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In this episode Taren Grom, editor-in-chief of PharmaVOICE Magazine meets with Paula Ragan, Ph.D., CEO of X4 Pharmaceuticals.

Taren: Dr. Ragan, welcome to the PharmaVOICE WoW podcast program.

Dr. Ragan: Thank you very much. It's wonderful to be here and I appreciate the chance to connect with you, Taren, and all of your listeners.

Taren: It's our pleasure. I am really intrigued. You made a big bold leap to found X4 Pharmaceuticals five years ago. I have to know, what were some of the key drivers that led you to found a company, especially in this space?

Dr. Ragan: I think it's a combination of a few factors. I think, first, intrinsically I've always been someone who's wanted to create and build something that could help a patient. As far back as seventh grade I can remember seeing the cover of a *Scientific American* magazine with a prosthesis, and it struck my cord of like wow, you can build something to try to make someone whole again. It's been kind of a lifelong journey since then just intrinsically.

And then I think my career intersections, I was so fortunate to connect with different companies and people within those companies who are so innovative and patient-focused. Probably one of the major imprints for me was my time at Genzyme – every single person there, the culture there was really always putting the patient first, and that was certainly driven by Henri Termeer. He was a true gift to the industry, and a visionary, and always anchoring to that point. I think his comment was always good medicine is good business. Everyone I think was very focused on bringing good medicine to patients.

A second person that I have been very fortunate to intersect with my life is Mike Bonney from Cubist. Again, he's been part of the X4 journey actually as of about five years ago and he's just been a very active and phenomenal mentor, and also a different, I think, type of role model for me in terms of company builder and what he did with Cubist.

I'm just grateful for that intersection as kind of my own intrinsic profiles with intersecting with some great people who built truly meaningful companies and products for patients.

Taren: That's wonderful. We're going to get back to your Genzyme days a little bit later in the podcast because I do want to talk to you about the influence that Henri Termeer had on you.

The name of the company X4 is also very interesting. Tell me about the name and how does it tie into the company?

Dr. Ragan: Again, there's a little bit of a twofold flavor to this; the receptor that our drug targets inside the body is called CXCR4. In the lab people would use slang as they called it X4, so they didn't have to use a mouthful when they were referring to the biology.

And then frankly, the flipside of that is I'm a bit of a superhero nerd. The X-Men in particular is kind of a cool group of misfits that make a difference in the world.

For me it was slightly both between X4 is the biology underpinnings, and then the slight kindred spirits to the X-Men superhero vein is sort of the Venn diagram of where it all came together.

Taren: I agree, it's cool. Congratulations, that's a good branding element. The company's focus is on oncology, and I'd like to talk to you about what sets your science apart in that therapeutic category.

Dr. Ragan: Again, it all comes back to what we believe is the underlying drive to cancers and our target has certainly been well-documented in a number of cancers that we think can really make a difference. I'll highlight a little bit of history and then forward looking.

We have our own studies that have shown that our drug increases the trafficking of the right immune cells so that your body can fight cancer. And then very specifically as we move forward there's an unfortunate type of lymphoma where R-receptor is mutated, so it's turned on. The lymphoma is called Waldenström's and it's well-documented that unfortunately people who have a mutation R-receptor have a much more resistant form of lymphoma.

We're really looking forward to marrying the drug and the driving mechanism that's causing the problem and bringing something that actually can stop that progression and we always will for cures, certainly we'll be aiming for that, but we certainly hope we can get as close as possible to make a meaningful difference in these patients lives.

Taren: I wish you all the success because we certainly are in need of something. Going back to the starting of the company, it's certainly not for the faint of heart. And I love your story about how it goes back to your childhood. But what were some of the biggest challenges you faced in launching the company?

Dr. Ragan: Think about successful launches, and I'll be transparent in my own gaps. But you need capital investors because it's a risky business. You want the right group of investors. You

want the right group of board and advisers, and then you want the right management team experiences.

I think I brought two of those three pieces; I think myself and then the network that I had we could start the company off with a strong management footprint. The network of individuals that we created with our initial board was very strong. And then the capital piece was tricky. At least in the Boston area there's a lot of homegrown company initiation, so the Third Rocks or the Atlases would like to grow from within, and that's just their business model.

I think perhaps the hardest was just breaking in a little bit to the investor world because they have their own sort of approaches. That was one of the trickier things. But we were very fortunate to have raised about \$75 million in two private rounds and bring in some very reputable investors in that story but it certainly wasn't easy.

Actually one of our current investors is OrbiMed and Carl Gordon is a well-known investor, and it actually made me feel a lot better because raising money is hard. Just to hear that come out of his mouth as someone as profoundly successful just to acknowledge it is a difficult process and investors have a high bar that they need to meet. And then as the portfolio companies that were all vying for that position is difficult as well. It's always a tough journey, but we're thankful for the successes we've had so far.

