Leadership in revolutionizing cancer immunotherapy, Garo Armen, Ph.D., Chairman & CEO, Agenus

Biotech 2050 Podcast

[00:00:00] Rahul Chaturvedi: Hello, and welcome to the Biotech 2050 Podcast. Biotech 2050 is a think tank, chronicling the disruptions, changing the biotech industry over the next several decades. Check out our website@biotechtwentyfifty.com or on your favorite podcast listening platform. I'm Raho Chuba, co-founder of this podcast and today's host.

[00:00:19] I'm also the founder and c e O of Clara. Clara is solving the biotech industry's talent crisis by organizing and providing access to worldwide life sciences expertise. You can check us out@clara.com. I'm excited to welcome Garrow Armen, founder, chairman, and c e o of Agen. Thanks for joining

[00:00:36] **Garmen:** us today, Gar.

[00:00:37] Thank you very much, Raul. Happy to be.

[00:00:40] **Rahul Chaturvedi:** Wonderful. So Garo, to kick us off if you could please walk us through the arc of your career all that you've seen and, how you got to where you are

[00:00:47] **Garmen:** today. Well, I'm a scientist by training. I came to the US at the age of 17 without having spoken board of English by some chance and series of [00:01:00] events I ended up on wall.

[00:01:01] After I got my PhD in physical chemistry and then on Wall Street, I specialized in specialty pharmaceutical companies as well as biotech because at that time, biotech was coming of age. And in the early nineties I was attending a conference in Washington DC about cancer immun. Cancer vaccines at the time.

[00:01:21] So, coming back from that conference, I was convinced that cancer could only be cured with the use of immunological techniques. And by some chance I was introduced to a company or a technology, I should say. There was no company at the time from Mount Sinai. It was an individualized cancer vaccine technology.

[00:01:43] So I. Due diligence for about nine months, and I took my time because I had no real plans to start a company. But the idea and the technology was so compelling that we started the company. And at that time it was called [00:02:00] antigens. And the name was introduced to us by the legendary Joshua Lederberg, the Nobel Laureate from Rockefeller University.

[00:02:08] And some years later we changed the name. Because it wasn't descriptive of all immunological processes. And so we changed the name to Agen and agen now is positioned as a cancer immunology company, but with capabilities that could extend beyond cancer.

[00:02:27] **Rahul Chaturvedi:** Garrett, talk to us a little bit about the founding story behind agen and, how it came to.

[00:02:33] **Garmen:** The founding story behind Janice is at the expense of peppering this with some personal stories. My grandmother. Turned out to be an organic immunologist without having gone to any school. I was the first grandchild. And of course at that time when you're the first grandchild you are regarded at a very high place by your grandparents.

[00:02:57] And so whenever I got sick with a [00:03:00] cold or the flu or something, she would come to our apartment with sheets of cutting. And she would heat those sheets of cotton on the ceramic stove and put them around my armpits for hours. Just she would rotate it for hours and I wonder what this lady's doing. And the truth was that she was activating my lymph nodes to be able to fight the disease better.

[00:03:24] Hmm. So that's a very, very old memory that persisted with me. But, my mother died of cancer at the age of 40. In 1972 and at that time I was desperate to come up with some experimental medicines and we didn't even have chemotherapy at that time for patients. And so I brought her to the US shortly after I arrived here for some experimental medicines.

[00:03:45] Unfortunately, she died after two months or so. And then, you know, I had some experiences with a dear childhood friend of mine my cousin, Three year old, beautiful child of a dear friend of mine. And so when all of these things are happening, and [00:04:00] in the meantime you are going on a journey to be able to do something about it, something sustainable.

[00:04:06] See for the last up 10 years, we've tried to deal with cancer in a suboptimal. Using all kinds of medicines. And of course, there has been some benefit, but relative to the effort put into it, that benefit is really minuscule. And

but 10 years ago when the immuno-oncology revolution started we started seeing a very tiny slice of specific cancers like melanoma, for example, being cur.

