3 Takeaways Podcast Transcript
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Ep. 140: The Man Who Led the Creation of Moderna's Covid Vaccine Shares His Powerful Insight and Vision: Tal Zaks

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INTRO male voice: Welcome to the 3 Takeaways Podcast, which features short, memorable conversations with the world's best thinkers, business leaders, writers, politicians, scientists, and other newsmakers. Each episode ends with the three key takeaways that person has learned over their lives and their careers. And now your host and board member of schools at Harvard, Princeton and Columbia. Lynn Thoman.

Lynn Thoman: Hi everyone, it's Lynn Thoman. Welcome to another 3 Takeaways episode. Today I'm excited to be with Tal Zaks, who was Chief Medical Officer of Moderna from 2015 to 2021. Before that he worked at Sanofi, GSK and the National Cancer Institute. And he's also been a professor at both the University of Pennsylvania and at Tufts. At Moderna, Tal oversaw the development of the Moderna COVID vaccine. So he's responsible for developing the vaccine that has protected hundreds of millions of people around the world from COVID. I'm excited to find out what we really know about the safety of mRNA vaccines, why the US is the leader in drug discovery, how he sees the future of drug discovery, and what it would take to accelerate the discovery of new drugs and treatments for cancer and other diseases. Welcome, Tal, and thanks so much for your work on the Moderna vaccine and also for our conversation today.

Tal Zaks: Thank you, Lynn. It's a real pleasure to be here today.

LT: The pleasure is mine. Tal, what makes mRNA vaccines new and different?

TZ: Well, the unique feature of mRNA vaccines really is part of what makes mRNA medicines at large unique, which is we figured out with messenger RNA how to turn something that is an inherent biological property of all of our cells in the body into a way to make new medicines. In essence, what messenger RNA is, it's the instruction set that tells every cell in our body which unique proteins to make. When you think about it, what makes a cell unique is the protein that it makes. For example, insulin is a protein. It is made by a very certain type of cells in our body, in our pancreas. If you can actually take that kind of molecule, a messenger RNA, and think of it as an information molecule. It's essentially the same molecule, but because it has different sequences, it ends up encoding for different proteins in different cells. And so the ability to take this molecule and change the information it encodes and then introduce it to cells allows us to essentially teach a cell to make a protein that has a medicinal effect.

TZ: In the case of the vaccines, what we do is actually a relatively simple application of this technology. We know what a virus is. We know what the proteins on a virus are. Everybody now is familiar with the spike protein of COVID as being the thing that our immune system recognizes. And what the mRNA vaccine allows us to do is basically code for the sequence of that spike protein, but introduce it in a way that teaches the immune system to recognize the virus without actually seeing the entire virus. We don't need the virus for our vaccine. In fact, we've never had the

virus at Moderna in any place in time. All we have is the information. And if we just take that critical piece of information of what codes for the right thing the immune system will recognize, which is the spike protein, and we introduce it in an mRNA molecule as part of a vaccine, then it teaches our body to recognize the virus before it has ever seen the virus, and that's exactly what a good vaccine does.

LT: So the mRNA vaccine is different also because it essentially tells the body to produce the vaccine itself. It's just the directions. It's not introducing an attenuated virus into our bodies.

TZ: That's exactly right. There is no risk of anybody getting infected from COVID from a vaccine with mRNA because there's no virus there. And in fact, it's just information of just that one spike protein. And once the immune system sees that, it generates antibodies, it generates the other elements of the immune response that are required then to protect us.

LT: And what do we really know about the safety of mRNA vaccines and how do we know it?

TZ: These mRNA vaccines are probably the best studied medicine in the history of mankind. If you think about it, we've treated billions of people with this, and we've done this in a modern era of data collection. We've done this under regulatory oversight that requires every company that is manufacturing and distributing the vaccine to actually very carefully record any adverse events, any side effects that people from the field tell us. And so when we launched this vaccine, there was a lot of effort.

TZ: This is kind of the iceberg that goes under the water, but we had to set up massive systems of data collection so that anytime somebody from the field gets any side effect that they're not expecting, they actually call us and we're obligated to look at that data, follow up and evaluate it. And the end result of that is a very good understanding of even the rare side effects here. And the proof of the pudding is if you look at some of the vaccine platforms, you've seen side effects that occur at one in several hundred thousand cases have still been reported, validated and at the end of the day deemed to be true.

LT: What makes the US the leader in drug discovery?

TZ: I think the US has two very critical components. The first is the depth and breadth of the science that we have. And the second is the unique ability for private-public partnerships at the deepest level such that we can deploy public capital through things like our National Institutes of Health to advance the science. And then we're able to deploy private capital or in some cases when the companies are public, public capital, but in the context of a commercial entity to seek a return on that investment and therefore enable risk-taking, which otherwise is very hard to justify. And I think those two components are what make this country unique. And if you look at the number of medicines and the quality and the effect of the medicines that have been developed in the United States in the last 50 years, it's astounding. And there's nowhere on earth that comes even close.

