Mike Milken: Jim and Pam, thank you for joining me today.

Padmanee “Pam” Sharma: Thank you, Mike for inviting us.

James “Jim” Allison: Thank you.

The sense of urgency, which we all feel – tomorrow will be different than today and the day after will be different – brings me back to a meeting almost three decades ago, Jim. I was sitting there and you were telling myself and the other researchers and scientists in the room at one of our scientific retreats that our immune system is smarter than all...
of us, and if we could just get it working at full strength, it'd be amazing what it could do.

[JA] Well I became fascinated with immune system when I was an undergraduate and learned that we had these things called T-cells that go through your body and screen every cell in your body and find out if anything's going wrong with them, whether infected with a virus or become a cancer cell or whatever, and can learn how to respond to it. The question is, how does that work? And the way it works, we're beginning to get some little insight into, but it's just truly amazing because our bodies can respond to anything that nature throws at us, or we throw at ourselves, by protecting us. If we could just learn the rules about how to help it sometimes – and why it fails sometimes.

As I think about both of your careers in immunology and trying to energize the immune system, it's hard for me not to reflect, Jim, on the fact that those melanoma cancer patients that would have had life expectancy of months are alive and in full remission today from what had been developed by turning on our immune system. And that my father, 30 years or more after he died, that there was a solution for his melanoma. Today we have people in many ways whose lives are being cut short. The question is, what should we be doing? What are the solutions?

[JA] I can see a three-stage, progressive way that I hope will be successful. The first is to find antivirals that will do something about the coronavirus. There's a lot of talk about chloroquine. I'm sorry – there's just no data to support that and it has adverse events, so you can't just go out and have everybody taking it. But there are many companies now and many scientists that are taking the structures of antivirals that are used against other viruses and trying to modify them a little bit and then run them through screens, which can be done to find ways of slowing the virus down once it's in people.

Simultaneously what's beginning in a number of major medical centers in the country is to use what's called convalescent serum – that is, the blood plasma from patients who have had the disease and successfully recovered, which indicates that their body, their system, did do something. There are a number of ways possible of either using that plasma or making it work better by making monoclonal antibodies from those patients that can be scaled up and actually given to people to treat them – again passively, at least – to reject the virus once it gets in them.

“If the T-cells can eliminate those [early infection sites] before the virus has a chance to continue to replicate through other cell types – for example, in the lungs – then you can really prevent the infection from becoming fatal.”

– Pam Sharma
Of course, the third phase ... is a vaccine. And it just takes a long time to do that. But, until the vaccine comes along, it's going to be difficult. I think drugs and these other things are going to help a lot in saving people from dying. But in order to really get rid of it, we desperately need the vaccine. But that's a year, year and a half away.

**So, Pam, Jim spoke about monoclonal antibodies. Can you explain to us what that is?**

[PS] Sure. I mean, the immune system is a, as you heard, it's very powerful as you know, and it's comprised of multiple cell types. T cells, which are the cells that Jim was talking about that go around looking for things that don't belong there and destroying them – destroying the infected cells, for example.

B cells are the other cell type that then produce antibodies against whatever foreign antigen is present, whether it's a tumor antigen or a viral antigen in this case. When those antibodies that are made by the B cells bind to the virus, it prevents the virus then from infecting the cells within our body. That's the importance of the antibody stage.

But of course the T cells then are also important because the first few epithelial cells, for example, in your throat or your nasal pharyngeal passages that are infected – if the T-cells can eliminate those before the virus has a chance to continue to replicate through other cell types – for example, in the lungs – then you can really prevent the infection from becoming fatal.

So I think initially, yes, the B cells are important for the convalescent plasma. T cells also become important for eliminating infective virus. The vaccine will hopefully allow us to have both a B-cell and a T-cell response.

Most vaccines have been very good at allowing for the B-cell response, for example. Just figuring out what the epitopes are, what the specific pieces of the virus that we can use in the vaccine to help the B cells and T cells have their response is where we're going.

And I have to say that this has been an unprecedented time in science. The collaborative efforts that are being put forward. The rapidity with which we're all coming together as one group in terms of science and medicine and how to take care of patients and how to really bring the best science forward to come up with the right drug treatments and come up with the right vaccine – it's been amazing. This collaborative effort is something...
that we all need, and it's hopeful for how we can keep moving forward to really win this battle.

[JA] If I could just add something: If we could get good antibody responses, they can do a good job as soon as the virus gets in your body of hopefully keeping it from infecting. But if that's not 100% effective and a few cells do get infected, then the T-cells could come along and eliminate them. That double-whammy – first decreasing the chance that the virus can infect anything and then also having the ability to clean up, if you will, and in a way sterilize the body of the virus – is really the long-term way to do it.