[00:04:41] Never happened before. If you had stage four melanoma, you were doomed to die. But with the advent of ervo, that small slice of stage four melanoma patients were cured. And of course, at that time it didn't generate all that much interest because the market was small. And, [00:05:00] but ask that of the patients who are alive today, who would've been dead if it hadn't been for this invention?

[00:05:08] And so since then, of course we've had a revolution of explosion in the treatment of cancer patients with immuno-oncology. But unfortunately, we haven't been able to expand that tiny slice of a single indication in the last 10 years, even with PD one s.

[00:05:30] Great help for patients, no question about it, but we haven't fundamentally licked the issue of curing cancer on a broader basis. Now, of course, what's exciting about what we're doing today with Agen is that we believe. We have the next revolution at hand in the form of a product called Botten Zumab which is not just a checkpoint anybody, but it does other things beyond binding to a [00:06:00] checkpoint receptor and with Botten Zumab, early indications suggest that we are broadening.

[00:06:06] the number of cancers that would've not responded to immunotherapy or other drugs. And we are also deepening the potential responses and potential cures. And so that's exciting. but the question becomes, is it one product that's gonna do this? And the answer is no. It's not one product. It's going to be an.

[00:06:30] Of weapons to obviously beat cancer on a much broader basis. And the thing that's unique about our company is that we've worked very hard over the last seven years or so and delivered on this a whole broad army of, weapons. And we can talk about the specifics of course, but it's really the criticality of being able to battle with cancer with a tug of war between the disease and the immune [00:07:00] system.

[00:07:00] and that's where we are today. Hmm. Tilting that tgo war in favor of the immune system. Yeah.

[00:07:06] **Rahul Chaturvedi:** and let's just double click on that Garrow. Based on your work at Agen, I'd love to hear your perspective on. Immunology and

immunotherapy and the immunotherapy landscape and the opportunities that it provides compared to other approach.

[00:07:19] **Garmen:** cancer UL is a, pretty challenging disease. You know, we used to think of, for example, many years ago that if somebody had breast cancer or lung cancer or prostate cancer, that it was the same disease in every single person. And so the notion that a drug would be able to cure cancer was flawed from the start. Now what happened was, of course, as I said, cancer is a tug of war between the disease or battling. Cancer is a tug of war between the disease, cancer and the immune system.

[00:08:28] And if you can, there are two ways, over three ways of tilting that in your favor. One is you can reduce the cancer itself and certainly something like chemotherapy does. if the immune system is competent enough to be able to battle that reduced cancer. And when it happens naturally, so in some patients, for example, that chemotherapy, they may be cured, but it comes in with all the toxicities and perhaps long-lasting toxicities of some of these drugs.

[00:08:57] So the real challenge for us [00:09:00] is With present day drugs or the previous day drugs chemotherapy, radiation, targeted therapy, and so on and so forth, we're doing something to reduce the burden of the disease and or we're making the disease a little bit more visible to the immune system, indirectly.

[00:09:17] Indirectly. So when you do that, the relatively competent immune system that is in that patient may be able to battle and. Without any immunological intervention, but as we know in most cancer patients, particularly in stage four disease, this doesn't happen. And so we need additional help to bolster the immune system to win that battle or under the defenses of the cancer that block the immune system from destroy.

[00:09:47] So it's two prong strategies and with, for example, with antibodies, checkpoint antibodies, it accomplishes both. It accomplishes both the job of the [00:10:00] cancer so it doesn't protect itself from the immune system, and also bolster the immune capacity to be able to kill the. Great. and

[00:10:09] **Rahul Chaturvedi:** Garrow, I'm curious, over the next, 10 to 15 years or so what's exciting you the most about the immunotherapy

[00:10:17] **Garmen:** space?

[00:10:18] Of course I'm very excited about what we're doing, . Yeah. Because what we're doing is really, you know, you have a multi-component

immunological process. So you've got, as I said, you have cancer cell trying to hide itself from the immune system. So we've done a pretty decent job of being able to undo that.

[00:10:35] But all of these things, Raul, come at a cost, if you don't balance that process properly, you can indulge. Overactivity of the immune system that causes self-harm. you can have, for example, self tissue harm in targeting some of the checkpoint receptors like CTLA four.

