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In this episode, Taren meets with Dr. Lan Huang, cofounder, chairman and chief executive officer BeyondSpring.

Taren: Lan, welcome to the pharmaVOICE WoW podcast program.

Lan: Thank you for the opportunity.

Taren: It's our pleasure to have you. I understand that you have more than a decade of entrepreneurial experience in both the Chinese and US biotechnology industries. I'd love to know what sparked your interest in the field.

Lan: Thanks for this great question. As you know, I'm a scientist turned entrepreneur, so my true passion is to bring scientific discoveries to become medicine and to help patients globally. So that sparked my interest to do what I do, and especially with my background as a Chinese, and also trained in the US, I think is just a perfect union to integrate US and China clinical resources and also pharmaceutical market together so we can develop a more cost and time efficient business model for innovative drug development.

Taren: With your background, you could have worked with any number of established companies. What gave you that entrepreneurial bug?

Lan: Well, I'm Chinese, so I think a lot of Chinese people do have entrepreneurial bug. But I think when I was finishing my research fellow at Memorial Sloan Kettering Cancer Center, at that time I was debating what to do with my training. I had my science article when I was in the first year at Memorial, so it really gave me a taste of being validated in the science field, but with that great paper and also drive me to think how to use the discovery to develop medicine and help patients. And I thought as a scientist I might be able to do it on my own – and that basically drives me; and definitely you would think I could go to a pharmaceutical company to do that, but we thought at that time, when you go to a pharmaceutical company, you start in very granular details, not so much more take the mission into your hands and then do it yourself kind of view.

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Also at that time in 2001, China got into WTO, so we thought with that, China will be opening up and then welcoming a lot of innovation and also broadening its market. So as a Chinese, I thought, it's a perfect time for me to integrate China into the global drug development; again, taking things into my own hands. So that basically taught me to start as an entrepreneur. So it's almost 20 years of journey.

Taren: That's fascinating. And the first company you started was a CRO. Correct?

Lan: That's probably not my first – probably the second. The CRO company – as you see, I was trained as a scientist, so I really need to learn by doing as an entrepreneur on the business world how to do business. So I had a few bricks] to lead me there. So one is the WuXi Company, which is an R&D company that trains me how to do innovative R&D, and then the CRO company which I started in China, it's to integrate China clinical resources and to do clinical trials in China for major companies according to US GDP. So basically it trains me how to collect quality data from China.

So both of these innovation company, R&D company and this CRO company, they were the building blocks for me and which I translate that experience into founding BeyondSpring, which is innovative but also uses a lot of China clinical resources so we can conduct trials much faster and cheaper.

Taren: Excellent. Talk to me about what BeyondSpring is doing. I think it's a fascinating area that you're getting into.

Lan: So BeyondSpring is a pharmaceutical company currently developing innovative oncology drugs, and our drugs currently – the lead compound is already in global phase 3 trial. So Plinabulin is an immuno-oncology agent, and currently is in two global phase 3 trials, one in the non-small cell lung cancer, another is in the prevention of chemotherapy induced neutropenia – both very large market. Also, we can help many, many cancer patients. Plinabulin actually is the first in class agent and we actually are developing it ourselves. So it's really the driving force of the value now, and then we'll also have other additional pipelines, which will create more value for the company.

Taren: Also in the oncology space, or will you be looking at other therapeutic categories?

Lan: Our company is focused on the oncology field, because as you see from my training background, my PhD from Berkeley is in the KRAS and downstream factor structures; and then at Memorial, of course, it's very much focused on cancer. So that's my field of expertise. So we

are focusing on cancer, but we do have a platform, which is called ubiquitination degradation platform, and that actually won Nobel Prize in 2004 and we are using that field not only to work on the oncology treatment, but also potentially can also be applied in other treatment areas, such as diabetes or Alzheimer's disease or those areas. But the current focus is definitely on oncology.

Taren: That's exciting. So let's talk about some of the science that's happening right now. What excites you about some of these breakthroughs that we're seeing?

Lan: I think for from an oncology point of view, I definitely am very excited about the IO field because I think it has such an evolution of cancer treatment. Now using your own body, the immune system to fight cancer, that's just the ultimate. But I think currently, the IO field still needs more improvement because even for the second line non-small cell lung cancer, the response rate is still only less than 20%. So there's still 80% of patients who need additional help.

