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In this episode, Taren Grom, Editor-In-Chief of PharmaVOICE magazine meets with Dr. Shannon Dahl, Chief Scientific Officer at Cell Care Therapeutics.

Taren: Shannon, welcome to the PharmaVOICE WoW Podcast program.

Shannon: Thank you so much, Taren, for having me here today. It's really great to be joining the group of women that you've featured with this podcast and I'm really honored to be part of the broader PharmaVOICE community as well where it's my experience that people have been very intentional about the impact of they're trying to make in this field and it's exciting to see that as we move forward as an industry.

Taren: We're thrilled to have you. And we're really thrilled to share your unique story with our audience. You are one of three women founders. You, Dr. Laura Niklason and Juliana Blum founded Humacyte. How did the three of you come together? And the follow on to that is did you know at the time that it was really something special being three female entrepreneurs?

Shannon: Well, we all worked together at Duke University where the technology was being developed. Laura was on the faculty in the Department of Biomedical Engineering and Anesthesia and as an M.D. Ph.D. and practicing physician she always had a very translational focus and was focused on bringing the technology towards patients. I joined Laura at Duke in 1999 as her very first graduate student and Juliana joined the lab several years later as a post doc.

So, I had gotten hooked on regenerative medicine and tissue engineering in the 90s where I was a student at MIT and in Boston at that time the field was really emerging and growing and I knew it was a field that I wanted to pursue because I was excited about the potential of offering natural solutions rather than synthetic medical devices to treat patients. And I was really excited about Humacyte technology, which eventually grew out of the lab at Duke which was really focused on growing a human blood vessel.

And so the way it works is that we start with human cells, grow tubes of tissues in custom made bioreactors and then wash away the cells that were used for their production process, resulting in a tube of human tissue that's available for use in any patient and available off the shelf meaning that the patient doesn't have any wait time for creation of the product. And after the blood vessel gets implanted into patient then the patient's own cells grow into it and it becomes their own living blood vessel with time. So that's pretty

cool and very different than a tube of polymer that was the predecessor technology for vascular grafting.

And so I was really drawn to this field and definitely wanted to work in bringing this forward. And so in 2003 at Duke, we started to lay the groundwork for Humacyte. Laura and Juliana and I worked over lab dinners and with support from many others in the Duke community and in 2004 founded Humacyte to advance this bioengineered blood vessel platform for vascular surgery.

To your question about did we think a lot about being three female entrepreneurs, honestly I don't think we thought about it at all. I didn't. I can't speak for the others, but at the time in 2004 in North Carolina coming out of Duke we didn't have a lot peers that were on a similar path forming companies and life sciences let alone companies with such an unusual technology that's not a normal drug or a small molecule, but a really disruptive regenerative medicine product. So being three female founders is not on my radar and it didn't hold us back I think in any way and we were really focused on moving the company forward and figuring out how to build it.

Taren: You were really at the forefront of this regenerative technology, talk about the excitement that you guys felt when you were starting up because it had to be really energizing to think wow, you're creating something that nobody has ever done before.

Shannon: Yeah. And it's a harvest kind of reward. We were in this young field of regenerative medicine and the point of our academic research was really to find alternatives that would provide better solutions for treatment of disease in patients and we thought that we had one, but as you mentioned we didn't have a lot of precedents to follow and did not have a clear path of how to bring it forward. So I think it seems for me that's always stood out about Humacyte and regenerative medicine in general is that in any young field really is that it's not only about innovating the product, but it's innovating about how you get the product forward to patients.

And so we definitely have the opportunity to work through all of those dimensions with Humacyte and it was exciting and still is seeing this technology and others in the field including my new company at Cell Care bringing technologies forward to offer a new type of treatment for patients where that type of treatment is really harnessing the body's natural regenerative capacity.

Taren: Exciting stuff indeed. I mean so much so that CNBC named Humacyte a Disruptor 50 regenerative medicine company. And what did this recognition mean to you all?

Shannon: Well, it was exciting. We received that at Humacyte in 20016 which was the same year that the Diruptor 50 recognized Uber and Airbnb and 23andMe. That was the year that Humacyte published the results of our phase 2 clinical trial data in The Lancet

and the same year that we opened enrollment for a phase 3 study to compare Humacyte's blood vessel to a synthetic polymer graft for patients with end stage renal disease who required hemodialysis vascular access and reaching that year in that stage there had been a lot of work that had preceded both milestones of 2016 and the Disruptor 50 recognition I think was really an exciting validation of how far we've come in the development path.

