3 Takeaways Podcast Transcript
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Ep. 174: Former Secretary of Health and Human Services Alex Azar Details Previously Unknown Reasons For The Stunning Success of Operation Warp Speed

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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 Alex Azar. Alex became Secretary of HHS, Health and Human Services, in 2018 and faced the challenges of overseeing the federal government's largest healthcare-related agency, with its $1.4 trillion budget and 85,000 employees. But in January 2020, COVID arrived. Under his leadership as head of HHS's Operation Warp Speed, COVID vaccinations were developed in a record seven months and were being distributed in less than one year, which was extraordinary, given that previous vaccines took 8 to 12 years or so to develop. I'm excited to find out how Alex did it and how his experience as president of Eli Lilly's US division helped him figure out how you could get a vaccine in seven months. Welcome, Alex, and thanks so much for joining 3 Takeaways today.

Alex Azar: Hi, Lynn, thanks. I'm glad to be with you and your listeners.

LT: It is my pleasure. And thank you so much for your work in government and your success with treatments and vaccines for COVID.

AA: Thank you.

LT: Alex, you had a call with Johnson & Johnson at the end of March 2020. You were going to put in half a billion dollars and they were going to put in half a billion dollars to jumpstart J&J's work on a vaccine. How did that call go and what did you realize?

AA: This was at the end of March in 2020. We had already been investing a lot in various, what we call countermeasures. So already in January and February, we had started with Moderna, our vaccine program. We had already gone into what we call phase 1 clinical trials, which is that initial human safety testing, I think on March 16th on the Moderna mRNA vaccine. We were already funding remdesivir clinical trials. We were funding monoclonal antibody clinical trials.

AA: And so, I had a call set up, and I had fairly limited information before the call. And I was speaking with the leadership of Johnson & Johnson about an announcement that was coming out the next day. It was sort of a touch base kind of interaction. I didn't have a lot... Oddly, usually you're pretty well briefed. For this one, I oddly didn't have a lot of briefing, and over the course of the call, I learned we were putting half a billion in to support their vaccine program. They were putting half

a billion dollars in.

AA: And I started asking some questions, such as when did we think this might enter phase 1 clinical trials. Well, I had just been touting the fact that Moderna had entered phase 1 on March 16th. And I learned that, well, this might get into phase 1 in September of 2020. I said, "Okay, that's interesting." Remember, this is the very early days of COVID, and we had been through SARS, MERS, monkeypox, various novel contagious diseases that would come out really strong and then basically disappear. And you didn't know if, frankly, we'd still have COVID in September. So, it wasn't clear that that was going to be terribly relevant. I asked whether this cooperation would lead to manufacturing. It wouldn't.

AA: I kept asking questions... Well, I went in the office the next day, met with the team, and I started probing. Because I'm a business executive, I started asking the sort of accountability questions, "Okay, what are we getting for half a billion dollars? How much manufacturing?" Nothing. "What price would we be able to buy it for?" Undetermined. "When will we have vaccine phase 3 clinical trials, the final stage [of clinical trials]? And when will we get vaccine?" Undetermined, that's not part of this. And I started really... It started coming into clarity that what we were getting was much more NIH [National Institutes of Health]-type funding, where we provide grants, and they aren't really accountable. It's not so much a contract with a demand like, "Here's $14 billion and you will produce an aircraft carrier within 2 years that meets these specifications," but rather, "You've got a good scientific idea and we want to support that and fund that. And so, here's some money."

AA: My team could sense my frustration and I said, "You know what? I want to do a survey." When we were at Lilly, we would do portfolio management, where you'd look at all of the bets that you're placing across the entire portfolio and determine have you placed the right bets and assess them. So, I created the Scientific Advisory Council with Francis Collins and Tony Fauci from NIH and Bob Redfield at CDC and Nancy Messonnier from CDC and Bob Kadlec from our preparedness and response group and our FDA people.