So actually from Plinabulin, all of these assets – this first in class asset point of view, we could actually add to the PD-1 and other probably combining with additional chemo, triple combo could have even better efficacy in the field. So definitely IO field is what I'm fascinated with, and this gives a lot of potential and also help for cancer patients.

Taren: Wonderful. I have to ask about the name of BeyondSpring. Why did you name your company that?

Lan: Okay, thanks for this great question. So the BeyondSpring basically means beyond seasons and beyond borders. So as you see with our company's business model, we are integrating US and China clinical resources together, and we are also speedily using this business model to get to the NDA. So the main use is beyond borders is to integrate US and China together. And secondly, beyond seasons is to go directly from the sowing and hope season of spring, and quickly and directly into the harvest season of autumn.

Taren: Oh, that's a wonderful story. Thank you. Speaking of the US and Chinese duality of your company, I have to imagine that those two different cultures have to really impact some of your strategies and your vision for the company. How are you melding those two very distinct cultures?

Lan: As you see, I am Chinese, but I was educated in the US. So myself can deal with both cultures. They are very distinct. I think US culture is more diplomatic, and China is probably more from top down rather than bottom up. So they are very different, but I think drug

development and with a mission actually integrates all of our people together and also the company culture because we do have a goal to get to the end of the tunnel, which is to bring this drug to the market not only in China, but also in the US. So that goal actually is integrating both cultures and both people. And then also, our people in the US – of course, they were only educated in the US; but in China, we also have team members who have worked for multinational companies in China. So they also are very familiar with this diplomatic and also integrated research model. And that's how I integrate them together.

Taren: Fascinating. And not only that, but you're having to deal with multiple time zones and a global R&D project. That's going to be challenging just on the face of it.

Lan: Yes. So my call starts at 8 o'clock in the morning, goes all the way to 9 or 10 in the night, and a lot of other people also do that. So it's almost like our company is running 24/7 because China and the US is just exactly 12-hour difference. All of our people I am so honored and the privilege to work with our excellent team. Everybody has this mission to bring this innovative and transforming medicine for patients, and they're all armed with a tremendous amount of experiences. So we have this drive to improve this drug to the end and in that sense, working hard is working hard, but working happily with the people who have the same drive and same vision is a godsend.

Taren: That's awesome. And so I heard you correctly, yes, you want to bring the drug to commercialization under BeyondSpring's umbrella?

Lan: So we are developing our company from R&D to R&DC, and we have had new people joining our team, including Mr. Richard Daly. So he actually had launched over 10 drugs globally and was the 14th employee for Takeda and have brought it to a few thousand people and to \$7 billion revenue. So we do have people who can do the commercialization.

Currently, we are also talking to global pharma, so this way, we might also be able to do this with them. So we are balancing those partnerships and also our contribution to this commercial landscape in the future.

Taren: Got it. That's fantastic. Well, I wish you a lot of success. So talk to me about some of the things you're doing that are a little bit different in terms of your R&D. Operating with a footprint in two different countries, no less two different continents, you have to have figured out some new processes in order to create some efficiencies. What are some of the things that you're doing?

Lan: Okay, so you see that our US headquarters are in New York and then China is in Dalian; and we actually have different focuses for our two geographic location operations. So in the US, it's very much the brain of the company. So all of the research development plans and protocols and regulatory filings, they all actually come from US first. So usually we get US FDA approval for our phase 3 protocol first, and then later we translate that into Chinese and then get this approved in China.

So Chinese operation actually, for us is very much like operation hand of the company because there are so many cancer patients in China so that gives us a lot of clinical resources. So for global trials, we go globally, and then certain amount of the patients actually come from China. So China is very much spearheading in the operation and also execution of our strategies from the US.

And in addition from a manufacturing point of view, we do outsource. So we do have manufacturing outsource in the US and also the global market in the future. We also have outsourced in China manufacturing facilities, and then later it can be also supplying for the China market, and there's also cost benefit in that and also this take away all the potential issues of tariffs and other geographic conflicts. That's how we planned it.

Taren: You are very smart, the times we live in, right? I want to talk about some of the duality in your persona. You are educated in the US, but you are Chinese. How does that influence your leadership style? You said earlier that in America, we're a little bit more diplomatic and in Chinese it's from the top down. So how does that impact you and how you lead your teams?

