

CONVERSATIONS WITH MIKE MILKEN



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Mike Milken: Welcome. Arie. Let me start with an important question. How is your health?

Arie Beldegrun: My health now is good. I'm back to full function, and it's been almost one month.

So, both you and your wife, Rebecca, were diagnosed with the virus. Do you know how and where you were exposed and how you got it?

It was a 2nd of March when, a healthcare conference in Boston took place. I attended it. Two days later I started a short cough, which, as a physician I can tell you it's a different cough than with flu. It's a very dry cough. On day eight, I had a temperature, low grade temperature of 100.7 and then muscle ache and fatigue. That night, putting all of that together, I requested to be tested and had a positive testing for COVID-19.

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And then the next day I insisted that my wife will be tested. She was asymptomatic. She had no symptom that time. That's what happened, and it was on the 14th of March.

You have been studying the immune system, uh, for more than three decades. What role is the immune system playing here in the coronavirus?

The immune system plays a major role preventing viruses from attacking and taking over. There are two steps in the attack, specifically with COVID- 19.

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The first one is when the virus enters the body and starts replicating or dividing and then it enters into the cell. That's the first phase.

Second phase is when our immune system is now stimulated to fight that virus and it mounts an immune reaction against that virus.

This is a brand-new virus that the immune system has not seen before. And therefore, the inflammatory process that's happening as a reaction of the immune system stimulated is what causes the severity of the disease in some patients. And we do not understand why some patients fight it well, and in others the immune system is not fighting it well.

Now, you've had this amazing track record of building biopharma companies. Talk a little bit about that.

I was an active surgeon/physician/scientist building a laboratory at the Johnson Cancer Center, at UCLA. I started realizing that while we are doing great surgeries, but there is a limit to what we can achieve with our knife. And I started looking for other alternatives. We started the first company, called Agensys, which was a gene discovery company that was fully dedicated to studying different genes involving cancer, creating monoclonal antibodies that at that time was quite new, but today is a household name. And these antibodies were then converted to medications, some of which are approved now by the FDA.

I have started another company called Cougar Biotechnology, which was interesting in that when we started that that company in the early 2000, there were very few new treatments for prostate cancer. You, Mike, were the impetus of starting the research then. We then established a company that developed eventually a drug called abiraterone, today known as Zytiga. That drug is now distributed all over the world by

Johnson and Johnson and making a lot of difference in the life of patients with metastatic prostate cancer.

And I would say Arie have probably visited with a thousand people who had failed surgery, had failed hormones, had failed radiation and are living normal lives today because of that drug. Just an amazing thing that probably all by itself has reduced the death rate by five to 10% in the entire world. One of the things we've been focused on here, Arie, is that everything that's occurred in cancer that you've been working on, we've been looking at how to apply that to this virus.... Talk a little bit about the therapies in cancer. You had this immune response as you energized the patient's immune system to fight cancer. These issues were addressed in research before to try to regulate the immune response so it didn't go to such an extent that we're seeing here in the coronavirus.

Mike, That's exactly the case. These proteins are not specific for COVID-19 virus. They are an inflammatory process that the body is using to fight diseases, whether it's cancer or viruses. For example, Interleukin 6 (IL6) is a very important protein that a body is using to create an inflammation and and fight invaders. This IL6 has been used by us in the last five years in treating patients that are receiving immunotherapy with cell treatment. We have been using that drug for now several years in patients that are treated with immunotherapy for cancer.

We've read a great deal about the Gilead drug. What do you see in the development of that drug?

Gilead is working on a different aspect of the immune system and developed an antiviral, that's called Remdesivir. The mode of action is completely different than the IL6. The IL6 antibodies, there are two companies that are now testing it against COVID-19. One is called Actemra, made by Roche. The second one is Kevzara, which is a made by Sanofi Regeneron. Both are being tested right now for treatment in patients with the inflammatory process of COVID-19. Remdesivir is an antiviral drug that essentially was developed originally for the Ebola inflammation. But recently it has shown, as other respiratory RNA viruses, that it can work against COVID-19 as well. And this is the drug that is right now being tested by Gilead.

What strategy would you recommend from how we've fought other diseases?