AA: And what we did was that matrix laying out where on therapeutics, on diagnostics and on vaccines, where are we investing? What bets have we made? And I guess my frustration kept growing. As my team came to me, they said they... I remember the moment when Paul Mango, my Deputy Chief of Staff, and Dr. Bob Kadlec, the Assistant Secretary for Preparedness and Response, and Peter Marks, who was the Director at FDA for Biologics, which has vaccine regulation under it, came to me and said, "Mr. Secretary, we can feel your frustration that there's not enough timelines, accountability, deliverables, that it's a bit loose."

AA: And they said, "To be honest, if we just rely on the pharma timelines, we're not going to get there. If we do it the old way, we're just not going to get there." And I said to them in this meeting, "We are the most powerful nation in the history of the Earth, with more resources than any nation in the history of the Earth. We are the country that developed an atomic bomb in three years. We are the country that put a man on the moon and returned him safely to Earth in eight years. We should be able to do things differently."

AA: And I said, "So here's the thing. Congress has just spent 2 trillion dollars of COVID relief money." So literally any amount of money we could conceivably spend on clinical trials or manufacturing of vaccines, therapeutics and diagnostics would have an infinite return on investment

if we could pull that forward by any, any period of time. And so, I said, "Take money off the table. I've got the money or I'll get the money. You... " And I don't know why I used this framing. I said, "be limited only by the laws of science and physics, and just take money off the table."

AA: And they came back with it. And it was actually originally code-named, I called it Manhattan Project 2, so it was code-named MP2, originally. And they came back and we worked together on this plan where with unlimited financial resources, we could completely change the paradigm of how drugs are developed, approved and manufactured. Once we got our basic game plan, the team rather quickly decided that Manhattan Project, while it was one of the most important public-private partnerships in history, might not be the best name for something that was dedicated to saving millions of American lives. [laughter]

AA: And so, Peter Marks, who was the vaccine head that I mentioned from FDA, was a Trekkie [a Star Trek fan] And so he proposed Operation Warp Speed as the name. And that's how it came about. I actually didn't like the name Operation Warp Speed because I was afraid it conveyed that we might be going too fast or cutting corners, which we both certainly did not do. But it was what the team found very motivating, and it certainly is a brand that has stuck with the program. But that's how that ended up changing.

LT: Alex, when you're talking about the Manhattan Project, you're talking about the United States World War II project to create the world's first atomic bomb. Is that right?

AA: Exactly. Exactly. Oh, yes, yes. And I quite consciously designed Operation Warp Speed on the blueprint of the Manhattan Project and how it was organized, including the choice of personnel.

LT: Interesting. Let me come back to that. Who did you involve and why was the Secretary of Defense and the involvement of the Department of Defense so critical?

AA: So, we came up with this idea, with this team together, me and Bob Kadlec and Peter Marks and Paul Mango, my Deputy Chief of Staff. And we worked out an actual game plan of how we thought, with unlimited financial resources, we could dramatically change the timelines and paradigm around developing vaccines, getting them approved and manufacturing them. And we agreed amongst ourselves that we would have, as the famous business writer Jim Collins calls it in his Good to Great book, it's called, "A big, hairy, audacious goal." A BHAG, that you lead by BHAGs. And our BHAG was that we would have enough vaccine authorized by the FDA for all Americans by the end of 2020.

AA: And we agreed that, yes, this was not something that was an accountability goal, not something that you could guarantee, but rather it was something that if everything went right, if the science developed right and the technology, the engineering all worked, that that was possible. And we agreed amongst ourselves. And I still remember the day. It was Saturday. I think it was April 25th or 26th. I started calling around to my Cabinet colleagues, because I... This wasn't an HHS [Health and Human Services] production. There are so many parts of the US government that have expertise in manufacturing, in biologic countermeasures, in science, in computational science. I wanted to make sure we were leveraging all of the government and that it was a whole of government enterprise.

AA: And I also didn't want... It wasn't a personal thing to me. It was just, "Hey, we had this idea.

We believe it can work. We have the resources. So, let's work together." I had already sold it on to the Chief of Staff and Jared Kushner, who was the Senior Advisor to the President. But I wanted to make sure it was very inclusive. So, I talked to most of my Cabinet colleagues. I talked to the Secretary of Agriculture, they do veterinary countermeasures, so they do a lot of biological research, the Secretary of Energy, they've got the largest computational resources in the world at the Energy Department.