Taren: Congratulations. I was thinking that Boston Cambridge area that there are some advantages as well as disadvantages to be in that locale. There's a certain level of energy and buzz around transformative science, but at the same time you all are competing for the same capital.

Dr. Ragan: Absolutely, capital and people. It's just incredibly competitive. But again, I think in a good way I'm a big fan of competition helps elevate. You want to elevate people through striving, through connections. I do think I am an intrinsically competitive person. I make fun of myself to a point, but I think that makes you strive to always try to want to win. And for me it's winning for the patient, so it's a nice kind of marriage of my internal burn.

I think in this entire ecosystem in Cambridge there's a lot of people with that same profile. It's a fun chess game that we're all playing and trying to attract the right investors, the right people, and playing for the long game to win for those patients. It's an awesome place to be.

Taren: That's great. You touched on a piece about your network, and especially speaking with women it's more difficult for women to build that strategic network than it is for men for whatever reason. How did you go about building your network that set you up for success?

Dr. Ragan: My mantra was I literally talked to every single person that every single person ever recommended that I talk to. That funny commercial from – and I’ll be dating myself, but the 70’s or 80’s – and it’s like...

Taren: The Breck commercial?

Dr. Ragan: ... and they told two friends, and they told two friends. First of all, at Genzyme I was very, very fortunate to kind of have that as an anchor to my network. My time there I do think this is where when I’m trying to coach people through their own careers, I think having some portion of your career in one of these larger biotechs is incredibly valuable because it has such intrinsic population of very talented people that you then naturally touch with through business interactions and they get to know you and what you bring to the table, you get to know them and what they bring to the table. You do build bonding relationships through shared experiences, and that almost becomes an intrinsic platform for your network.

And then from that platform, when I left Genzyme I used that network. And then hopefully the mutual respect that we had for each other to then enable them to feel comfortable to introduce me to even a broader set of network.

I’ll give you one great example. When I was at Genzyme I had a wonderful HR business partner. Again, not high up in the organization at all but she was phenomenal support to me. I really enjoyed her support for my team in particular during supply crisis. She left and went to Cubist, and she introduced me to the VP of HR at Cubist who then introduced me to Mike Bonney. Again, anybody who was gracious enough to spend their time with me facilitated the journey forward, and so I would really encourage people to try to... Women or men, I do think it’s that shared experience that forms the bond and mutual respect. And then don’t be afraid once you leave to try to rely on those. I think that’s actually...

Again, I don’t know if it’s men or women thing, but people tend to almost feel shy about it. But I think we want to do the best for patients in supporting innovation and exploration, whether it’s human exploration or a product exploration is I think what is in the profile of most people in Cambridge and they’re very generous with their time and support for that.

Taren: I think that’s great advice, talk to anybody who will talk to you. I think you’re right, it’s that respect piece that goes a long way. You mentioned something that dated you, but my mother always said ‘don’t ever burn a bridge because you never know when you’re going to have to cross it.’

Dr. Ragan: I always try to say thank you in both directions, letting the person who facilitated the conversation know, like ‘thank you, this was helpful to me,’ because it gives people feedback to keep doing it. I think people do want to be helpful. And then of course to thank forward to the

new person that I did meet who then helped create a new set of connectivity with others. So it's important.

And it's a silly thing, but I think it's just a human element that sometimes we're so busy we just forget to say 'hey, that was really helpful. Thank you.' I try to be really mindful of that, even in my own family.

Taren: That's really sound advice, so thank you for reinforcing that. Before we get to Genzyme I'd like to hear a little bit more about what are some of your shorter term and longer term goals for the company? Where do you see yourself in five years with the organization?

Dr. Ragan: In five years I expect that we'll be a global commercial organization, hopefully serving our patients and improving their lives through the approval of our first indication, again, hopeful for the treatment of this very rare form of immunodeficiency.

I actually hope, certainly in five years there's actually one or two additional wins that we'll have for broader patient populations, so to serve a broader footprint of patients with different forms of immunodeficiency.

And then I mentioned this interesting form of lymphoma that unfortunately is so heavily driven by our target. Within that five year scope we have that potential to be treating a very broad swath of patients, and I hope we get to all of them. I really do. That would be an absolute dream come true for me personally. And certainly I hope it helps with the dreams of some of these patients that have these diseases.

That would absolutely be my long-term vision as a global commercial organization where we are able to directly market and sell our products into the different communities that need it across the world.

Taren: Fantastic. Let's go to Genzyme. You mentioned your time there. How did your leadership role there help prepare you to lead X4? You touched on it a little bit ago about making connections and those relationships. But what other skills did you develop at Genzyme that put you in a position to be a leader for X4?