The challenge here is controlling the spread, treating the underlying cause. This has to go hand in hand when you ask, what can I do today? Today is controlling spread. And we cannot emphasize enough how important it is because when you look at an interesting group in Italy, which discusses the importance of social distancing, you have number one,

a group in Italy in an area called Lodi that started to shelter in place on February 26 and then next to it there is another area called Bergamo which started to shelter in place about 10 days later. The difference in the spreading of the virus in the community is like day and night. It's amazing to see. In one area it was about 50 to a hundred patients a day. In the Bergamo case, 600 patients a day.

The immediate need is for controlling the spread, and I think that's what Anthony Fauci, the entire team, is emphasizing day and night.

The second one is what's called the Manhattan Project. How do we treat the underlying cause of the disease, and what do we need to do immediately? Obviously, as a scientist, as a clinician, as a biotech person, I would say clinical trials. You have to test it. You have to see exactly what works, what doesn't work. You have to do a very well-controlled study. But this takes time. So therefore you also have to factor in – it's not what we know how to do ... it's how you do *it today*.

The WHO study, which is not perfect – there will be a lot of criticism to that – but it started just now what's called the “solidarity trial.” Lots of people, thousands of people, all over the world, the physician will be able to participate, and it will have Remdesivir from Gilead; Avigan, that was actually developed as a treatment for flu; and then all of that with combination of a drug called Interferon Beta.

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But these are different approaches that eventually we'll know what works and what doesn't work. Most likely we will meet this virus. If not now, we'll meet at the end of the year or beginning of next year. So, we need to know the facts.

With the disaster that this has brought to families, individuals and death to so many people, we have to push on every path. So, on March 16th, Moderna put a vaccine into the first patient. We're going to get feedback. But this vaccine is for people who don't have the virus.

As you said, this is a vaccine, this is not a treatment. And therefore you should look at 16 to 18 months to get the results.

But meanwhile we need to treat. And in the treatment, there are different approaches. Those of us like myself who recuperated from the COVID-19 virus have developed antibodies. Obviously, there's discussion taking the antibodies from one patient and

transfusing to the other patients. That's one way. But what we'll do is they will clone and create multiple antibodies that can be treated for a lot of patients, and these antibodies would then be the treatment. And it will become extremely important in controlling and treating the disease.

So as we look at what has the best chance in the short run, whether they're antivirals, whether they're antibodies today, one of the questions that has to be answered is how long do these antibodies last? Do you have to continually get them? We know in some cases they last a decade or more. Do you have any insight into that?

Not much more than you or any scientists in the world. This is a new virus. The immune system has never seen that virus. And therefore your guess is as good as ours. You can say it will last for at least two to three months. It's also a great story to look. Is that all globally a single virus, the same virus that was sequenced in China several months ago? It did not

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mutate? So, all of these questions are extremely potent. Usually the viruses tend to mutate. If that's the same virus, there are so many questions. Why are some areas extremely aggressive versus others where patients have very mild symptoms if it's exactly the same virus?

It appears in many cases the virus started in the GI track in Italy, different than it's occurring here or say in the United States or other places.

That's correct. I have seen that information as well - that in Italy, many of these patients first appear with diarrhea and GI symptoms that then, later on, becomes a respiratory problem.

In the States, most of them are through the respiratory system. So yes, these are different modes of entry of the virus and creating the first step, which is the replication and the entry into cells, to which cell it enters.

Is there anything we're not doing that we should be doing today?

Personally, I don't think we are skipping any opportunity in this world. We are all together. If you think of sequencing the gene in China in four weeks, I would have never believed that that can be done in four weeks. Up to few years ago it would take me a

year to sequence the entire gene and come up with the sequence of coronavirus. Once you see that, you start believing that everything is just a matter of time. Time is of essence. But I have personally no doubt that we will control that disease rapidly – and when I'm saying that, it's within the next three to probably six months. This is work that otherwise would have taken 10 years. So, with the technology that we have today, with the multiple companies all using all their technology and everything that they have in development entirely, with old drugs and new drugs, and just testing it against the virus. I'm quite confident that we will have a drug to treat the disease. I believe that patients will not die from the disease and that will be the first step. If we will know that it's not a deadly disease, that we can treat that, then all the rest will come in steps.

Well, Arie, one, thank you for your commitment to serving the world with your treatments and the company that you've built. And as you know, that motto of our *FasterCures* center is “time = lives,” and hopefully we'll be able to compress time with technology today. Thank you for joining us.

Thank you so much for the opportunity to be here.