AA: I talked to the Secretary of Homeland Security, the Science Advisor to the President, the Office of Science and Technology Policy, many others. And I called Mark Esper, who was my colleague, who was the Secretary of Defense. I laid out for him how I was thinking of this White House-led, very big, cross-Cabinet board of directors that would lead this Manhattan Project 2. And Mark said, "No, no, no. That's making it too complex. This is you and me. You've got the brains. We've got the brawn. This should be just a joint project. The Defense Department and HHS, we work together and we can get this thing done."

AA: And that's really how we formed it. And I have to say that for all the credit HHS gets, Operation Warp Speed could not have happened without the Department of Defense and especially without the personal buy-in and leadership of Secretary Mark Esper and his top leadership team. I've been around many Secretaries of Defense, I cannot tell you how unprecedented it is for a Secretary of Defense to say to a member of the JV [junior varsity] Cabinet, you know HHS, to say to the HHS Secretary, I'm putting the entire power of the US Department of Defense at your disposal, full cooperation, full resources, full personnel. That is absolutely unprecedented. And so that's how we built it. We created a streamlined board of directors, that was me and Secretary Esper as co-chairs. We included Dr. Deborah Birx, because she was, of course, running all of the COVID response from the White House. She was in charge of the entire US government response. Jared Kushner, because he was essentially the top liaison to the president for us, because I did insist this would have to report directly to the president because I wanted absolutely no political or bureaucratic interference in this project. And he lived up to the promise that he would ensure that. And then we also had the critical partnership of the Office of Management and Budget. So, I don't often say positive things about the Office of Management and Budget, no Cabinet Secretary ever does. But they were part of this and they were able to able to look at the contracts, the procurements, the money being spent, the money being committed all along the way as full partners and never were a barrier, but actually a key enabler in our ability to spend really considerable sums to get this done.

LT: And Mark Esper, the Secretary of Defense, contributed a four-star general who is the head of the US Army Materiel Command. Can you tell us about that?

AA: Let me talk a bit, if you don't mind, about personnel and organizational design, because we approached this like a business problem. For me, history is quite important and informs very much how I lead, in addition to microeconomics and how I think about government policy problems or execution problems. And I had studied quite a bit of the history of World War II and what were called the Dollar-a-Year Men, if you remember that, the folks like Henry Kaiser and Bill Knudsen from GM and all those folks who created America as this manufacturing powerhouse, but also George Merck, as in Merck, who really led the biopharmaceutical innovations in World War II, including penicillin and other products that really enabled America to win the war.

AA: And so, I had this vision in my head of what I needed was somebody who was, say, a retired

CEO of a pharma company to lead it. And I actually talked to one of the greats of the biopharmaceutical industry in the history of the industry, a fellow named Art Levinson. He really helped me think this through. He said, "Alex, you need to be thinking about what do you really need? What are the jobs to be done and the problems you're trying to solve? Over the course of a couple of phone calls, I actually figured out that a pharma CEO, that's about big finance and a lot of marketing and sales. Those weren't the issues. That's not the challenge of Warp Speed, of getting vaccines across the finish line.

AA: There really were three key jobs to be done. One of them was what we call development, which is how do you actually run clinical trials quickly, studying in humans whether vaccines or therapeutics are safe and effective and then get it through FDA's approval, development. The second is manufacturing. You often think of manufacturing as pressing out a pill, oh, not a big deal. Well, first, that is a big deal.

LT: At scale.

AA: But secondly... Yeah, at scale. But secondly, we're talking here about vaccines. We're talking about proteins and biologic products. And it is going from a 20 liter bioreactor where you produce the vaccines for your clinical trials to commercial scale manufacturing where you're doing it in 2,000 liter bioreactors that are producing hundreds of millions of doses of vaccine is not just a mathematics problem. It's not just multiply by and get something. The techniques of how you cultivate a protein, what feeder cells do you get it to grow on, how do you replicate and get adequate yields of them, how do you filter them properly, how do you make it sterile, fill and finish. This is where one of the... I think having been at Lilly and being from the industry, I knew that manufacturing would be the critical defining trait on whether we got to the finish line or not and had to invest in that in a way that perhaps other people wouldn't have known to focus so much on manufacturing.