We've taken the idea into reality and really built a company to support it and also recognition of the fact that we had demonstrated clinical potential for addressing a serious condition and unmet medical need and the excitement around the potential of what was still to come with the technology and the field and our ability to improve patient care in an innovative way.

Taren: I'll tell you that's big stuff. And then you guys received the FDA's first ever regenerative medicine advance therapy designation for Humacyl. So, how did that change what you all were doing?

Shannon: We had a long and collaborative partnership with FDA I would say and so being granted the first RMAT I think was a nice thing and representative of the collaborative relationship that we had had. Again being a first in class technology, Humacyte was one of the first companies with an engineered tissue to be regulated by the Biologics Division of FDA and so we had collaborated very closely with FDA to pave the path of how to demonstrate safety in the sector of regenerative medicine and engineered tissues and had been working collaboratively with them starting in the early days since our preclinical development.

We had taken the approach of being data driven and developing clear rationale based on data and removing ambiguity to really establish the safety of bringing the technology forward to patients and had the opportunity of a really great regulatory lead on our team who guided as well through all those interactions. And so before the RMAT, we have received the FDA's fast track designation and the addition of the RMAT which is the Regenerative Medicine Advance Therapy designation which is sort of similar to a breakthrough designation promise to further facilitate the development and expedited review of the human vessel for patients who required life sustaining hemodialysis.

So, it was pretty exciting and I'll add that after spending the past two years working closely with Medicare to help develop a path through reimbursement for a Humacyte's vessel and to align on the scope of data sets that would support a reimbursement decision making I truly have tremendous respect for the regulatory agencies and the decision makers that work with companies to bring new technologies to patients. And along that way I feel it's critical for companies to act as collaborators and partners working with those regulatories to ensure that we as companies really clarify the opportunity to have patients ultimately benefit from the therapies we're developing. So I think to me the RMAT kind of solidifies the bringing together of regulatory in company and the opportunity to really develop a therapy and bring it forward to patients in a good way.

Taren: Congratulations to you and the entire team for laying such tremendous groundwork for other companies to follow. So breaking new ground is not really new for you, you are now continuing to break new ground at your new company as Chief Scientific Officer at Cell Care. Talk about your role and the innovative approach that you're bringing through the company's technology.

Shannon: Sure. I believe that Humacyte is on great path forward. I'm excited to see its future success and in 2018 I left to join an early stage company called Cell Care Therapeutics so I could "do it all again" and you'll notice some themes here about where I see the opportunity for the field. So Cell Care has an off the shelf version of cell therapy and I think that's really exciting because I think it offers tremendous commercial potential to have off the shelf regenerative medicine product.

Taren: Talk about what that means off the shelf regenerative medicine.

Shannon: So in some therapies it's autologous, so if you need a treatment they'll take a biopsy from you, generate a cell therapy or grow a tissue for you and then return it back to you. There's a wait time associated with receiving the therapy. There's a variability from patient to patient in terms of effectiveness of the therapy. To me, off the shelf is really the allogeneic platform where you're taking allogeneic cells, creating cell banks and deriving a therapy from that. So in Cell Care's case, we're deriving therapy from an allogeneic cell bank and instead of delivering the cells themselves, which have shown clinical potential that has logistical challenges of keeping them alive and delivering effective doses, we're capturing the secretions in cells, and it's been shown in cell therapy that with mesenchymal stem cells that the mechanism of action is really derived from the secretome of the cells and their ability to trigger paraffin signaling that changes the response of host cells. It's the new behavior of host cells that drives the treatment.

And so the Cell Care is capturing the secretions of stem cells, packaging them in a way that they can be readily available to patients without any wait time and we can make large scalable batches of products so we have a lot of consistency from dose to dose. We can deliver locally in a way that with stem cell therapies sometimes it's intravenously delivered and it relies upon the cell to hone to the site of injury where with a solution of proteins and exosomes which we believe are the key therapeutic aspect of the secretome of stem cells we can deliver locally in our case in the eye where we're treating ophthalmology indications and have the potential to downstream through the more broad array of clinical indications in the future.

Taren: What's the next step for Cell Care?