And just to build on what Pam said about collaboration, most of the universities and medical centers that I'm aware of that have been in involved in the immunological assault on cancer, developing new immunotherapies, are now shifting attention to this COVID virus. Many of the lessons are similar, not the same, but similar. And there's an amazing collaboration of institutions across the country to bring all our knowledge together and try to do this as fast as we can.

[PS] At MD Anderson for example, we've also set up a task force here where although we've been MD Anderson cancer center focused on cancer care, we now need to focus on cancer care as well in terms of covid 19 infections in our cancer patients. And we're doing that as part of the task force where everyone's collaborating.

You've brought up a very important point here, and that's the fact that MD Anderson has been one of the leading cancer centers in the world. What is happening to the reorientation of MD Anderson? How are you dealing with cancer patients? Because you can't tell cancer today, you have to stay on hold while we deal with the virus, and also those cancer patients whose immune systems might be compromised. What is happening at MD Anderson?

[PS] Our leadership team – I have to give them a lot of credit here – they've really put in place a processes where we're able to continue to see our patients in one part of the hospital. Another part of the hospital was then completely reoriented and reorganized so that we can take care of COVID-19 patients. We are moving now from that scenario to having telemedicine and have it helping a lot of our patients receive their medications closer to home so that they don't have to travel.

These have been detailed conversations also that each physician is having with their patient about the pros and cons about continuing certain treatment in this period of time where they may be susceptible to the infection because of immunosuppression of certain agents such as chemotherapies. And whether or not, for example, drugs that we developed that you heard about from Jim – the immune checkpoint therapy agents that we're giving to treat cancer – whether or not those immune checkpoint therapy agents
that accelerate an immune response may be helpful or may be worse in the setting of a COVID-19 infection.

We don't have the all the answers, but we're having these very transparent conversations with our patients weighing pros and cons and making decisions together between the physician and the patient for each individual case. MD Anderson has moved very rapidly to enable telemedicine so that we can have these conversations with our patients wherever they're at – we don't have to have them travel in – and then we can help set up a oncological care or cancer care closer to their homes. We also set up a database system because we don't have a lot of the answers. We need to know how our patients will do over time as we're taking care of cancer patients who have the COVID 19 infection so that we can learn from it.

One of the things that makes me optimistic is that collaboration at every level is with us today: government agencies, academic centers, clinicians. And not just in the U.S. but around the world. And the ability to accrue patients, which challenged us many times and delayed treatment – particularly in adults with cancer – does not seem to be an issue here today. Let's talk about acceleration. Is there something – a call to action [you] would suggest that needs to be done that we could accelerate faster?

[PS] I think one of the calls to action is something we've been doing in these different task forces between the government agencies, the medical centers, the philanthropic groups such as yours, Mike. We've been having these calls to action where we are trying to engage patients who've recovered from the infection so that they can come in and donate their plasma for us to learn how we can then start giving this convalescent plasma to other patients who are infected.

We also need a call to action for developing the serology tests so that we can make sure that we are testing these patients and we understand the titers from these patients who've recovered, so we know that they have the right amount of antibodies that we need in order to give to other patients. I think we've seen, for example, Mount Sinai reported recently about 500 patients lined up to give their plasma to donate after they'd recovered from the infections in New York. So that's been an incredible outpouring of support from the community, but we need to have this on a larger scale.

[JA] I agree. I think that what Pam just mentioned, the patients who've recovered, if we could identify the individual B cells that would give us a real quick head-start on making monoclonal antibodies from their own cells that that could be made in massive quantities to use to treat other people. That could be doable within months I believe.

In the meantime, this virus is with us and it's going to stay with us and we need to keep doing what we're doing now to keep it from spreading, with social distancing and all that, while we're working on these other efforts that are going to buy time until the ultimate
treatment appears, hopefully within a year or so. But it's just going to take all of us behaving ourselves and doing the right, socially responsible things.

[PS] I also want to say that we have to have a call to action about how to help the healthcare system and public health system, because this is teaching us a lesson that maybe we weren't fully prepared, and we need to be better prepared when the next one comes because I do think that these are global health issues that we're facing, that things will spread from one area to the next and we have to be prepared to deploy people and protective equipment for our health force and different tests for these. So maybe we need to start investing in the science of public health policies and epidemiology a little bit more. And I hope that's another call to action we can have.

We often say it takes courage to be a cancer patient or a patient with life-threatening diseases to want to know and take action.... But we also looked at all those that went into clinical trials as heroes. It might not have worked for them, but it gave us the knowledge that allowed us eventually to find the solution for so many others. And today you've raised this issue here of giving blood and people that have successfully fought the virus. The more of them that give their blood and we can test their antibodies, it seems to me, the quicker the results. Has MD Anderson put anything in effect that you've spoken about similar to Mount Sinai?