AA: And then the third is just logistics, operations and procurement. How do you pull this together and make it happen? God bless HHS. We've got a lot of really great scientists, but we are not known as logisticians, operators and procurement people. And that's where the Defense Department comes about. So, I lay all this out to Secretary [of Defense] Esper, and we have a summit meeting actually over at the Pentagon. And I'm saying to him, "Okay, here's how I'm thinking about it. We need basically three heads: development, so the science director, a manufacturing head and a logistician procurement operations person who also is the government. I'm thinking I'm going to bring in from the outside, from the pharma industry, the first two people. I need a government person to really to be in charge."

AA: And as I said, I used Manhattan Project speak. So, the science director is Robert Oppenheimer, the manufacturing head, not a perfect analogy, but Enrico Fermi. And then my logistics operations procurement person is General Leslie Groves, the guy who built the Pentagon and then ran the Manhattan Project. So, I'm laying this out to Secretary Esper, to his Deputy Secretary and to the Chairman of the Joint Chiefs of Staff Mark Milley. Esper leans over, I remember the moment he leaned over to General Milley and said, "This is Gus." And they said, "Yeah." And then Milley returns and said, "Yep, it's Gus."

AA: And I said, "Who?" He said, "Gus Perna, got the guy for you." This is the guy to lead the project and to do the logistics operations procurement. Well, at the time, he was a three star general

about to be promoted to four star, the head of US Army Materiel Command, the former Deputy Chief of Staff of the US Army. When you think about Materiel Command, this is literally everything that goes into deploying the US Army. So, think about the decisions, the choices, the supply chain management, the critical chain project management that has to go into deploying a million soldiers to a field of battle somewhere. Everything from food to weaponry to latrines to housing to airplanes, all of it. He's got to figure out how to do that. And so that was our guy. Then we convened an interview board where we were talking to people to run the manufacturing and the development side of things, the Oppenheimer and the Enrique Fermi-type characters.

AA: I actually called Jim Greenwood, who was the head of BIO, which is the trade group for the biopharmaceutical industry. And I asked him, can you ask around, you know, for recommendations? And he actually called me right back. like a day later and said, I got the people for you. One of them is Monsef Slaoui. Dr. Slaoui had been the long time head of research and development at GSK, had brought, I believe it was 14 vaccines across the finish line in ten years at GSK, unprecedented in the history of the pharmaceutical industry. And another name Carlo de Notaristefani for manufacturing. Carlo had been the global head of manufacturing for Bristol Myers Squibb, a classic big pharma global company, and then had been head of global manufacturing and supply chain for Teva, the world's largest, I think it's the world's largest generic company out of Israel.

AA: What was neat about that is he knew the big pharma way of doing everything super, super right, process based, but had the speed of the generic industry of how do you set up a hundred new production lines each year. So that combination. We interviewed candidates and Monsef Slaoui came in and he had the belief, he saw the vision. He said, literally, everything has to go perfectly. You can't have something that delays it by one day. If everything goes perfectly, yes, it could happen. And Carlo, the same thing with manufacturing, understood the gravity of the problem, the public private partnership that would have to happen and how we needed to get started on manufacturing right away. And so there was our team.

AA: So, our General Leslie Groves at the top, like the Manhattan Project, was General Gus Perna, promoted to four-star general. Our scientific director was Moncef Slaoui and our manufacturing head was Carlo de Notaristefani. Honestly, three American heroes as far as I'm concerned.

LT: Wow. I had no idea that Operation Warp Speed was informed by the Manhattan Project. Let's talk a little more about the structure of it. The structure was also informed by what you learned as president of the US division of Eli Lilly, one of the largest pharma companies in the world. Before we talk about the actual structure of Operation Warp Speed, can you tell us about drug development, how much a new drug costs, what percent of drugs actually succeed and go on the market and how you de-risk drugs?

AA: So, if we're talking just generally across the drug industry, a big pharma company or a biotech company may look at thousands of candidates and do initial testing on thousands of candidates to eventually winnow that down to the one product that ends up going to the FDA and getting approved and going on the market. And interestingly, of those, even only a fraction of those recover the costs of getting it to that point. So, it takes a couple blockbusters out there to really subsidize the entire risk-based enterprise that a big pharmaceutical company is engaged in. It can cost upwards of $1.5 to $3 billion dollars, start to finish, to discover a drug and get it across the finish line.