[00:10:54] You can cause colitis. Or you can cause other autoimmune diseases. So [00:11:00] it's a very fine balance and the challenge is this is different from person to person and it's different from cancer to cancer. so being able to have agents that can help you modulate that process smartly is very helpful.

[00:11:16] Now then second step is, let's say that you win the initial battle, okay? But you haven't won the war. In order to be able to win the war, you have to have the ability of generating immune cells that are in a high state of alert. And that means that what if, for example, some residual cancer cells remain and they poke their head out if the, the initial battle is over.

[00:11:42] So do you have, for example, the memory response of the immune system ready to go and as soon as they poke their head, It will destroy the residual disease. And then you have these offsetting elements of the immune system. For example, they're regulatory T-cells. [00:12:00] Regulatory T-cells are cells that try to minimize the damage.

[00:12:05] it's a, regulatory process that, for example, if the immune system is overactivated, the regulatory T-cells get in the way of allowing that overactive immune system from, causing damage. But sometimes these regulatory T-cells assume a mind of their own and they do too much of regulation and they inhibit the ability of the immune system to kill the cancer.

[00:12:28] So we have agents that can. Address each one of these elements. And then we have cell therapies with our mink therapeutics. Subsidiary and cell therapy is also very interesting. The innate immune system is also very interesting. It's almost like. Envisioning, for example, a military system, and I'm not a violent person, but imagine it in the context of a military system because you can't win the war with just the Marines or the Navy and the Air Force and the [00:13:00] Army and Special Forces.

[00:13:01] You need all of these elements to be able to be deployed at the right time. And this is what's required with the immune system and, and companies

that have thought, one trick pony is the way to go about it, I think will not deliver on the final or the appropriate mandate of curing cancer. We can make important strides in treating cancer, but cures are the holy grail and that's what we need to look.

[00:13:31] Great. Thanks for

[00:13:32] **Rahul Chaturvedi:** sharing that. Perspective Garrow. Let's switch gears a little bit and talk a little bit about the current environment in biotech. You know, we're coming off of some great years both the public and private markets from a financing perspective, but there's certainly a correction underway across all sectors right now.

[00:13:48] I'd love to hear your thoughts on. What's going on in biotech perhaps you know, some of the silver linings of what's going on. It seems like you've been through corrections in the past, so we'd love to hear from you [00:14:00] how you've also navigated these.

[00:14:02] **Garmen:** So there, are two separate silos of topics here.

[00:14:06] One is what you mentioned, Raul which is really a reality beyond biotech. And I'll tell you what I mean by it. And the second piece of it, Is more specific to biotech. What is it going to really take to be successful in the future? Is it driven by an exit strategy to make a lot of money? Or is it Driven by delivering on the mandate of making profound differences with diseases? So take cancer, for example, that's our sweet spot. How do we cure patients? In order to cure patients, we need to innovate and we cannot stop innovating. The standard model in the pharmaceutical and the healthcare business has been, you know, you come up with a product and you introduce the product into the market and you have a 15, 20 year monopoly with that product and what that product does.[00:15:00]

[00:15:00] Versus the next product that's gonna be launched isn't very different. So we're dealing with incremental changes, and those incremental changes can only be demonstrated with very fancy footwork, with statistical analysis of trials that are gonna meet the regulatory standards of today. and so, then you need a huge infrastructure to do this with a regulatory and clinical infrastructure.

[00:15:27] And then you need a huge commercial infrastructure to convince doctors that having this much improvement is worth prescribing the drug. I think this is not going to be the way of the future, in my opinion. I think that the

future is gonna be driven by innovation. And rapid innovation as well as containing costs of medicines.

[00:15:51] That's what's gonna drive the future. So if we don't innovate rapidly in order to be able to deliver on the mandate of curing [00:16:00] diseases or allowing patients to have a very appropriately high quality of life while. Have the disease, but it doesn't cause harm to them, to keep a disease static.

