be unethical to run a placebo-controlled trial, for instance, in a country where vaccines are available.

There are two things you brought up I'd like to touch on. One, children. Most trials have started with adults. Do you feel vaccines will be given to children when they're available?

These vaccines would need to run clinical trials in children. I know that they have been tested in children for other vaccines, for instance, like an RSV vaccine that's being developed by Moderna. But this very specific vaccine has been taken into adolescents, age 18 to 12, as part of the Phase Three trial that Pfizer has run. The Moderna vaccine has stopped at the age of 18. I think it was really an important and the right decision to not go into the below 18 as long as we didn't have an evidence of benefit. Once we have now evidence of benefit, we are planning as we speak to start imminently clinical trials into adolescents, and then into toddlers, and then into infants. You have to show you're safe in each age bracket. I would expect adolescent immunization to be approved by the

agency, maybe on the basis of the Pfizer data that they already have, or maybe more likely in March when more trials have been conducted in adolescents. And I would expect to go lower in the ages. I hope to be approved before the start of the next academic year, in the fall of 2021.

What about the distribution? How does it get out, and what is the most effective way to do that?

One of the visionary aspects of the operation was to associate the academic and industry ecosystems with the Department of Defense and the army logistics and project management and operational capabilities. General Gustave Perna, co-leader of the operation with me, is an outstanding leader who is providing incredible input in that regard. From day one when we started, planning the distribution started to be thought through and all the steps analyzed. And one of the biggest decisions that was made was to say, between 80 million, 120 million doses of vaccine are distributed every year in the U.S. And what we're talking about, maybe three times that number, maybe four times that number, over a period of six months or something like that. We don't need to invent something different. What we need is expand and consolidate what is already used.

Can we do it that way? And the answer is yes. And I think learning from the tests and the fact that no system existed to distribute the tests all the way to every CVS or Walgreens or whatever place, turned out to be an incredible challenge because you had to establish the routes. Here, the warehouses are there. The distribution companies are there. Really the biggest challenge is the cold chain, and it's of course a higher challenge with the Pfizer vaccine that requires minus 80 degrees as compared to Moderna that requires a minus 20-degree cold chain. But even then the work was to say, okay, how can we make that cold chain a challenge that is contained? And Pfizer was very creative in designing a packaging system that allows for two weeks stability at minus 80 with dry ice, renewable at least once; both Moderna and Pfizer demonstrating or measuring and showing stability of their vaccines at two-to-eight degrees at the fridge temperature for five days for the Pfizer vaccine and a month for the Moderna vaccine.

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Why is that important? Because the last step of vaccinating people once you take the virus outside of the minus-20 or minus-80 cold chain, it was very important that the level of flexibility exists. We have rehearsed every aspect of this, first in tabletop exercises, conceptual to make sure nothing fell between the cracks. And every time we did it, new things were improved. But also more recently in mock distribution of vaccines. I'm pretty sure that will be hiccups. I hope the hiccups will be 1% and the perfect would be 99% of the time.

So, let's talk about preparation. You spent considerable time trying to convince the world of the need for having manufacturing capacity and other things in place if we had a pandemic. The creation of these new RNA vaccines with the potential that they might be used in this technology for many, many different things in the future. What do we need to know going forward?

This partnership between public and private in a way that was unencumbered by bureaucracy is super important. The system knows it can do it. So that's one. The second I would say is the incredible level of alignment. Really I have never seen as fast decision-making on all aspects. It was amazing. I could call Pfizer CEO Albert Bourla literally many times; he was somewhere in Greece at five or four in the morning. I wake up very early in the morning and we would discuss something and Albert would call the teams in Pfizer and things were aligned and we didn't have to go through 10,000 discussions. It was immediate.

I think the other thing is redundancy as a means to manage risk is very important. We need to really be careful not to think that now we know what to do, therefore next time we're going to take just one approach, because for the next pathogen, unfortunately it may require something else. I think the one thing that is more difficult is nobody has an idle manufacturing site waiting for the next pandemic. These manufacturing sites were being used for something else or just been built from scratch. We worked incredibly, thanks to the Department of Defense, to enable access, to accelerate, import, authorize, engineer, you name it, anything, to build manufacturing facilities from scratch. We did it, but it's tough. It takes time. You need to validate them. You need to hire the people and train them; that takes time.

We could have gone faster if there were dedicated manufacturing facilities for this; have a nucleus of a permanent facility to discover development manufacturer. And then if there is a crisis, you can overlay that with a very strong partnership with the Department of Defense. I completely changed my perspective on the army; it's all about leadership. It's absolutely exactly like in industry; make sure we create that integrated partnership next to a permanent facility. I think that would be my way forward. We are bleeding $20 billion a day; let's spend $300 million a year when we don't have a pandemic. Let's be preventative.

When you talk about leadership, how fortunate the world was that you answered that call to lead our efforts during this period of time. Thank you for joining us today, and we look forward to people in the United States, joining the U.K. and others around the world and taking the vaccine.

Thank you.