AA: The first thing that you have to do is discover a molecule. So, whether that's a vaccine or a pill, you have to discover it. So, you need scientific insight. You have to have drug candidates and you have to then do initial testing to just determine if you think it might possibly work. That's discovery. You then enter what we often call development, which is clinical development, which is testing in humans. And that has three phases. Let's talk vaccines in particular here. So, phase 1, when you're doing vaccine clinical trials, will be the basic testing to see does it meet basic standards of human safety. So, you might have testing in, say, 10 to 50 clinical trial subjects, individuals who volunteered to get this shot and see if, frankly, there are really bad adverse safety events. So, these are quite heroic individuals willing to... But these have been tested often on animals. There's a reason to believe it should be safe, but still, they are making themselves available for the benefit of all of us to test these products.

AA: And often that takes one to two years to get the results from. Once you've shown that it's safe, then you move into what's called phase 2. The phase 2 studies are where you're trying to then demonstrate the efficacy of the vaccine. Does the vaccine actually provide protection against this virus or protection against the adverse consequences of this virus? In addition, you're in a larger population. Now, let's say hundreds of people that are in the clinical trials, you're going to get better safety data. So, you get increased safety data and you're testing, does it work? And if it works, you're doing what's called dose ranging studies. Ethically, you need to give the minimal viable dose to somebody to produce the effect. You don't want to over-drug someone. And so, you'll test 5 milligrams, 10 milligrams, 15 milligrams, and then see how that comes out on the efficacy curve and try to pick the optimal dosage.

AA: That can take 2 to 3 years, that study, where you're testing efficacy. Then you go into what's called phase 3, which are the definitive studies the FDA relies on for approval. Those can take 5 to 10 years and involve thousands of subjects. Here's the good question for you, Lynn. When we're talking about a therapeutic, you have someone who's sick and you want to have them get better. How do you test a therapeutic? Who do you test it on? Well, you test it on people who are sick. You find people who are sick, you give them the therapeutic. Do they get better? Okay, fair to me. Not a simple enterprise, but at least a straightforward enterprise. You know who to test it on. They're sick. You give it to them and you can see, do they get better?

AA: How do you test a vaccine that's meant to protect somebody who is not sick to see either do they get sick or if they get the illness, do they have better health consequences such as reduced hospitalization or death? Well, you can do what's called a human challenge study where you take a perfectly healthy person, you give them a vaccine and then you expose them to a virus. We literally test to see will they get it or get sick from that. Highly ethically challenged. You can imagine the ethics of that. And in the context of COVID, remember when we're talking about here, which is March, April, May of 2020, we don't have reversible therapeutics. So, if we have an individual who gets very sick, we don't have the ability to just turn it off. So that's one problem.

AA: The other is the people you want to be testing in are some of the most fragile individuals. The elderly, the people with co-morbidities are those most at risk. And so, you, of course, can't do a human challenge study on them. So, the way you test a vaccine is you take healthy volunteers. You vaccinate half of them with the vaccine. Half of them get basically a sugar water vaccine. And you say, "Go out into the population," and you wait for them to get sick. When a certain number, and there'll be statistically... There'll be a number of people out of that pool that when they have gotten sick will present a statistically significant result based on that data. You collect the data and then

you open the black box and you look and you say, "Okay, 100 people got sick. 99 of those people who got sick were unvaccinated. Only 1 of them was vaccinated." Those are clinical trial results.

AA: And so, you can imagine this is something where you don't control the timeline. You're subject to the vagaries of the spread of the disease and people getting sick, and also people who are in the clinical trial, the odds that they end up getting sick. So, these trials can take 5 to 10 years when you're talking about vaccines. And so that's why, Lynn, as you as you mentioned in the opening, 8 to 12 years would be the norm. I think the fastest in human history up to this point a vaccine had ever gotten through was 4 years, if I remember correctly. And then add another about 2 years for FDA approval on top of all of that.

