

June 12, 2019

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In this episode Taren Grom, Editor-In-Chief of PharmaVOICE Magazine meets with Dr. Joan Mannick, Co-Founder and Chief Medical Officer at resTORbio.

Taren: Dr. Mannick, welcome to the PharmaVOICE WoW Podcast Program.

Dr. Mannick: Thank you, Taren. I'm delighted to be here.

Taren: Well, we're delighted to have you here as well. You made a pretty bold leap to co-found resTORbio after a very successful career as executive director in the New Indications Discovery Unit of the Novartis Institute of Biomedical Research. What were some of the key drivers that led you to make this transition?

Dr. Mannick: The program that I was involved with at Novartis was targeting aging pathways as a new way to treat aging-related diseases, and Novartis decided to spin out the lead program into its own separate company, which is resTORbio. So I actually was just given the opportunity to spin this asset out and form a company by Novartis. I was delighted to do it because we'd had positive data at Novartis in two phase 2 trials, so I wanted to move the program forward and determine if we continue to see positive results in later phase trials.

Taren: You say given to you, but that sounds very humble speak to me because obviously you had to be the right person with the right credentials, with the right knowledge to be able to take this program to the next level.

Dr. Mannick: I think what helped me with this program was that I was very passionate about it and was excited because there were positive results in two phase 2 clinical trials. And Novartis allows some programs to be spun out into new companies and some may move forward internally and some they just discontinue. And I think because this program did have positive results and I was very passionate about it, I was able to advocate for getting this spun out into its own separate company. So it may have been the only credit I think I could take is that I was passionate and excited about the positive results that had been generated at the time it was being considered to be turned into its own new company.

Taren: Excellent. We'll talk about the therapeutic focus in just a minute, but even with the advantages of spinning out from Novartis, starting a biotech company is not for the faint of heart. What were some of the biggest challenges you faced in launching the company?

Dr. Mannick: Yeah. So when we started the company, we were two people. It was a CEO – my CEO and it was myself; I was the CMO. So there weren't the resources you have when you work at big pharma. Novartis has over 100,000 people and whole teams of chemists and preclinical toxicologists and clinical development people and suddenly you have to do drug development with a much smaller team and so you have to get your hands dirty and do all sorts of different jobs. Also, with all little startups there are bumps in the road and you have to be resilient and just keep your eyes down the road on the prize and ride through the bumps.

Taren: Yeah, it is. It's like being chief bottle washer and cook at the same time too, right?

Dr. Mannick: Exactly. Exactly.

Taren: As I said, I am excited about the focus of the company – age-related diseases; as somebody who is aging this is really important research. Talk to me about what excites you about this area of focus for the company. And then as a follow up, I'd like for you to talk to me about the company's lead program. Is it T-O-R-C-I? How do you pronounce that?

Dr. Mannick: It's TORC1. There's really interesting high-quality science in preclinical species suggesting that aging isn't just due to random wear and tear and it's actually a biology that's regulated. It's regulated by a few specific mechanisms that have been identified to date. And one of the best validated mechanisms is the activity of a protein complex called TORC1.

So what's interesting is when you inhibit the activity of this protein complex in every specie study to date – in yeast, in worms, in flies and in mice – life span is extended and the organisms not only live longer, but they stay healthier longer.

And what's important about the fact that it's in so many different species that the benefit of inhibiting TORC1 is that these very evolutionarily diverse. So if throughout evolution this mechanism that seems to contribute to why organisms age has been preserved it's likely that TORC1 may also play a role in human aging. So then the question is if you

want to in drug development look at whether TORC1 inhibition impacts human aging, you need to pick some endpoint that can be analyzed in a relatively short period of time to see if you are impacting aging and that's the tricky part of drug development in this field.

What is an endpoint? You're not going to look at lifespan in a clinical trial, but what's the endpoint that occurs in a shorter timeframe that can be accessed in a clinical trial. So we look at what are the things that get better when an old mouse is given a TORC1 inhibitor and we saw that the function of some organ systems but not all organ systems get better, the function of the heart, the function of – neurologic function, physical activity and the function of the immune system get better in old mice given TORC1 inhibitors.

So it was first indication and this was to your question about our lead program. We said if we give elderly people TORC1 inhibitors, can we help the function of the aging immune system? And if you can make the immune system function better, one of the endpoints that should occur is that older people will get fewer infections and in particular they should get fewer respiratory tract infections which are the most common infections that occur in the elderly and are a leading cause of morbidity and mortality.

So that's the background for our lead program, which is giving older people our TORC1 inhibitor called RTB101 to see if we can reduce the incidence of respiratory tract infections during winter cold and flu seasons.