TZ: And for me and what I've actually lived through in the last several decades has been that marriage of depth in science, public commitment to science, but also the ability of a capitalistic for-profit return on invested mindset that allows us to take risks even when many of those ultimate endeavors will fail. And look, if you talk about a cancer vaccine, which is close to my heart, we've tried many, many times and have failed many, many times. I think more recently we've had what

looks like finally the beginning of a success with an mRNA vaccine, a personalized vaccine for cancer, but it's that kind of investment and persistence that is required. And you can have that if there's an expected return on that investment. I don't see that same level of commitments in other countries.

LT: The COVID vaccines were not developed by the largest pharma companies, but by smaller companies and ones that were not vaccine makers. Why do you think that was the case?

TZ: I've often scratched my head on that one. I think it's a combination of two factors. I think the first is, and I'll speak for Moderna and BioNTech, for us at Moderna, it was clear from the get-go that there were many potential applications for messenger RNA, but vaccines was probably the low-hanging fruit just from a technology standpoint. And without going into too much details, if you think about vaccine as a medicine, it's a little bit of medicine and you give it relatively infrequently. So that's easier to envision than taking an IV infusion once a week. So we knew that for this technology, vaccines made sense. And in fact, back in 2015, when I had just joined Moderna, in my first all-employee town hall, I sort of tongue-in-cheek gave a presentation that explained to everybody why it was we cared so deeply about vaccines.

TZ: And I used the story of influenza, the flu pandemic of 1918. We always feared that the next one is around the corner and we believed that this technology was uniquely well-suited to that. And so if you fast forward then just five years to 2020, by the time COVID hit, we at Moderna had already been able to immunize people to use messenger RNA as a vaccine for eight different viruses. And in small clinical trials and people, we were able to demonstrate that in all cases, in eight out of eight, we were able to mount an immune response that we thought was going to be relevant. And so COVID for us was actually the ninth one that came along. It was the big one. But we were well-prepared with this technology.

TZ: And frankly, BioNTech who was doing similar technology development alongside us, in 2017 had already partnered with Pfizer to look at influenza, flu, and whether mRNA would work because we'd published our data in flu as the first publication of a messenger RNA vaccine that actually works in people. And I'm very proud to have been part of that. Back in 2016, we showed that this could indeed work. And so I think BioNTech and Moderna were very uniquely suited from a technology development standpoint to start chasing this. Our technology also enabled us to move quickly. I think the other pharma companies, and I give Albert Bourla and Pfizer a lot of credit for having seen the potential and jumped on it. And they were there neck and neck with us. And that's why the world today, the Western world has two very successful mRNA vaccines for COVID.

TZ: I think the other large pharma players had technologies that were a bit older and they were slower to get there. By the time they reacted, we were off to the races and their technologies were slower to begin with. But it was the small companies who were more nimble, who had technology that could move quicker that ended up being the ones who actually proved this. And I think it's a combination of being at the forefront of scientific innovation and having the agility to move. And frankly, look, in a small company, and this goes back to the capitalistic environment, your success is not guaranteed. Your back is to the wall. And so that creates a sense of urgency that is quite unique to small companies who are still not bringing in any revenue.

LT: You just talked about scientific innovation. How do you see the future of healthcare and developing new drugs and treatments with mRNA, artificial intelligence, and other new

technologies?

TZ: I've never been more excited. In fact, one of the reasons I left Moderna was because I had to take some time to satisfy my curiosity in terms of everything else that was happening that was not just mRNA. I think we've proven the concept for mRNA, certainly in infectious disease vaccines, it's probably the most successful vaccine platform to ever have launched. So I'm very excited about the potential opportunities for that technology. You mentioned artificial intelligence and machine learning. I think that that is where we're going to see a huge change. It's going to take time because one of the interesting aspects is that science and technology actually operate to a different time cycle than drug development does.

TZ: Science moves very fast. Machine learning moves fastest than anybody could ever envision. But medicine development actually takes time. You have to go enroll patients, you have to figure out what it is you need to do, you have to wait, you have to show an effect. There's regulatory considerations. But I do think machine learning has many interesting applications that I'm just curious to see evolve and be part of. And as a result, the ability to actually diagnose and ultimately treat people is going to significantly improve. It will change our relationship to knowledge in all domains, including medicine. And that will, I think, change how we look at medicine writ large. And I think that revolution is going to be fascinating to watch and hopefully be part of.

LT: I can't wait for that to happen. And how can government accelerate other discoveries and treatments for other diseases?