AA: So multiple billions of dollars, tons of candidates, thousands of candidates to get to one that might work, and over a decade to go through this very long, drawn-out statistical human clinical trial process to get clinical trial results. And then you get to FDA. Oh, and guess what? Then you get to figure out how to manufacture it, as we talked about, then you've got to figure out how do you take a very small batch production you've been able to figure out to make the materials for your clinical trials and now start making it for tens or hundreds of millions of people. This is so complex. It is more art than science.

LT: Can you talk about how you de-risked and the portfolio approach?

AA: This is where having come from the drug industry was very helpful, because I had the insight that the drug industry, for reasons we just talked about, the drug industry is the riskiest business on Earth run by the most risk-averse people on Earth, which sounds like a contradiction. But in fact, what it is, is it's people that are very smart at reducing risk. So, if you're running a drug company, how do you survive when you're placing multibillion dollar binary events? There's a yes or no outcome at the end, after having placed billion-dollar bets. So, it's like you're going to the casino at the roulette wheel and you're making a bet. How do you make that seem rational as an investment hypothesis?

AA: Well, the first thing you do is you diversify your bets. You don't put all your bets on one number on the roulette wheel. You bet in multiple therapeutic areas and you invest in multiple theses about what a mechanism of action might be. So, you've spread your bets around like that. Then within each drug that you decide to invest in, you vertically de-risk based on information and time. So, the way you do this is you invest a little bit of money, you learn, you study, use that information to decide whether to further invest in that molecule. Every step of the way, you are de-risking your future investment, because by getting more information, you have increased your probability of technical success, as we call it, of the ultimate molecule.

AA: You might start in phase 1 with a 5 percent estimated probability of success. But once it succeeds phase 1, maybe that's 10 percent. Then you invest in phase 2, get phase 2 data back. Maybe you're up to 30 percent. So, you de-risk horizontally with multiple products. You de-risk vertically by pacing out your investments over time. And then on that over time, you de-risk, as I said, on manufacturing by holding back on the massive capital infrastructure and learning process that's needed to figure out how to do commercial scale manufacturing.

AA: So, this is really one of the core insights that we were able to bring to the table with Warp Speed, knowing how the pharmaceutical industry works, is if we have that money, we can de-risk

all of that. We can basically pre-fund all of that, take that risk off the table for the drug companies, and we can invest in multiple molecules to do this horizontally. And so that's what the team did. We ended up investing in what proved to be three different mechanisms of action. One was an mRNA approach. The other was what we call adenovirus approach. And the third was a protein subunit approach.

AA: And then within each, we invested in two different drug companies and molecules in each of those. So, six bets. We had others we were considering, including other mechanisms of action that we ended up not finding fruitful enough or have enough probability. And so, we kept our focus on those six.

LT: How did the funding work?

AA: This is where Secretary [of the Treasury] Steve Mnuchin and our appropriators deserve a lot of credit. So back in March, when we were doing those COVID relief bills, we had put, I think it was over $7 billion into the COVID relief package in order to fund the replenishment of the strategic national stockpile for masks, for ventilators, et cetera, and for vaccines and therapeutics. And that was thought to be as much as one could credibly spend. But as they were negotiating up on the Hill, as often happens, there was a desire to put even more money in. And I remember getting the call at night saying, "Would you be willing to take another $10 billion in the strategic stockpile?" I said, "Sure." Again, early days, if we don't end up needing it, it's there. And if we need it, it's good. It's there.

AA: And so, Secretary Mnuchin got, I think it was a total of $17 billion. Then that gave us a lot of the seed money that was right away immediately deployable. And then we had other monies that were available through the COVID relief packages that the appropriators and the lawyers all agreed were appropriate under how the funding was written to be able to use as a source of money to fund vaccine and therapeutic production. So, it was very important that the money was there and available. I don't have any doubt whatsoever that with this vision, the appropriators and Congress would have under the duress that we were feeling at the moment, have funded additional monies. But it was good that we had it already instead of having to worry about the process of getting it. So, we were able to really get off to the races right away.

LT: Alex, you started to talk about manufacturing. When did you start the manufacturing?

