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In this episode Taren Grom, Editor-In-Chief of PharmaVOICE Magazine meets with Andrea Pfeifer, Ph.D. CEO at AC Immune.

Taren: Andrea, welcome to the PharmaVOICE WoW Podcast Program.

Andrea: Thank you.

Taren: You made an amazing leap moving from head of Nestlé’s Global Research in Lausanne, Switzerland to co-founding AC Immune in 2003. Please tell me what led you to form the company and then as a follow up, you really broke a big barrier for women to start a bio pharma company. So let’s start with the first question. What led you to form the company?

Andrea: I think it goes back to my childhood almost where I always felt I have to be an entrepreneur and was quite vocal about this, and actually even when I was working at Nestlé as head of research I was very much interested in innovation and in particular, in the healthcare sector. My approach was always about how can nutrition, for example, improve the well-being of people, how can we prevent diseases. So that was always very important to me.

I was one of the first one looking into positive aspects of coffee on brain function because I felt it has a very important function. The brain is such was something which very much interest me. But the other aspect to being really able to help people to improve their quality of life probably also goes back to my childhood because I had countless chronic diseases, and I felt strongly that I have to use my energy, my knowledge, my interest, my curiosity in bringing something positive to people. So this people aspect and making a sort of better world – and don’t take this in the wrong way – was something which is probably following all my professional life.

Taren: That’s fascinating. So when you were a child and you had this vent to entrepreneurialism, did you have a business as a kid?

Andrea: Well, you would be surprised; I always had a small business actually. Yes, I did, and I sold it because I’m still embarrassed about it – cigars. I’m very much embarrassed about it because later on I worked in lung cancer and this was definitely not compatible. But yes, I did and I sold them for a lot of money.

Taren: I love that. Talk to me about breaking that barrier and being a woman and starting a bio pharma company. There weren't a lot of role models for you.

Andrea: Yeah. And I think you know I have never thought about this I have to admit, but what really opened my eyes in Switzerland was an event, the first meeting of the professor speakers. As you know, I'm also a professor at the local university and there were actually 11 professors and more than I think 300 male professors and to me this was the sort of imbalance and in fact we had a first launch – and I'm saying this because it really is quite important to see the context. We had the first launch and we all sort of exchanged why are we doing what and why are we there, and that we were all different in experience, different in our life, different nationalities, different languages, but we had all one thing in common, and that was we all worked years in America, by and large where you're not asked if you're a woman or a man, we don't worry about it. If you have an idea and you really want to get something done, don't think about it if you're a woman and you are a mother, just have a plan and do it because you believe in yourself.

This experience with these 11 professors that I would never forget in my life really helped me to finally see that there is a difference in culture and that the good thing I had, in fact, extends in America and I never asked this question, I just thought well, I do it and I make it. And that's the attitude which I used actually in my former career also at Nestlé – I never ask a question, you know, why am I doing this? As a woman I just said this is my job and I'm doing it.

I think this is sort of – you can almost call it naïve attitude. I overcame very many hurdles and for me, it was just normality. And of course later on I had to realize that it's absolutely not normal and that what you're doing is potentially special and is sort of helping other women. I was always refusing all of my life in a professional environment to be a role model because of what was not needed. But later on I realize that actually by just showing that a woman, even in a culturally complicated environment, can actually succeed in not only what is even keeping many of the female attitudes, for example, being very interested in shoes and fashion, is not a contradiction. So I do try to keep my female attitude.

Taren: I love that. Yes. Because it shouldn't be a stereotype that all women do is shop, but you can have a fashion sense and still have a very good head for business.

Andrea: Part of it I think you should not as a woman in business become a man, and this is something I really stand for. You should keep your female sensitivity, your female senses and use them as an advantage. And I always believe if you have a mixed population a company and we are, of course, quite female oriented, we are more than 60%, it's very positive for a company.

Taren: I think that we've seen study after study that shows diversity within an organization, especially in those seats of influence is just good for business.

Andrea: Yeah. So to come back to your question, I don't consider that my achievement is special. I do accept that I might inspire this my sort of career many other young women and I'm actually proud of this, if this is the case, and I do support many of our employees to actually just believe in what we're doing and moving forward. And that's all we do and actually, I think we are probably one of the only companies in Switzerland that is 65% women and they're all outstanding in what they're doing. So this is – these are like the few things that I'm proud of, and that's certainly one of them.

Taren: That's wonderful. You started the company just about 15 plus years ago. Has your initial vision for the organization changed or are you holding steady?