Shannon: Yeah. So, Cell Care is at an exciting time. We're at preclinical stage as a company and our next steps are really about focusing on getting to a pre-I&D meeting with FDA so we can start that collaborative process with the regulatory agency of moving

forward. And so we've been doing some good work really demonstrating the potential of our manufacturing platform and technology platform for capturing these secretions in cells and delivering them and then as well really connecting the data set so the composition of the product to the preclinical data to the unmet clinical needs and make sure we're setting ourselves up on the right path for future success.

Taren: You really are doing it all over again, aren't you?

Shannon: I seem to have enjoyed it.

Taren: Good. You are a prolific inventor from what I have read that you have 20 patents to your name, what drives your innovative spirit?

Shannon: I think I'm ultimately focused on reaching the goal of bringing new innovative therapies forward to help improve patient care and to me it's an added bonus if it reduced healthcare costs for the healthcare systems as well. And when I think about innovation, I think it tends to come from when you're looking forward looking at the biggest areas of challenge that could hold you up in the future and saying how am I going to not let that challenge be a real challenge and persistently work through it. I mean a lot of those face of challenges is really opportunity for innovation and I think innovation comes in two ways.

One is the more obvious example of patent that I think you alluded to in the question. For example at Humacyte developing our product, developing novel methods for scaled manufacturing and developing a pipeline were really critical for us to advance the technology to support our work with FDA and surely demonstrated control of the manufacturing and done our business in a way that moved those therapies forward. And as a result of all these efforts, we were able to capture the new value we created and patent to cover key aspects of composition of matter, manufacturing and use and so that becomes key assets of the company and patent is our one way of innovation.

I also want to point also that I think there's another equally important side of innovation. So, I see innovation also occurring at interdisciplinary interfaces whether it's a need to merge expertise and drive clarity, so while it might be surprising when people think about innovation and patents, I do a lot of the work that we did at Humacyte to define the path forward in collaboration with FDA and Medicare as being highly innovative. And so that process of helping to collaboratively set the path forward for regulation now and especially when you're dealing with first in class technologies requires innovation. It requires new thinking. It requires sharing what you know, understanding what the other person knows or the other entity knows, putting them together and new paradigms, new ways of thinking of that interface of technology, strategy, healthcare and policy.

So I mean that's an important other dimension of innovation and then now being at Cell Care Therapeutics I think it's exciting we're engineering cells to capture an enhanced

secretome profile that delivers exosomes and proteins in an off the shelf formulation which is another new exciting platform for innovation and what I'm excited to help bring forward through those other dimensions of setting the path with regulators.

Taren: I couldn't agree with you more. I do think that innovation is more than just an end product. It is about looking at different ways of changing the healthcare system, so kudos to you and your team for really forging a new path.

Shannon: It's actually quite fun to do that as well. When you're operating those interfaces you really get to meet a lot of different people with different expertise and I value that, so it's been an enjoyable process.

Taren: That's great. I know you also serve as a mentor at Stanford StartX Med, which is a medical vertical of StartX. What does this role entail? What are you doing at Stanford?

Shannon: I work with founders of life science companies most of whom are spinning out companies from Stanford to support their early effort so they're focused on shaping their companies and clarifying how they'll focus moving forward. And a lot of what I do is really support the founders of CEOs on honing in and clarifying and communicating their value proposition and ensuring that their company goals and investor pitches are fully focused on advancing the technology and the company to realize the value proposition.

I guess when I think about value I see it having several dimensions, value of the patients, value of the competitive advantages of the technology, cost savings to healthcare systems, asset value such as patents, value of the team, you know the experience behind them, the size of the market, etc. So really helping them think strategically about putting all that together and communicating it effectively and brainstorming with them that they see challenges ahead on how they might think about navigating those challenges that they have a successful strategic path forward.

I view it as a fun way to give back to the community. I enjoy meeting these energetic early stage founders and one that simultaneously allows me to see a broad range of interesting technologies across several sectors that are spinning out of tough institutions.

Taren: Yeah. I would think it's very exciting to be there on almost at the ground level and seeing what's percolating up, so that's wonderful. You and I had the chance we ran into each other by coincidence at the J.P. Morgan conference back in January. I'd love to know what are some of the key takeaways you came away from?

Shannon: Well, wear comfortable shoes. I'm joking with that.