[00:16:13] TNF inhibitors, for example, have done a pretty good job of containing arthritis in patients who are severely affected by arthritis. Not a perfect solution, but a certainly a much better solution than we're facing with cancer so far today. Okay. that's the future. And how do we do this?

[00:16:32] Well, the current pharmaceutical model, Isn't going to deliver this because as I said, the current pharmaceutical model is huge. Infrastructures to be able to demonstrate minuscule improve. Huge infrastructures to demonstrate min, minuscule differences. That's one issue. Now, if I may to indulge in the previous, the first question that you asked what's unique about biotech and what has driven biotech in the last 20, [00:17:00] 25 years?

[00:17:00] Well, it's beyond biotech. Really, if you look at the world at large, I'd say mostly the western world, it's been driven by financial greed. That's the fact, And the fact is financial greed drives in people's minds. How do I make a quick buck tomorrow or as soon as possible? Not for the long haul.

[00:17:21] and that has driven entrepreneurs, that has driven Wall Street, that has driven venture capitalists, that has even driven companies because most companies have CEOs that have a tenure year of about six to eight years max. so they're not thinking long term. Now this in contrast to the way Chinese.

[00:17:40] Implemented their strategy. There's a wonderful book that we can learn lessons from called the 100 Year Marathon. It's about Chairman Mao's strategy from the 1940s to teach the West because the west humiliated him and he wanted to teach the west about [00:18:00] the ability of the Chinese. And the China country, and he embarked on a 100 year plan to do this.

[00:18:08] Imagine a man who knows he's not gonna be around 100 years from then, but he wanted to embark on this 100 year plan. Can you imagine trying to convince the west. To do something like this, it's impossible. and I'm not suggesting that we need to be on a 100 year plan for biotech. That's not what I'm suggesting, but I think the greed of trying to deliver something tomorrow.

[00:18:33] Or as soon as possible, and having companies form so that you can become a serial entrepreneur and have an exit strategy so you can go on to your next gig. I think that really is something that's harming us today, and it needs to change. So I'm a believer in the innovation, the work ethics, the value system of Elon Musk.

[00:18:56] I'm not a republican. Or a [00:19:00] Democrat. I'm just an independent minded person, but I think my experience has taught me what is right and wrong, and without hard work and some longer term planning, I don't think you're gonna be able to battle what we need to battle today, which in our case is cancer.

[00:19:19] **Rahul Chaturvedi:** And Gar.

[00:19:20] I'm curious in terms of approaching things similar to Elon Musk, what are some of those core similarities that you share?

[00:19:27] **Garmen:** I think, you know, of course Elon Musk is a much smarter man than I am, and he's been a brilliant innovator. A brilliant innovator. one of the things that we need to be cognizant of is, If conventional ways of doing things is breathing mediocrity, we need to break that convention.

[00:19:50] You know, when Ilan Musk decided to go about his business model, he didn't take a American made car or a Japanese made [00:20:00] car and take it apart and try to improve on that model. He built something from. For example, an average Tesla car has about a hundred or so moving parts as compared to a thousand plus moving carts in a conventional car.

[00:20:19] Imagine. All the advantages that come with it, but that's just a, tiny piece of what we're talking about here in terms of innovation. He then brought in all of the algorithms and the software and, you know, for example, if you want to have an improvement on your Tesla that you thought about within few days or a.

[00:20:40] That improvement already has been engineered by brilliant software engineers of Tesla, and you get an update that you can install on your car immediately. so that's why I gave the example that typically, you. Launch a product and that product gives you a 15, 20 year monopoly.

[00:20:57] That's shameful. I think because that [00:21:00] impedes innovation. Whereas, for example, I give the example to my team members, if Apple. Had stopped innovating when iPhone four was introduced and said, we're the king of

the hill right now. We can kill research and just capitalize on our iPhone four because it's the best selling product and the best of breed.

[00:21:20] Where would Apple be today? Yeah. Okay. Where would it be today? So that's why I think the speed and the magnitude of innovation is going to be critical for our.

[00:21:32] **Rahul Chaturvedi:** Certainly agree. And Gary, I'm curious, given the current environment How have you adapted your approach in terms of hiring, how you get work done, leveraging external providers and and

[00:21:46] **Garmen:** so on?