Andrea: Nothing has changed in a sense that my primary objective was from the very beginning and has definitely not changed to generate a treatment for Alzheimer's. This was what I wanted to and this is still what I want. I have to admit that I thought it would be easier as an objective and more straightforward, etc. But we did a lot of learnings during the last 15 years and actually probably not so far away even from a treatment, so in that respect that has not changed.

What has changed of course is the large learnings we did in terms of that you have to treat early, that you have to be much more specific when it comes to diagnostics, that you have to potentially do certain of these clinical trials in modifying genetic populations, that you have to add inflammation as a very important part of the causative root of Alzheimer's.

So a lot of these aspects we did not know 15 years ago, and for in particular that you need to use precision medicine probably in the same way as you do it in cancer research is becoming so important. Whenever I'm getting depressed because of some negative study coming out again, I always have this picture in front of me of one of the first mutations specific cancer treatment for breast cancer, which was coming out of the laboratory of Genentech. I always remember when I was a young post working at the National Cancer Institute in Bethesda there I was so disappointed until, in fact, we learned that if you select the breast cancer patients there's a certain mutation – meaning precision medicine – that actually the drug really works. And I think that now translated into where we are, it's certainly one of the big learning in 15 years that you really need to understand what the pathology is in the brain of these Alzheimer's patients and treat them according to their pathology.

Now, in contrast to cancer we're speaking about proteins and in cancer we are speaking about DNA, so that is certainly a big difference. Also to add to the 15 years, the toolbox – meaning that we have now diagnostic means imaging which allows you to look in the brain is something

we created, we added to the field at AC Immune, and I think it might be decisive for finding this treatment which remains our ultimate goal.

Taren: Well, first congratulations on the diagnostic and second, I wish you all the continued success in your development program because as we all know Alzheimer's is just – it's just been fraught with so many trial disappointments as you said, but you're taking a very unusual approach. What led you to look at the pathology of the disease rather than at the amyloids or the Tau protein?

Andrea: This was part of I would say our learning in particular with Genentech collaboration. In fact, one of the best things which could happen to us was this early collaboration agreement with Genentech where we really took a lot of learning on how you approach a complete unmet medical need, how important the science is in that you go really to the basis of the science, so what is really causing the disease, what is the mechanism. So we had the wonderful experience to work with one of the best biotech companies in the world sharing actually the scientific approach and as you probably know, we had outstanding founders. I mean one has a Nobel prize in chemistry, where the second one [inaudible 12:46] prize, the third one many important awards from Harvard. So our scientific founders were top class. But what we added to this was development experience and the clinical experience from a company like Genentech and actually continue, if you look at our company, then the second Genentech and actually we added Janssen, another outstanding company. We added Lilly last year. So we are really working with the best companies in the world all trying to understand the science and to do with development, the clinical development based on this very sound scientific understanding.

And I do believe that what went wrong, if you like, in neuroscience in the past was that this rigorous scientific approach which we had in our team for many years in cancer and that this rigorous approach has to be applied to be successful in neurodegenerative diseases as we were in cancer. And we as a company are certainly applying this rigorous scientific approach to go step by step look into the brain, look at the pathology and create compounds.

I just had a recent learning actually from a person who works for one of our collaboration companies and he actually said the future of drug development is actually not anymore to treat symptoms. What we will have – the first generation was we had small molecules. The second generation was of drug development; we added antibodies and certainly Genentech was one of the leaders. Third is like now where we have small molecules. We have antibodies. We have vaccination. And we are certainly covering all these three areas, but the future is actually that we are treating this disease; we are not treating the symptoms of the disease, we are actually treating the pathology of the disease. And I think probably Alzheimer's is one of the best examples of this future orientation where we really need to treat a pathology before any symptoms, any of just cognitive declines actually happens. So in a way you can say this approach we are taking we are really building or influencing the future of drug development.

Taren: I think that vision is quite inspiring. I don't need to tell you that the past research into Alzheimer's and even dementia has been these solo projects, but it's really taking that collaborative approach as has been done in oncology is the path forward and sharing of data. That's part, I would imagine, is part of the collaboration is right now the companies, the walls are coming down and that you're sharing data amongst each other to show, to see what works and what doesn't work much more to create increased efficiencies?

Andrea: Mm-hmm. In fact, data sharing is, of course, a big question mark in a way because these are very competitive data sets, etc., etc. But I do believe that I think the view of many of the companies, even the big pharma companies, is really changing in our area because we all learned unless we are working together, unless we are sharing this data, we will not be successful as a field. And honestly, we cannot afford as a generation to be not successful because we cannot leave this burden of Alzheimer's on our next generation. We as a generation have to solve it, in my view.