Taren: That's exciting stuff. You are looking for that fountain of youth. Ponce de Leon would be very jealous.

Dr. Mannick: This is just for a baby step. This is breaking it down into little pieces. First we've observed that in initial trials that the incidence of respiratory tract infections are decreased, but we have to confirm this in phase 3 trials, and then even if those phase 3 trials are positive, we don't know yet what other aging-related conditions may or may not improve.

Taren: Sure. But it sounds like you're hitting the top four, right. You mentioned cardiac, neurological, the immune system and what was the fourth one again?

Dr. Mannick: Physical activity.

Taren: Physical activity.

Dr. Mannick: Yes. Well, we don't know. That gets better in a mouse. What we don't know is will any of these things improve in humans that we have to do the clinical trials to find out.

Taren: Sure. So you have a lot of old mice running around now in better shape, right?

Dr. Mannick: This is work done in many different labs around the world; not work that was done at resTORbio.

Taren: Got it. So another exciting thing that you all had happened to you is the company announced its IPO. Tell me about this experience.

Dr. Mannick: Yeah. I had an unusual experience with the IPO because I actually thought it was fun when I think it's not fun to a lot of people. I have a wonderful CEO Chen Schor and the two of us went on our IPO road show where you meet with many many, many different investors before the IPO to see who was interested investing in your company and who isn't and because Chen and I get along well I think it was just kind of fun and it was – I liked meeting all these different investors. I think I had an unusual response to the IPO road show that I think sometimes can be not fun.

Taren: Right. I understand it can be quite grueling and it's telling the same story over and over, but yours is such an exciting story, but it's fun to tell, but it's fun to watch these investors. Their eyes light up when they hear the progress you're making, too.

Dr. Mannick: Not every investor, but I think it was fun.

Taren: You've got enough of them.

Dr. Mannick: Right. For me, I have strong connections – this program is like a child for me so it was like convincing a college to accept your child for admission. I care about this program and I hoped I could get other people as excited about it as I was.

Taren: That's great. I wish you continued great success, and I hope it really does prove out the way you think it's going to. We'll keep our fingers crossed. Not that hope is a strategy, but we'll still keep our fingers crossed.

Dr. Mannick: Sure.

Taren: You are very inspired by this project, and I want to ask you how do you inspire your teams.

Dr. Mannick: I think one thing that I really like about our company like getting so far is because we're a small company. For me inclusion is important, that everybody feel included and that communication – nobody is left out of communication and that also their contributions are valued. Everybody brings in a different set of expertise. So right now the company – I used to row crew and the company is like a boat where everybody is rowing together and it's really moving down the river well and when you're rowing and the rowers on your boat aren't rowing together and it gets very choppy, what I like is sort of including everybody so we are rowing together and acknowledging because people work so hard in these little startups, acknowledging their contribution. They are doing really hard work and good quality work and letting them know that they're appreciated.

Taren: Nice. You are quite an inspiration to so many women, but I'd like to ask – and not just women, men as well, but who do you look to for inspiration?

Dr. Mannick: It's funny but one of the people who philosophically has inspired me and this is very odd is that coach of the New England Patriot Bill Belichick. It's a strange thing, but he has said two things that really have helped me when I'm at work and one of them through within a press conference asked as a patriot that had a terrible loss and everybody said to him in the press conference, your team stinks this year, your quarterback is too old, everything is going down the tube. What's going to happen? What's going wrong?

He answered the same response to all these questions and all these predictions of doom and gloom. All he said was on to Cincinnati and his next – the game the next week was in Cincinnati and he just refused to go there about the doom and gloom and he just said on to Cincinnati, on to Cincinnati and I think that it's such a good philosophy is that when things are going badly and there are bumps which there always are in biotech and in drug development just move on, put it behind you and just keep moving forward. So that particular on to Cincinnati philosophy I found inspirational and very helpful in this particular career.

Taren: That's great. What was the second quote that he inspired you with?

Dr. Mannick: So the other thing he said to his team, he just goes just do your job, just do your job like take out all the noise and just do your job. And I also find that helpful. There's so many fireworks and dramas and things that go on around you and just kind of by keeping focused and do the job I think is an important way to get through it all.

Taren: I agree. That's great. You mentioned something just a second ago that sparked the questions for me. Having come from a big pharma company, as you said Novartis was over 100,000 folks in it and now in a startup biotech, what do you see as the main differences – obviously resources, but do you find that you have more agility and more flexibility than you did in your previous role?