AA: Right away. And we also built duplicated manufacturing capabilities. So, we supported or stood up over 26 manufacturing facilities with redundant capabilities. We went into commercial scale manufacturing on vaccines in June of 2020. So, think of that. We were scaling up the production of tens of millions to hundreds of millions of doses of vaccine, even when we didn't know if these vaccines would work. So, when we were still in phase 2 clinical trials, to determine whether these vaccines are going to be effective and whether they're going to be safe, we're making basically, if you want to think of it, vats of vaccine at risk that could just have had to be thrown away. But that was one of the key insights here - if you want to de-risk things the way pharma would normally do or often how government would do, that will slow things down. You have to be willing to place bets that will not turn out, or you can't do this. So, we did. We placed bets that might not, and in fact, in many cases, did not turn out. But that was part of the process of maximizing your odds by diversifying your risk across a portfolio.

LT: When you say "we," do you mean that HHS did the manufacturing or was it in partnership with Moderna and Pfizer?

AA: Oh, yeah. No, no. This is another key aspect. This is a public-private partnership. It's very important. We are the funder, the accountability, the pusher, the enabler. But we can't do what they do. We cannot rebuild their expertise, their capital infrastructure, their manufacturing capabilities. Remember, with some of this manufacturing, there may only be a handful of people on earth who even know how to do it. And they're not sitting at the Defense Department or at HHS necessarily. We very much partnered with them on manufacturing. What we did was solve the business problems that slowed things down. We basically pre-funded development.

LT: And the military was also key with the clinical trials?

AA: Absolutely, because they provided that logistics and operations support. Let's say you have a study that you're doing. You originally planned to have one of your major clinical trial sites in Nashville, Tennessee. But what if there's not a lot of disease going on in Nashville, and in fact, Omaha is having a major outbreak. But you don't have any clinical trial set up there. With the US military involved, you can rapidly pivot and move what was going to happen in Nashville to Omaha and basically follow or anticipate that disease burden, which is so critical, of course, to getting the clinical trial results in a timely manner that you need.

LT: That's just phenomenal. Alex, can you summarize the critical decisions that enabled the development of vaccines in record time?

AA: I would say, and we've covered really almost all of them, I'd say there were seven key decisions or problems that had to be solved to make this happen. The first was getting vision and buy-in. That big, hairy, audacious goal [BHAG] that we're going to shoot for having enough vaccine for every American by the end of the year authorized by the FDA and getting people to buy into that. I accidentally would steal from Wayne Gretzky when I would talk about this. I often said that you fail to achieve 100 percent of the goals you do not set. And eventually someone said, "You know Wayne Gretzky says that you miss every shot you don't take?" I was like, "Oh, yeah." So, I always have to credit Gretzky now. Then there's people and organizational competencies. It's about the people, stupid, as they say. Picking the right people, setting up the organization the right way is critical in any business problem or government problem to making that work.

AA: Execution risk, minimizing any execution risk. Do what we know how to do, minimize novelty. Development risk, portfolio risk management, vertical and horizontal the way we talked about it. Commercial scale manufacturing risk, invest in that immediately so you solve that question up front rather than waiting to solve that later. Commercial risk, create a guaranteed market for the product, so that there's not concern and delay because people, or lack of investment because people are afraid if they'll be able to sell. And then finally, something we didn't talk about, distribution risk. How do you minimize the risk of the ability to actually get the product out into the marketplace and get shots in arms? And again, a lot of that is around execution risk, use existing systems that are proven. We do vaccines in this country -use those systems. Don't try to build new when you can use existing.

LT: And what lessons did you learn throughout this process of development and distribution, and what are the lessons for the future?

AA: First, I learned the incredible power of partnership, whether it's partnership within the government, the US and DOD [Department of Defense] working together, the public-private partnership, working together as real partners, not as adversaries, but as real partners. And then we didn't talk a lot, but on the distribution side, the federal and state partnership. We are a very decentralized, diffuse public health and health care system. And it's actually more than just federal states, federal, state and private sector. To get any job done, you really need all of those partnerships to work quite effectively. The other thing, in terms of lessons learned, and I often get asked, could you use Warp Speed for other things.

LT: Yes, exactly. Could you use it for cancer or for other diseases or anything else.