Taren: I completely agree with you. I think you are spot on. The timing of our talk is really timely because June is Alzheimer's and brain awareness month. I understand you're a member of the CEOi Initiative on Alzheimer's disease, and with your company so focused on neurodegenerative disease research my curiosity is what drives your passion around this therapeutic area?

Andrea: Actually, I'm not just with CEOi, I'm even a founding member, if you like.

Taren: Oh!

Andrea: Yes, because when I met the George Vradenburg the first time in Washington and he told me about this initiative. I said 'okay George, I think it's a great idea, but don't make it a national initiative; make it an international initiative. You have my help, but only if it becomes one of the first international initiatives, which are absolutely needed in order to move with the field forward and the fact that it is even having a lot of major annual meeting in Lausanne is not for nothing. It has certainly to do with the first conversation I had with George.

Now in terms of what gives me this unshakeable, unbreakable, I would almost say motivation is simply that I see everyday how many patients, how many families of these patients are affected, how what the impact is on society in terms of paying as much money. I mean the impact we have with this disease costs one trillion today and it will cost us 2 trillion in 2030 is just unimaginable. It's this part, but it is also the part that I believe that we as a company, I as a person, that we can actually do something about it, that we have technology which allow us to make molecules that you can specifically target with proteins. We're speaking about mismodeled proteins in these Alzheimer's patients more specifically than maybe many of our

approaches, and that in fact we have some of the best people working on that and some of the best collaborators working with us in that. So we think besides the motivation, the curiosity, besides this completely unmet medical need, there's also the strong belief that we can make a contribution to that which might change, may be a bit too much – but could change the world. So we really believe in that.

Taren: I think that the work you're doing is so important. At the same time I have to ask how do you keep your teams inspired to keep moving forward in such a difficult therapeutic area because it's hard what you're doing. It's really hard.

Andrea: Yeah. I have to say then Concizumab was discontinued in January, this was very hard for my team and myself obviously because we were so convinced that, we were convinced our original objective was achieved, and then we had to learn that this is not the case and not just for us, but also Aducanumab, which was the second compound also didn't work. So we knew that we have to rethink the whole treatment approach to Alzheimer's and other neurodegenerative diseases and this was, of course, a difficult message.

But I think what helped was that we immediately looked into it. We accepted the data. We looked in to it and we developed a five-point plan – five-point hypothesis, our roadmap as we call it, which is now actually discussed and taken by many of the institutions earlier treatment, working in populations like Down Syndrome which are more genetically defined, precision medicine, so having the diagnostic available, and inflammation – all these five points. And I think our team strongly believed that if anybody can analyze and contribute along these five points, then it's actually our group. And because we have this pipeline and we have these platforms which could really lead to the molecules and the drugs which are needed to test this hypothesis. So immediately with depression – a short depression phase – we accept that we failed, but now what do we do. Obviously you can imagine as a leader, as a CEO, it is extremely important in this space is to show confidence, which I have; I mean it's not that I'm saying this, I believe we can make a difference. But it's important that you show leadership, that you show how you move a company forward, that you give confidence in the people, that your analysis of the situation actually made sense.

In the meantime, our five-point plan has gotten a lot of positive feedback and is almost a sort of framework for the overall field. So we are very happy about that. So anyway, we are beyond that and we are now looking forward to the next milestones and readout, which obviously one of them is Tau.

Taren: I love that, onward and upward. So as you have to inspire your teams and keep them motivated and keep them on the good path, who do you look to for inspiration? Is there anybody you can point to where you draw strength from?

Andrea: Number one, I'm extremely curious in terms of, I mean for me if I have time the biggest pleasure is if I can read a new publication, which shows the aspects of a disease or a new target. For example, one of the most recent publications on Tau being completely correlated with disease progression and the clinical symptoms was one of these highlights of my month where I could finally here is the proof – the Tau, and we have the biggest Tau program, the biggest Tau pipeline, we have invested since 2007 was the right decision.

So this sort of scientific inspiration is very strong. But there's also one event which I will never forget in my whole life, and this was then I think it's now quite a few years ago when I went to South Africa and I met actually Nelson Mandela and I had the chance to talk to him and to speak to him about my work. Very proudly, by the way, I told him about Alzheimer's and all the rest of it and he looked at me, he was very quiet and he said, "You know, I did something for my country and I'm very proud that I've changed many things in my country, but you are doing something for the world." I almost had tears.

I went home, the next day I organized a meeting with all my staff. I told them about my experience and I said, "You know what, this is exactly how you should see it and by the way, we will go – and this is where a common saying actually in AC Immune – we will go to the moon. We will make it to the moon and our moon is, of course, to have a treatment for Alzheimer's. At the moment, I would say it's probably Mars because it's so difficult, but this event is something which influenced the company and myself.