Lan: Actually, for me I lead my team because I am a woman... I'm a woman scientist, so that seems to be my trademark. I think I lead my team by integrate. So actually, my leadership is very much diplomatic because all of our C-level people, they came from large pharma. They have plenty of experiences with 30 NDA approved globally, with 10 drug global sales to the tune of \$2 billion. So they are very, very experienced. So all of them are very visionary and also have the same vision to have the best channel for Plinabulin to go to the market. So I listened to them, and everybody has the best intention, but I integrate all of their ideas and then find the most efficient and effective way for Plinabulin in development and also the company's pipeline future growth. So I do the integration because I think as a woman, we usually like to take a lot of advices and then digest them and synthesize them and then get the most efficient product.

But secondly as a scientist, I think it's data driven. So in the end, everybody is putting their contributions and thoughts, but in the end, I have to look at the data as a scientist thinking about this logically and get to the right conclusion. And with that, everybody respects this

conclusion because it is based on data. So that's my leadership – as a woman, as a scientist. So integration and data driven.

Taren: That's fantastic. How did you assemble this superstar team of individuals in the C-suite that have gotten so many NDAs to market? What was your secret sauce?

Lan: I said build it one by one. So they came actually in sequence, not at the same time. So first is, because Plinabulin actually we acquired this from R&D company in San Diego. The old company is called Nereus – it basically means god from the sea. And then with acquiring of the asset, we also acquired the talent. So Dr. Ken Lloyd, he actually was the CSO from Nereus, and he really loves Plinabulin, so he came with Plinabulin. And Dr. Lloyd actually was the head of R&D for a while in UK before he had brought six innovative drugs to the market under his belt. So that's first one.

The second one is Dr. Gordon Schooley. He is our head of regulatory. He actually brought 19 drugs to the global market. He really wants Plinabulin to be his 20th baby. So same vision and same drive. So he came in because at that time in 2013, we want to bring Plinabulin in the global trials, and he is spearheading in our discussion with the US FDA on the protocols for the phase 3.

And then later we brought in Dr. Ramon Mohanlal, who is our chief medical officer. He was the clinical head of Novartis in the oncology products before he worked at GSK, Vertex, and some other major innovative companies. He had five drugs under his belt, and he actually was trained in immunology at GSK and also oncology in Vertex and also Novartis. So his background is very helpful for bringing Plinabulin as an IO agent to the cancer treatment market. So he came in to really get all our clinical development protocol down and also get the two indications started.

And then later, we brought in Mr. Rich Daly, who is our COO, and also, he has this extensive experience in the marketing side and also in company alliance management, and that just complete the whole realm. So we went from R&D to R&D and C, which is R&D and the commercial.

So I filled them one by one because I think the company grows, it has an evolving growth. It's initially in the research and development, and understanding the mechanism that the science is very important, and then later after we understand the mechanisms, then we need to develop the protocols to target the targeted population, and that's why the clinical people, regulatory people come; and then later when we already understand the profile and then the stage of clinical development, then the commercial person has to come to get the company commercial ready. So that's the evolving process, and I think it's a logical way of building the C-level team.

Taren: Logical and impressive. Congratulations. You alluded earlier that you're a woman scientist, but you're also one of the few founders, chairs and CEOs of a biotech company, who also happens to be a woman. What are some of the lessons you've learned along the way in having to navigate this biotech space? Because it's not easy when there aren't a lot of other women who have paved the way.

Lan: I think for me as a woman, and a professional woman, and also a mother and a wife, I think it's the best time for us to shine in this world because we get so much equality now, and people do treasure and trust women as a force to bring change to the society and bring transforming medicine to patients. Harvard has a woman president and UPenn has a woman president and there are many prime ministers who are women, right? So I think we are very lucky to be living in this time. So that's a given because we cannot achieve what we have achieved if the society is not ready for a woman like in the 1930s. So that's the backdrop.

Secondly, I think, for me, my mother was an architect by training, so she always worked. Growing up, I always felt a woman should be excelling in a professional life and also can be a mother – a good mother and a good wife. So I never had this impediment that, 'oh, you cannot have it all.' But I think that we can have it all but at different times. Different time you have different focus. So I have never set boundaries for myself, and I think I contribute anything which wasn't satisfied into be a process in the growing and then learn from my mistakes or from my growing pains. And with all of that, I got my PhD when I was 27 years old from UC Berkeley, and the chemistry department is number one chemistry department in the world. So I did it in four and a half years, and usually it costs seven years there.

Taren: Wow.