AA: Or Alzheimer's.

LT: Exactly.

AA: And I'd say the answer is maybe. You have to have the insight about what made Operation Warp Speed work at its outset. It's important to remember Operation Warp Speed was not a discovery problem. We didn't have to discover whether a vaccine would work, whether there would be vaccines, whether there could be a vaccine. We went into this knowing something about COVID and vaccines that you may not know. Let's compare, say, to HIV/AIDS. What's the difference between, one of the key differences between COVID and HIV/AIDS? Well, in HIV/AIDS, other than one reported case in history, the human body doesn't have the ability to cure itself. COVID, we knew the body could cure itself of COVID. Now, obviously, a lot of people would get sick and die, but the body has the innate ability to recognize COVID, produce antibodies to it and fight it. That's the key to vaccines.

AA: We knew we had a vaccinable target. If we could just trick your body into thinking it had COVID, your body could manufacture the response and build protection against either infection or serious illness. And so, what it was really more about than discovery, we already had 140 potential candidates that we had to choose from when we got this going in May, was about execution, just brute force, quality execution against a target. It doesn't mean that things couldn't have failed. It doesn't mean that things couldn't have delayed manufacturing, development. Yes, that's all. But it was about executing against a known target, as opposed to, for instance, I get nervous when people talk about using Operation Warp Speed to create a pan-coronavirus vaccine. Well, that would be just delightful. It would be delightful to have a pan-flu vaccine also. Well, we've been trying for decades to do that. We don't know that it can be done.

AA: So, it's not just about brute force. We don't have a proof of concept and it's about the brute force of quality execution against it. I mean, remember the Manhattan Project for the nuclear bomb, the Apollo Project for going to the moon, Warp Speed. In each of those instances, we had effectively proven technology and proven proof of concept already that simply had to be executed against, brought to scale and risk-minimized to achieve. And so, if we had a cancer target, the validated genetic target or human autoimmune target, yes, you could brute force against that, against a validated target. But if it's Alzheimer's, where I guess we're now getting a bit of clinical trial validation around the amyloid hypothesis, but I would have said months ago where you don't know if it's amyloid plaque or if it's tau tangles or whatever else, you're still in the discovery phase. That's not really a Warp Speed-type endeavor.

AA: So, I think, use it in the right places. You have something that's a pretty well-validated and knowable hypothesis, and it's about the brute force of using the incredible power of the US government to drive accountability to results, quality execution to make that happen. But again, with the right people involved.

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

AA: I'd say, first, that it's vital that leaders and participants in a great venture have boldness. There was a tremendous amount of courage from everybody involved in this endeavor to say we were going to lay out a goal of having enough vaccine for every American approved by FDA or authorized by FDA by the end of the year. And there were a lot of naysayers. When we laid that out as a potential that we were aiming for, not as a guarantee, but as a potential, I mean, you can look back, the commentary was scathing, that it was lies, that it was political, that it was nonsense. And yet the people involved, they were willing to believe, even while being scorned, that it could be done. And they did it.

AA: The second is what I touched on before, which is partnership, the power of partnership, of not going it alone. The partnership with DOD and across the federal government, the partnership with the private sector, really treating the private sector as a partner in this, not as an adversary, but as a partner. And then the federal, state, local and private sector partnership. And then finally and most importantly, is the issue that we talked about early on, which is people. People drive everything. People are policy. The ability to get the right people from the government and the private sector made all the difference here, because a good leader gets the right people in place, enables them, removes barriers, holds them accountable and gets out of the way. So, boldness, partnership and people would be the three key takeaways.

LT: Thank you, Alex. This has been wonderful. Thank you for your service in government and especially for our COVID vaccines. And thank you for joining 3 Takeaways today.

AA: My pleasure. Thank you.

[music]

OUTRO male voice: If you enjoyed today's episode and would like to receive the show notes or get new fresh weekly episodes, be sure to sign up for our newsletter at https://www.3takeaways.com/ or follow us on Instagram, Twitter, LinkedIn and Facebook. Note that 3Takeaways.com is with the number 3, 3 is not spelled out. See you soon at 3Takeaways.com (https://www.3takeaways.com/)

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