Taren: One of the questions that I always ask during our WoW podcast series is to identify a wow moment in your career. I would think that is one of your wow moments.

Andrea: It was. It was. It certainly was. And something you never forget.

Taren: I have chills. That's amazing. You have garnered a lot of awards. You've been recognized in 2009 as a technology pioneer by the WEF and Swiss Entrepreneur of the Year by Ernst & Young. You won the bio ops prize in 2013. You were named as one of the top 10 women of biotech by FierceBiotech and one of the 300 most influential personalities in Switzerland. What do these accolades mean to you?

Andrea: Well, it's a nice recognition for your work. Whenever I get such a prize, I always take it back to my people because it's not me, it's not my work; it's actually their work. It's very important that this is a shared recognition. But for me, what is probably one of the events, which you didn't mention by the way, was very important to me and this was this year when we took Alzheimer's the first time to the World Economic Forum in Davos. We were fighting, I would say, probably for 10 years to bring this subject to Davos because we felt it's something which is of interest in the world, the society as a whole and we succeeded. I'm not sure if you had a chance to look at this session which we had in Davos; it was very important, very much

appreciated. There's many, many, many questions by the people, and as you know we're all in very important functions, but it really came down to the fact well what does this disease mean for the world, for the society, for the economy of the world and for myself.

And many of the questions we got in this session was actually about themselves, because each of the people – no matter politician, queen, we had all of them – was actually that they had a family member with this disease and that it really had an impact on them.

So for me, it was bringing this to the world, making the world aware of the problem of 150 million people very soon, 50 million people now, every three seconds a new Alzheimer's or a new dementia patient – all of these numbers are very important to the awareness and actually these governments whoever is in a position to move something – entrepreneurs, people who can donate money to research – to actually make them aware that we have a real problem and that we have to work altogether in order to find the solution for this generation, not for the next one, but for our generation.

Taren: Again, I'm blown away by your passion around this and by your dedication to this disease that is, as you say, is so devastating to so, so many people. We know – I talk to a lot of CEOs and I ask the same question – what are some of your biggest challenges in leading a company, aside from the development issues and looking at drugs and bringing them to market, but other than that, what is your biggest challenge as a CEO and then finally I'm going to ask you how you define success for yourself.

Andrea: That's a good question. Success would be I think that's the latter, to have a drug for Alzheimer's, and that's the only success I would accept. So anyway, we'll see if we will succeed with that one.

What I would say is a big challenge as a CEO today of this company listed on NASDAQ – and I'm using my words here very carefully – it, of course, is that it's much harder to run a company out of Switzerland which is NASDAQ quoted because you have to do a lot of communication about the company. You have to be all the time present in America to speak to investors on a continuous basis. So there's a lot of travel involved and a lot of absences in the company. So to really balance this communication invested, the external part is your internal responsibility making sure that the milestones are achieved, that people get right input, that they're motivated, that they're happy. I would say that the most important task of a CEO is to make sure that the people in the company are happy because if they're happy, the rest will come by itself.

So to have enough time to generate this happiness is a challenge. So I think the timing, balancing the time for all the different tasks of the CEO is probably one of the biggest challenge.

Taren: You know I said that was going to be my final question, but I do know that you also co-founded the Nestlé Venture Capital. How does that help you with your financial responsibilities with the company? Does it give you the particular insights?

Andrea: We were two people, so we were co-founding this venture at Nestlé was an internal fund. Again, we were speaking about entrepreneurship so I was definitely one of these internal entrepreneurs. I just felt as head of research that you have to do in the food industry also R&D differently. You have to look more in innovation. For me, this venture fund was a vehicle, if you like, to tap in more and more rapidly into innovation in the food industry. So that my motivation came really from that.

But what it certainly helped me is to build the investor network, which was very important for the foundation of AC Immune, to understand how investors actually think and what we are looking for. So the whole aspect of how investors look at their company, look at people, what is important to them, I definitely took back from this venture experience. Obviously, that science has a value, has a price tag which sometimes when you are doing internal R&D you miss, you don't realize.

So for me, first of all, and actually having the confidence honestly also to say okay, as a quite senior executive in a company – in a big company – would I be able to be a CEO and would I have all the different experiences which you actually need to be a successful CEO and it was one of them, which I think is important when you do fundraising. So I think all of that, the whole financial aspect, the whole business aspect was really supported by this experience.

Taren: Andrea, I can't thank you enough for spending some time with me today and talking about your vision for the future of treating Alzheimer's. I wish you continued success, and I am really inspired by the work you're doing. So thank you so much.

Andrea: Thank you very much for your questions. I really appreciated that.

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