Dr. Mannick: Yes. The 100,000 people also means things can get done very much faster in a little company, so we're able to get things done at a speed that we never could at Novartis. So that's the plus side of the little company. There are layers and layers and layers of their management that they could get approval for things to get done.

Taren: Sure. As chief medical officer, I would imagine you have to manage many different hurdles and opportunities. What are some of your biggest challenges and what are some of the biggest opportunities you see in your role?

Dr. Mannick: I think one of the challenges I have is there's a lot of work that I need to just roll up my sleeves and do and then there's a lot of work managing the people who are my direct reports and getting that balance right of managing versus doing the work yourself, that's one thing that I always want to try to get right and not spend all my time for instance just doing work and not helping the people who are reporting to me make sure that they're doing okay, too. I want to get that balance right.

I think for opportunities there's a lot on your shoulder in a little company in terms of making decisions for the company on next indications and next targets and that's a huge opportunity, but also one where there's a lot of responsibility to get it right.

Taren: Yes. And balancing that, it takes a lot of leadership skill. What are some of the things that you learned along the way that helped you develop those kinds of skills?

Dr. Mannick: I had a really great mentor at Novartis who was I think another one of my inspirations and he's actually come to be the chief scientific officer at resTORbio, so I'm really blessed with that. It's Lloyd Klickstein. As a leader and a manager, he always made us feel heard. He gave us air cover so that if there were any problems from upper management he provided air cover for us, and he also made sure that our contribution was seen by upper management and so that we got credit for the work we're doing. And that's the kind of leader and manager I want to be, that I really take care of the people who are reporting to me and make sure they get credit and make sure they're protected. Give them the air cover they need.

Taren: Sure. It's wonderful. And so as you are celebrating the successes of those around you, how do you define success for yourself?

Dr. Mannick: I want resTORbio to be a place where people love working. They love coming to work and they're inspired by the work they do. If I can create a company that is a really wonderful place to work I will consider myself to have had a success in life and then sort of the bigger goal is within this company we can develop a drug that moves the needle and really helps our older population that I think is not getting adequately sort of taken care of in drug development and really start developing drugs that help people have the better older life and live healthier longer, you know that's the ultimate goal where I really will feel on a more macro scale that I had a success.

Taren: That's fantastic. There are a lot of women who look to you as a role model, any advice you can provide to others who might be contemplating taking an entrepreneurial leap as they maybe look for new opportunities as they look to phase out of their current career and maybe do something a little bit different?

Dr. Mannick: My interesting sort of Eureka moment in life came when I was 50. As a woman, I had come from a family where academic medicine was sort of the family business. My father was in it. My mother was in it. My aunts and uncles and I just assumed I'd always have a career in academic medicine and so I was in academic medicine at age 50 and I was running a lab and I was seeing patients and I was trying to raise a family and I didn't feel like I was doing anything as well as I wished I could.

So I didn't feel like I'd take patients, giving patient care as well as people who just did patient care. I didn't feel like I was doing the basic science as well as the people who spent all their time doing basic science and I didn't feel like I'm raising my kids as well as the stay-at-home mom might be able to raise their kids and the whole thing just didn't seem to me like maybe it was the perfect career for me. And I talked to my father at the time who had a career in academic medicine. He said, "Joan, you know at age 50 is one of the last times you can actually change careers and try something completely new."

So at this time I was starting to get some executive search people talk to me about whether I wanted to look at some jobs in the biotech space. And I had some friends who had left academics to go into biotech and loved it, so I just decided I'm going to take a risk and try something new. I left academics and I went to biotech and I eventually ended up at Novartis where I was in translational medicine when you translate the basic science to the patient.

It was the perfect job for me because I knew the science and I knew the medicine and I wasn't the best at either of those, but I was really good at bridging the two. So I think taking a risk in your career for women and not being afraid to try something new is one piece of advice I would give.

Taren: That's awesome. And it's a calculated risk. It wasn't that you were just going to go hither another. You really looked at where your opportunity was and curved out a new path for yourself. Congratulations! That's wonderful advice. That sounds like a pretty big wow moment. But is there another wow moment that you can identify in your career?

Dr. Mannick: That was my wow moment.

Taren: Yeah. I was going to say. It's a pretty big mike drop, yup.

Dr. Mannick: Yes, I guess I could give that one as my wow moment and then the advice for women I would say be resilient, like don't worry when you hit hurdles just keep – find a way forward because there usually is a way forward and don't take no for an answer.

Taren: I love that. It's been really great speaking with you. I love your story. I love the science you're pursuing and I wish you all the luck in the world. And I hope that we get to meet sometime in person.

Dr. Mannick: Absolutely. Thank you so much.

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