[PS] Yes, we have that in the Houston Medical Center area too. The hospitals here are also collecting samples and MD Anderson is also doing that for us to get the patients who have recovered to bring them back so that we can get samples from them. We're also trying to figure out how to set up digital health platforms so that the patients who are not admitted to the hospital for recovery, because a lot of patients can recover just staying in their home, by reporting in through the digital health platforms, then we can find out about these people and have them also come in for us to receive the blood donations from them.

Walk us through, Pam or Jim, the process for our listeners: After you've taken some blood from people that have successfully fought off the virus, what are the steps that happen before we could put it in that serum into an individual?

[PS] Well, one of the first things we're going to need is a good serology test so that we can actually make sure that we're looking at correct antibodies in that blood towards the
correct virus. Cause as you know, many of us have had coronaviruses. They're quite frequent. But this is a different virus, this COVID-19 is very different. So we have to make sure the serology tests can accurately look at an antibody response to COVID-19 as opposed to all of the other viruses that we've been infected with. And that serology test becomes important. So having a serology test that gives us the right information is the first step that we're going to need.

Once that is done, what are the next steps?

[JA] Well I think with that we can begin to treat some people and get them back in the workforce. But we can also then – again, using blood from those patients, for example – isolate and detect the individual B cells that are making those antibodies and through a number of different ways immortalize that to where we can mass produce the right antibodies in sufficient quantities to treat the people who are beginning to get sick or at risk of getting sick across the country.

So obviously one of the first groups we'd want to give it to would be healthcare workers.

[JA] Exactly.

And what about those where the infection has advanced and they're now on ventilators, does it work for those?

[PS] It can, it absolutely can work. We still have to test where it's going to be best deployed. Once we understand a serology test, then we can determine the amount that we can give back to patients who are sick and then test it out into different groups of patients. The ones in the ventilator. Do they need one dose or they need two doses and the patients who are just presenting with early symptoms, how do we treat them? But these things will have to be tested. We don't have enough data now to make those decisions.

But if we're viewing, once again, every day as a month or a year, who is going to prepare those tests? And if I get that serum, how do I know it's going to work if you give it to me?

[PS] I think one of the things that we're going to monitor obviously are clinical symptoms. The other will be viral load. So we can actually have a virus test right now where we're doing a PCR analysis to look for the viral load. So maybe as we're giving these treatments, we see the viral load decreasing.
That's a very critical thing that unfortunately we're lagging way behind on. We need to have better tests that we could get to a large number of people in order to measure the viral load and be able to monitor how they're doing once they get therapy. But we just don't have them that in the scale that's necessary right now.

We're doing a much better job in this last several weeks, I'd say, than in the beginning when we first recognized that the virus was here in the U.S. I think this is improving, so that will be good to see as we have more and more people tested.

Are both of you together working at home or are you going into the office? How are each of you operating?

Initially, I was still seeing patients in clinic. But since the hospital has now made this change to mostly telemedicine, I'm not really in the hospital anymore. About a week ago, our research labs were shut down as well at MD Anderson. So, we're no longer going into the research labs, we are working with our laboratory teams virtually. So, mostly working from home.

Now that you're working remotely, what's been the reaction as you interact with your teams?

I think it's very frustrating for them, for the same reasons it is for me. These are young people, early in their careers, who are trying to generate new data, doing experiments, and now not able to do that. But we've set up a couple of ways of communicating with the whole group instantly, basically. We're looking at the data that's out there instead of the data that's generated by them. And I think everybody's itching to get back.

Yeah, I think people were a bit surprised and I think confused as to how quickly we were shutting down everything. Imagine over a hundred clinical trials that we were involved with in terms of collecting samples from the trials, understanding the data from the patients and starting new clinical trials based on our data. All of these things shut down very quickly.

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– Jim Allison

But I do think a lot of people have come to understand the severity of the crisis that we're facing and the importance for us to all stay at home as much as possible instead of interacting in the hospital or research labs in order to flatten the curve.
What they're doing in terms of staying at home is the best thing is to keep them safe. We have to come back to research and science and data so that we can propose other treatments for other diseases that are out there. We don't want to have a delay in treating other diseases. We don't want our cancer patients to have a delay in their treatments. So we have to think carefully about how to balance those things.

[JA] I think that there's no doubt that is frustrating for us that when we've made such great strides in the last few years on treating many kinds of cancers that were inevitably lethal. We've just, of necessity, had to suspend that because this is a much more immediate danger.

Well, I want to thank the two of you for joining us today and our, what seems like a lifelong partnership we've had. Jim, once again, congratulations on your Nobel Prize last year and we look forward to your creative ideas in helping us stop this pandemic and your continued work to eliminate cancer as a cause of death.

[JA] Well, thank you very much. It's a pleasure to continue to work with you on trying to bring some good to the world.

[PS] Thanks, Mike. This has been great. Thank you so much for all your support over the years.