TZ: Well, I think there's really two critical components. The first is to continue in terms of the investments in basic science. And I think the other one is really to think carefully about the regulatory framework by which we approve drugs and we reimburse drugs. I worry about a regulatory framework that is easy to point to the risk, but you have to remember always that approving a drug is a question of benefit versus risk. And I give the current FDA leadership a lot of high marks.

TZ: In fact, the FDA in my book are the unsung heroes of the COVID vaccines because while the private sector could always go hire another thousand people, build another factory, the FDA as our civil service actually with the same headcount, more or less, went to phenomenal length to cut timelines, give guidance, look at data and come to the conclusions. So I do think we need to strengthen the civil service institutions, first and foremost the FDA, and make sure that they have the tools they need and the resources they need in order to streamline and make development, make this translation of science into medicine faster and more possible, not just under extreme duress circumstances, but as a matter of course.

LT: Before I ask for the three takeaways you'd like to leave the audience with today, is there anything else you'd like to mention? What should I have asked you, Tal, that I did not?

TZ: Well, I think we hit on the relevant highlights. The fascinating thing for me personally was that we could pull this off by all working through Zoom remotely in our bedrooms or our living rooms. And if you had told me in 2019 that I could get a vaccine approved within 11 months, working closely with four government agencies on every major decision, and I would do this in a team that I don't have yet, but that I will all hire, and I will do this without actually leaving my house, I would have said, give me whatever you're smoking. The reality is that we did this and that has caused me

to think really about how we align ourselves and how we work and how important it is to have shared purpose alignment on what's important. And I think there's a learning there for how to work in this new future that is upon us where we have this hybrid way of working. You and I are able to connect wonderfully, even though we're recording this podcast completely remotely.

LT: Tal, what are the three takeaways you'd like to leave the audience with today?

TZ: I have to start with something I heard David Petraeus say on one of your podcasts here, and he was quoting the Roman philosopher Seneca, which is, luck happens when preparation meets opportunity. There's no better quote for me to describe why we were successful at Moderna, but the preparation for that opportunity starts at an even more fundamental place, which is having a vision for what the future is like. And that I find really striking. If you look around us physically, our world is the function of the vision of those who came before us. Everything that surrounds us, putting Mother Nature aside, is a function of people's vision. And that's what makes us as humans so unique. And so I really took that lesson to heart. And every time that I am now looking at an endeavor, I always try to start with, okay, what is the vision here? If this is successful, what will we accomplish? The second takeaway, and this is a personal one for me, I'm a physician. And what I learned at Moderna is the importance of engineers.

TZ: [Moderna CEO] Stephane Bancel, I think one of the best CEOs in history, certainly in living times, is an engineer. And it taught me the difference between physicians and engineers and how important an engineering mindset actually is. As a physician, we're taught to treat sick people. So I don't make healthy people healthier. That's an engineering mindset of continuous improvement. And yet, a COVID vaccine, that's exactly what it does. It takes a healthy person and essentially makes them healthier, makes them better prepared for the future. And if you take that to the next step, I think we as physicians should think about preventive medicines. And others smarter than me have come to that realization much before me, but I do take it to heart in that preventive medicine and how to make healthy people seemingly healthy, healthier, I think is going to be something I look personally more and more to. And I think it's going to be enabled by all this machine learning because disease as a manifestation of things that are wrong, well, those things that are wrong may be evident earlier.

TZ: And if we get smarter at detecting them earlier, then we can actually intervene earlier. And instead of treating sick people when they're sick, actually treat healthy people and try to make them healthier for a better future for themselves. And the third one is that what COVID has taught me is that if we don't learn how to translate medicine into politics, and politics, I don't mean as a bad word, politics is the thing which unites us as human beings. If we can't translate our medicine into a political understanding of the value of that medicine, people won't have access to our medicine and all that will have been for naught. So I've taken it personally, I think those of us who are in the trenches doing that first bit of translating science into medicine, we also have a duty to be able to speak to our medicines in a way that makes them understood and accessible so that they can actually get translated and do the good in the world that we had intended them to do when we developed them.

LT: Tal, this has been great. Thank you for your work and that of your team on the Moderna vaccine and also for our conversation today.

TZ: Lynn, thank you for having me and for giving me this opportunity to fulfill that duty I spoke

about. Thank you.

LT: For anyone who's interested, we have several great related episodes Former FDA Commissioner Scott Gottlieb on uncontrolled spread, why COVID crushed us and how we can defeat the next pandemic. That's episode 59. A unique model of innovation, making breakthrough discoveries and turning them into real world products at an unheard of pace with Harvard's Don Ingber, that's episode 35. And harnessing the power of artificial intelligence and synthetic biology to usher in a new age of drug discovery with inventor Jim Collins. That's episode 44. Hope you're enjoying 3 Takeaways. See you soon.

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