Dr. Ragan: I think Genzyme did a great job at helping people get exposure across different aspects of the business, which I do think is really important. One of my views as a successful leader is that you can empathize and perhaps have some glimpse into walking a mile in the other person's shoes because I think again, a shared respect for what people are going through can help always through the both the ups and down times as a leader.

For me, I was really fortunate to have a couple of different roles there which helped me appreciate the miles that people were walking. I spent some time in corporate development,

which is a role that really needs to integrate with the functional experts across the entire organization to really help assess whether or not any particular deal was appropriate to build a business. At least I think the way that the team there mentored me and helped me grow as a professional is you really need to feel like you own this yourself. The risk assessment, the understanding of the opportunities across all these different functions, you need to own that. You can't just rely on someone else's commentary, but to be that close to them that you're in-sync with them.

I just had this great opportunity to partner very closely with experts and understand what experiences they could use to help de-risk and build that product to move forward or the different targets we were after.

Then on the flipside, I also had the opportunity that's a complete inverse opportunity where I was in manufacturing and supply chain during supply crisis. It was very operational and it was very quantitative. Like we need to get this amount of medicine out the door today because these patients are waiting for it and pick a country. So I loved that aspect of the business because I like to have my own scorecard and see if we're winning or if we need to kind of apply some – do we need new positions or new resources to try to tip the scales in a more winning direction. And so I love that aspect of that.

Because for me as a leader I do think we need to be accountable. We need to think about what does good look like, how far are we away from it, and what can we do to invest, whether it's in our people, our vendors, our culture, you name it. We need to kind of know what good looks like and always be steering the ship towards that and in manufacturing, I have a profound respect; it's such an amalgamated and challenging effort to produce a medicine. I really am thankful for that very different experience, which again, I think helps round me out as a leader and prepare me as best possible. And I don't think anything fully prepares you to be a CEO, period, until you're in the hot seat. But I think it gave me the confidence to move forward.

Taren: Now that you are in the hot seat analogy and we know that drug development, especially in the area that you are addressing, is just fraught with disappointment a lot of times. There's just clinical trials that don't work the way you thought they were, the molecule or the biologic doesn't work out right. It's tough to keep your team uplifted all the time. How do you inspire your team through some of those downturns?

Dr. Ragan: We do have down days. I think acknowledging them and not pretending they don't exist, like we're all human beings. Absolutely you need to acknowledge the feelings of disappointments, of wishing something were otherwise. And actually it's always founded. We're disappointed for the patients. That's the culture here where we all want to win.

And so for me, it's just trying to absorb it and share it, because I think, again, sharing the burden is a way of working through it. And then frankly, tomorrow is a new day. We always learn from

self-examination of our products, of our approaches, and then we can then see where we can build.

Sometimes you truly can't build. And again, there are products in our industry that have failed because of safety. You've done the right thing, you've learned the right information, and you move on from that knowing that you've done the right things and you stopped that.

Or in our case we're learning mechanistically. Going from animals to human is a huge jump, so you're starting to learn mechanistically in humans this is better, where we should play better, and some of that is our cancer story where we keep on narrowing as we learn our disease what is the kind of highest probability of success for our first cancer patients, and that's where we've evolved and learned even in cancer about how to better target the right patient population. It's always a blend.

There are the down days being there to support them, and then at the right moment when people feel like they've kind of worked through that first wave, kind of turn it into how do we build off of this in a positive way, learn from it and think about our next set of patients, because unfortunately there's always another set of patients that need to be helped and addressed, and that's who we have to kind of re-focus on.

Taren: That's fantastic. Let's switch it around; how do you all celebrate your successes?

Dr. Ragan: That is so great. It's funny – and again, this group of people where they're like, 'yay, we're successful today. Okay, back to work. We've got work to do.' We're actually trying to get better at being celebratory. But we've definitely started to get in that direction. We certainly acknowledge individuals on a company wide perspective; we actually try to give folks some extra time off for their families as a company.

I'm a big fan of the way to honor people and their success is to give them a little bit more breathing room to enjoy broader things in life. I think that's what we've learned is a good way of recognizing corporate success here.

And then there's the fun stuff. We have a group of people in the company – they're called The Ambassadors. This is an organically-driven group of people who have come together to have the Cinco de Mayo party, or on Valentine's Day they put together a Valentine's Day playlist that we all got, with little Valentines like that. I loved it. It made me feel loved. When was the last time I got a Valentine other than something from my family. It was just a really uplifting, positive, kind of the little things that keep us feeling connected and I think happy in our daily lives. Halloween is also a big one here, believe it or not. We are all competitive Halloween costume folks. If you're in the area, you should stop by at Halloween and we'll see how that goes.

Taren: Don't leave me hanging. What were you last year for Halloween?

Dr. Ragan: Last year I was the bride of Frankenstein. Again, my husband and I often do couples costumes, so he was Frankenstein.