[00:21:47] This is a beautiful question Raul, because, many years ago as we got into the field of checkpoint antibodies, we didn't venture in. Prior to 2014 we made a very critical [00:22:00] acquisition of a company. It was a private company called for Anybody which was a result of a, spin out from Roche Research Institute in Buzzell, Switzerland.

[00:22:09] We acquired that company and that gave us the basis for creating antibodies. And so when I wanted to get the first. Experience with manufacturing clinical grade antibodies. I dealt with a couple of CDMOs out there And so we made a strategic decision immediately to get into our own manufacturing operations. And so we bought the Zoma manufacturing facility in Berkeley, ca. Before a very modest sum, but it wasn't a manufacturing facility that we bought that really interested me.

[00:22:52] It was the team that came with it. It was a stellar team with many years of experience and many, many [00:23:00] years of fantastic deliverables. So when we acquired this facility Reduced our dependency on outside CDMOs and most recently we just finished a soup to nuts commercial manufacturing facility by the mile down the road from our original acquisition in Emeryville, California.

[00:23:20] And that will give us the flexibility to make product from soup to nuts, I mean all the way product with VI and labeling and storage facilities and so on, so, To get back to your question, we had a similar experience with CROs. So my philosophy is if we're going to succeed, of course you cannot completely reduce your dependency to third parties, but you need to be as self-sufficient as possible.

[00:23:49] So today we have our own manufac. Today we have started [00:24:00] assembling our own cro, r o teams. We made two acquisitions and yes, we will use high quality third party providers. When needed. But I think the plan is to be as self-sufficient as possible.

[00:24:13] And in this world of, by the way all kinds of supply chain disruptions and so on and so forth you need to really be in control of things and to compliment what we're doing. For example, we didn't talk about this in the last 10 years. If you look at our trajectory in the last 10 years, we have raise.

[00:24:30] 900 million from corporate collaborations and royalty monetization. And I'm not talking about 900 million worth of bio dollars. I'm talking about 900 million that has come into our pockets in the last 10 years. And we continue to perform in that regard, by the way. so right now we're burning cash.

[00:24:52] And, but most of the cash that we burned in the last 10 years has come from our creative transactions, and we're [00:25:00] gonna continue to do that of course. And how do we go about the future? Well, you've got to be very efficient. Very innovative. You've got to be self-sufficient, and you've got to make sure that you have alternate means of cash acquisition, not just being dependent on third party investment banking units or typical investors.

[00:25:23] **Rahul Chaturvedi:** Yeah. Appreciate that, advice. Gar, you've certainly seen a lot being at the helm of agen for over two decades. So thanks for sharing those insights. If I could ask you to reflect and take a step back for a minute. Given all that you've seen and all the experiences that you've had, what's one piece of advice you wish you could provide your younger self knowing all that you now know?

[00:25:45] **Garmen:** I think the key Raul is to do it right and to do it right, to me means to work hard, to think hard, to be innovative. Never give up. and [00:26:00] built a company, a team of your colleagues with a very high standard, a high value system with high integrity. You know I think this is what keeps our team together.

[00:26:11] One common driver, one common objective of our team is the end game. And the end game is to cure cancer. But not just do it in a sloppy fashion, but do it with the right standards. And there are no shortcuts in pursuing the right standards. There is no quick buck to make here. I have invested 28 years of my life in this company and thank goodness that I didn't have the need to make a lot of money.

[00:26:37] In fact, I am net in the hole by. A number of million of dollars net of my pay because I could afford to do it. So I haven't done this for any other reason than meeting the objective of curing disease. Mm-hmm. , that's the only objective.

[00:26:54] **Rahul Chaturvedi:** Great. Well, on that note, Garrow, thanks so much for joining us today.

[00:26:57] It was a pleasure speaking with you and wishing you [00:27:00] and your colleagues continued success as you pursue this important mission at Agen.

[00:27:04] **Garmen:** Thank you very much, Raul. Thank you very much for having me. My pleasure.