Taren: That's for sure.

Shannon: There's a lot of running between meetings, but all joking aside I think we observed a lot of excitement throughout the meeting focused on cell therapies and that's where we are really interacting in the meeting. We noticed the team of investors looking at novel cell therapies and gene therapies and regenerative medicine technologies and increasingly looking at them at critical early stage, which I think is a new stage for their attention and an exciting observation for the field, an exciting time for the field that this is the area of focus at an investor conference such as J.P. Morgan.

Taren: To switch topics just a little bit, talk to us a little bit about some of the lessons you've learned along the way that might benefit others who aspire to reach the executive level.

Shannon: Yeah. I think about this one a lot. I think I've learned two areas I'd like to focus on. One, it's important to continuously develop yourself and other and two, it's also important to be courageous about adding your key value. So first, focus on continuously developing yourself and other. I think becoming an executive requires building leadership skills and many of these are skills that require building, not skills that we're necessarily born with. So, you need the skills to build businesses and teams to clarify ambiguities and to establish how you're moving forward.

And so I think really speaking out the opportunity to build those skills and get coached and mentored in that is helpful. I also think to become a good leader is to really take stock of who you are knowing your values and strengths and knowing the impact you want to make so that you can focus your efforts with intention. And then I'd add it's good to take time to reflect on your experiences and to learn from them and I'd also say progress is a team sport. So I think one thing that a lot of executives do well is pay attention to how to interact with others, how to have teams work effectively together, how to engage others and how to learn from others and how you develop and coach others as we go so we can continue to build the pipeline of leaders for the industry.

And then the second part I think is really knowing and focusing on adding your key value as you intentionally build skills to develop your executive abilities. It's important to figure out number one, what you think your key value is because it's not always obvious. I think it's usually what comes to you naturally and important to identify that. So for example, I think my unique value is focused on being very comfortable at the edge of ambiguity and using five skill sets to define the path forward.

So for me it's:
1) clearly formulating the value proposition,
2) driving priorities to realize strategic goals,
3) developing rigorous data sets to support decision making,
4) putting a stake in the ground with strong rationale and justification, and
5) really collaborating with internal and stakeholder team.

I think about leaning in to those at the edge of ambiguity and it takes the ambiguity away for others. And so I think it's important for everybody to understand what is their unique value that they're bringing to the table and how can they focus on adding that value while building skills that will really allow them to maximize their impact for their teams and organization and maximize the impact of those around them as well.

Taren: Those are five great key takeaways. You've been wildly successful in your career, but how do you define success for yourself?

Shannon: I think it's really about moving forward with intention and that may look different for everybody, so at a professional level I think about developing novel therapies and that every milestone we achieve is what bringing us one step closer to the end goal of improving care for patients. And so anything that brings us closer to those milestones is success and being intentional about how we're getting there. So I think it's again important for companies to build strong data sets to support FDA and Medicare's missions, important to build the data sets that support clinical adoption and really demonstrating that the new therapy is the best for patients and has the support and understanding from the clinical community and creating and capturing value that you can communicate along the way so that's really communicating the value proposition.

I think being intentional about what you're trying to achieve is helpful. Personally, I also think about managing my time and my energy. I want to ensure that I spend time where it matters to me and I do that with intention. I like multipliers. For example, I like to ski with my family and friends where I can spend quality time with people and exercise, both of which give me energy and help me in turn with that energy to be more impactful with my professional goals. So I think for me it's all about intention and choice and making a choice about moving forward and what impact I'm seeking to have.

Taren: Fantastic. Finally, what has been a wow moment in your career? Is there one thing you can point to to say wow?

Shannon: I think I've had many wow moments and I'm grateful for that. I will say the first time we put a blood vessel in humans was a big wow moment.

Taren: I would think that's a big wow moment. Yeah.

Shannon: Yeah. And I would say seeing the end of development and all the kind of the tail end of the steps to get to commercialization has been really exciting as well and then I'd say going to an early stage company and seeing the tremendous opportunity to accelerate development based on the experience that we had with Humacyte and how to apply that elsewhere has been really exciting as well, so many wow moments and hopefully many more.

Taren: Congratulations to you and I do wish you many more wow moments. And thank you so much for spending some time with us today for our WoW Podcast series.

Shannon: Thank you Taren. It was a pleasure.

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