Taren: That's great. I think it's important to have those kind of light moments because what you're doing is such serious business. You are literally looking to cure cancer. You need to have some of those moments of levity.

Dr. Ragan: Absolutely, absolutely.

Taren: I was looking at – obviously in preparation – looking at your website, and I have to say, and you can say no this is not... two-thirds of your management team is women. Was that purposeful?

Dr. Ragan: We hired the best talents that we are fortunate enough to attract, and that's where our management team has shaken out. I am sure there's an element of people being inspired by folks they feel connected to. That's always the case no matter where you go, feeling included and maybe again the concept of shared experiences. I have a family. I have two young girls. I think in general women historically have had a longer road to figure out what's the right workplace balance for them period as kind of a gender.

I just think it's a bit of a symbiotic situation in terms of trying to lead by example give people the right career opportunities. The talent at this company is amazing and the culture is amazing.

My biggest fear is we're going to be continuing to upsize the company and we hope that we can keep up with this ability to attract the right talent and diversity and commitment. Because really at the end of the day that's what it's all about, is being committed to our patients.

Taren: That's great. Because you do know whether or not, you are a role model sitting there as a CEO and president of a biotech biopharma company. Because there just aren't that many women who sit in those seats of influence. Do you stop to ever consider that you are a role model?

Dr. Ragan: I do, absolutely. I do think there are a few of us in the industry. So in some ways the role model percentage of the pie, so to speak, is almost a bigger footprint, so I try to remember that. I do think the total pie is growing which is a good thing, but I always want to make sure that I'm almost aware of the fact that maybe it's a big fish in a small pond.

I don't know if that's the right analogy, but I do want people to see that you can do it. Anybody can do it. Male or female you can do it, you just have to keep at it. I'm telling you, if I could quantify the number of times of no or not you...

Again, sometimes it was constructive negative feedback, sometimes it was just plain negative. It is what it is. You just have to keep going until any person decides to do something differently. There were times where I felt like is this really the right path for me? But I said I still intrinsically feel like this is the calling that I am drawn towards; I'm going to keep at it until I feel differently or the world has told me otherwise.

Taren: That's fantastic. You touched upon one of the areas that I think really makes for a successful leader, especially if you're starting on an entrepreneurial path, and that is resilience. Any advice to somebody, again, man or woman, who might be contemplating taking that entrepreneurial leap; what are some of the things that you know now that you didn't know then?

Dr. Ragan: Advice, honestly do it. If you have the bug, do it and call me and I'll help you in any way that I can. I would say there's a fine line between being brave and naïve. You definitely have to have a very strong element of being brave.

I remember the first person I asked for money to invest in X4 I was so cautious and almost apologetic about trying to ask someone, because I knew this person would be making an investment in X4. And I'm telling you on the flipside now it's been five years and we had a very successful recent fundraising... and it's the complete inverse; this company is going to make a difference; I believe in it and oh by the way, add a zero to what you're thinking because you'll be happy you've done it in a couple of years.

Asking for investments in a high risk business is always something... like I don't know where that naturally comes from in your own career growth. But it's something that you have to just work through and get comfortable with pretty quickly. And again, it's part of this ecosystem, it's just another element that you just have to appreciate.

Again, that was my kind of blend of bravery/naiveté because I just had no idea the types of decisions that investors do need to make. They are making investment decisions 10's, 20's north of that millions of dollars depending on the size of their fund, and you have to figure out how to connect with those people and tell the story that you believe in. If you believe in that story it's going to resonate somewhere. You just have to be patient.

Taren: That's fantastic. I love that story. That's great. Just do it. And thank you for being so generous to say call you too for advice. Finally, you've had a wildly successful career. Can you identify one wow moment that kind of either changed the trajectory of your career life, or that has stood out to you as one of those exceptional moments?

Dr. Ragan: That's a tricky one. One of the things that I think of, and again, it's a bit of a non-sequitur but I'll share it with you, is I was actually in graduate school and I was trying to figure out whether or not to do my MD as well as my PhD. I was volunteering on the wards at

Massachusetts General Hospital and I was shadowing an anesthesiologist, of all things, who was very kind with his time and allowed me to shadow him. And I met a patient. It was woman who had been in a plane crash. She had gone through multiple plastic surgery investments, a long road to recovery. She was amazing. She was a gift of light and love. To had gone through what she had gone through and to inspire people... Everybody around her was, frankly, inspired by her presence. That's something always to aspire to, so I think that was a really strong imprint in me personally.

For me, it's a long journey for me to even try to come close to her in that level of inspiration and fortitude. But it is a great role model for me and it stayed with me for a long time.

Taren: I can't thank you enough for sharing some of your insights, your wisdom, and some of your great stories with us for this podcast program. Thank you for being with us Paula, I really appreciate it.

Dr. Ragan: Thank you so much, Taren. I really am grateful for this opportunity, and certainly enjoyed the conversation with you.

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