Lan: I actually received this big award from the International Women's Association called the Soroptimist International Women's Organization, Graduating PhD Woman Award. So I was the only PhD woman from Berkeley to get this award. At the interview from these 10 brilliant women, they asked me, "Do you ever see prejudice against you?" I said no. So I think I never see prejudice, and I really think if a woman can do your best and work very hard, and then you will shine through; and if you are doing the right thing and also work hard, there will be people who will help you to achieve this mission.

So I always have this mantra that working hard, doing the right thing, and your goal will be achieved. I think for the other women should do the same like what this article about is just don't set boundaries for yourself. You have to set a goal and work hard to achieve it.

Taren: I think it's amazing advice, so thank you so much. Lan, talk to me about what drives you everyday.

Lan: Well, thanks for this great question. So what drives me every day is from my childhood, my grandpa died of cancer and as I just said before, every cancer patient is like my family members. So every day I'm fighting to bring innovative drug to the market so I can help them. That's number one, from my early childhood.

Another one is from my own son, because my son actually donates to send to Children's Hospital every year, and he understands that mother has to travel to China very often to treat and help cancer patients. So he's very supportive of this mission. And he wrote in his book that if I can read it to you, he said, "My mom is a scientist trying to find a cure with cancer. I would like God to fulfill this and help my mom with finding a cure for cancer. And this is important to me because this would help millions of people and would make my mom and her company succeed in life." So that's my drive, because not only my grandpa is my mission statement to help, but also my son as a young child is already instilling in himself to help mommy and then to help patients globally. So that's my drive every day.

Taren: That's amazing. Thank you for sharing that very personal story. I had chills. I got goose bumps. What an amazing young man you're raising.

Lan: Thank you. Yeah, I think that's why we are role models for our children, and we want them to bring kindness and help to the world as well and following our footsteps.

Taren: Let's talk about how you define success for yourself. It is working hard. It is doing the right thing. But to you, what does success mean?

Lan: Well, success for me is of course, there's a professional success and there's also personal success. So for me, professional success is also very personal because actually, when I was nine years old, my grandpa who had raised me died of cancer. So from there on, in my little heart, I always wanted to do cancer research because I want to develop medicine for other cancer patients. They are like my family member, they're like my grandpa. So that's why success for me is to bring transforming medicine to cancer patients globally, and they are like my family members.

Taren: That's an amazing story. In that same light, R&D is fraught with pitfalls. So how do you overcome those obstacles and then pick yourself back up again and lead that team because it's difficult?

Lan: Yes, that's true, it's difficult. But it all comes down to your vision, right? And also data driven. First is we're doing the right thing. We are bringing transforming medicine to patients. That's the goal everybody believes in. So that's where we want to get to. So when there is difficulty, the goal doesn't change; you still have to go there.

And number two is, where you have difficulty, you look at the data. As a scientist, if the data shows that actually it's working, you're probably just a little bit here, there, you have to fix it and certain things which can be fixed, probably not... it's not a scientific risk. If it's operational risk, then we'll just get together and isolate the problem and fix the little problems, and then you move on to the next level. When I see obstacles, I'm systematically dissecting them into problems, little problems, who can solve; and then when you solve the little problems, the big problem is solved.

Taren: That's wonderful. Finally, with all the success you've had in your career and your life, can you name and identify one wow moment of your career so far?

Lan: I think the wow moment is like a building block for me to achieve all the goals and to make who I am today. So I think probably in my life, if I can identify three wow moments to get to where I am, number one is to get a PhD at 27 years old and also receiving this Graduating PhD Woman Award. I think that, for me, is a good validation point for the hard work I did.

And then number two is I was in one year as a research fellow at Memorial Sloan Kettering Cancer Center. I solved the first E2E3 ligase structure in the world, which was accepted in *Science* within one month of submission. It's a science article and I think that's another gratifying moment to show that actually I have certain skills as a scientist.

Number three is I received in 2009 the Thousand Talents Innovator Award from the Chinese President in China. And then that, I think, is a validation for me as an entrepreneur.

So those are the three wow moments of my life, and I think all of this will build up to the future which I aspire to have the wow moment is to bring Plinabulin to the market which can help many cancer patients.

Taren: All I can say is wow, wow, wow and wow. Amazing conversation. Thank you so much for sharing your story, and I look forward to seeing what happens with Plinabulin as we go forward. So good luck in your venture.

Lan: Thank you so much.



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