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In this episode, Taren Grom, Editor-in-Chief of PharmaVOICE Magazine meets with Oreola Donini, Ph.D., Chief Scientific Officer, Soligenix, Inc.

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

Dr. Donini: Thanks for having me. I'm delighted to be here.

Taren: Oh, we're so delighted to have you to have a chance to get to know you a little bit better. I know looking through your résumé and background that you have more than 20 years of experience in drug discovery and preclinical development experience with startup biotechnology companies. Talk to us about your journey. How has it been for you in the last 20 years or so?

Dr. Donini: Thanks for the question. Actually, it's an interesting opportunity to look back. I started by studying chemistry in university and really that was motivated by my father because he was a chemist, was a strong believer in chemistry and he had instilled the love of science in general in me. And while I was in university, coupled with my interest in mathematics, this led me to the fields of quantum chemistry and molecular mechanics and sort of that interface between chemistry and math. And so from there I went on to a graduate school in computational chemistry at Queens University.

My Ph.D. supervisor at the time, Dr. Donald Weaver, he was a practicing neurologist, as well as a chemist, and that was really my first introduction to the world of pharmaceutical development and the idea of a chemist and drug design. I really loved that idea of potentially contributing to society as a whole and patients in particular, and so I followed my Ph.D. with postdoctoral studies at the University of California, San Francisco with Dr. Peter Kollman who is very well-known in computational chemistry and drug design, more specifically.

It was really at that point I think that I had to make one of the more pivotal decisions looking back on my career, and that's when I decided that my interest really aligned more with working in a small company. I think what I felt at the time was that I would be more able to contribute to many different aspects of drug design and development studies in a small company as opposed to a bigger company where I might have more resources but a smaller overall impact, and I really wanted to be engaged and involved.

So the first biotech company I worked for was based in Vancouver, Canada and it was bought out by a larger company, which is a common outcome for many companies and often a great outcome. And I chose again at that point to move on to another smaller biotech company, and this sort of plan and path allowed me to develop a broad range of skills across a lot of different indication areas in both scientific work research, but also in terms of speaking with investors and outside collaborators and engagement with a lot of different people with different skills.

Taren: That's awesome. What a varied and interesting journey you've had. Going back to your earlier days back at university and then in your post-hoc work, I can't imagine there were a lot of other female computational chemists. Is that a fair assessment?

Dr. Donini: So that's interesting. I really have to think back. In graduate school I would say my cohorts that was in the same lab with Dr. Weaver we were probably half and half I would say, which was really great. We had representation all the way through I would have said, although the emphasis on math skills and the training there may have skewed that representation a bit, as you would expect.

Taren: Got you. And the only reason I bring it up is because we hear and we speak to so many scientists, especially women who really look to other women for role models and here you are one of those role models for women who are coming up through the sciences. And what does that mean to you to be a role model?

Dr. Donini: I honestly don't think of myself that way. I take your point, but it's not something I've really thought of in those specific terms, so I'd have to think about that for a moment. But I will say that I think what's really important always, and I think it's part of the ethos of science, is that we all try to work together to solve problems. This idea of academic rigor and academic comradeship, I think, is very strong and I've always felt that throughout my career from mentors around me, and I would hope that I would give that back to other people as well.

Taren: Excellent. You talk about the scientific rigors, let's talk about some of those challenges. You had been instrumental in leading some early stage development of several novel therapeutics into the clinic. So when you look back at your experience, what are some of the biggest challenges in getting a therapy into the clinic and then as a follow up to that, how do you keep your teams motivated and inspired when the science just doesn't work out?

Dr. Donini: Right. I mean that's always very interesting from a variety of different perspectives, but I would say one of the biggest challenges in biotech is really deciding which experiments are the most worthwhile. And I don't just mean in terms of success, although clearly you want success, but also in terms of generating the most amount of knowledge possible in the scope of the limited funds and limited timelines that most biotech companies experience. So really what we're looking for is not only a great outcome, but also if it happens not to work, what will I anyway learn from it, and I think that's very important.

As you know, surprises always happen, and I think the motivation, both for myself and for my teams over the years, has come from those surprises actually and knowing there is always more to learn as well as the hope that with perseverance we'll be able to ultimately produce products that will make patients' lives better.

Taren: That's fantastic. What are some of the tools you use to effectively lead and manage your teams?

Dr. Donini: One of the key tools I think is really open and transparent communication. I always believe that your best path forward is dictated by your data, and so jointly understanding that data as a group and all of its implications is a driving force, I think, for most scientific teams. I also think it's really important to understand your employees as people, and just as the company might need extraordinary effort from the employees at certain points of time, like when you're filing an IND or an NDA for example, you should also offer your employees flexibility when life events happen. So I think it's a mix of those two and all of it is driven by the communication.

Taren: I also understand that you were the co-inventor and the leader of SGX94, which is an innate defense regulator technology that you developed at Inimex Pharmaceuticals which was then later acquired by Soligenix. What is SGX94 and how is it being applied today?

Dr. Donini: SGX94, which is also known as Dusquetide now, is as you point out an innate defense regulator. This discovery really came out of research that was being done at the University of British Columbia in Vancouver, Canada. And further research on the mechanism of action and discovery of specific drug-like compounds was undertaken at Inimex as you pointed out. Innate defense regulators are really unique in that they target your innate immune system.

So just to back up a little bit and put that in some context, most people think of immunity in terms of T-cells and antibodies and those really represent your adaptive immune response, the part of your immune response that learns over time. Your innate immune system represents the immediate response of your body to an insult, such as an infection or a cut or some kind of tissue damage. So it's only if that innate immune system failed that it activates the adaptive immune system to respond. Your innate immune system is preprogrammed, so you have hundreds of receptors constantly scouting for signs of trouble that can activate your innate immune response. The innate defense regulators are unique because instead of trying to change the surveillance system, they instead change how the innate immune system responds when any insult isn't detected.

So we used to think that innate immunity was inflammation, that that's all it did. But actually over the last 20 years it's become increasingly evident that innate immunity is really a few different things and it has two major proponents, the inflammatory component, but also this direct anti-infective and tissue healing component. And so what the innate defense regulators do is really leverage that understanding of the difference between the components and tries to change their balance. So we reduce inflammation a bit, but not a lot because you do need some

inflammation, but we try and modulate it and control it more and we also enhance the anti-infective and tissue healing response of your body.

So we obviously thinking of that mechanism, we were initially developing the innate defense regulators as sort of broad spectrum alternatives for super bugs and antibiotic resistant bacteria, but as you probably know the investment environment in that space is really challenging and has been for a number of years. So we then turned our attention to other aspects of the drug mechanism and we're now developing SGX94 for the treatment of oral mucositis in head and neck cancer patients. The exciting thing is that SGX94 is just completing a phase 3 study in the oral mucositis indication, and we're really excited to see the outcome of the study later this year.

Taren: That is exciting because there are very few therapies out there for head and neck cancer. How does your drug differ from some of the other therapeutics that are in development or even on the market?

Dr. Donini: As you probably know, oral mucositis is a really debilitating side effect of most cancer treatments. It doesn't only happen in head and neck cancer patients, although unfortunately they are very susceptible to it. What it amounts to is these sores in your mouth that are so painful that even opioids can't control the pain. And so what happens is the patients will stop eating or drinking and as you can imagine, if you're trying to fight cancer you don't want to be not eating, not drinking and feeling all of that pain all the time. So it's really hard on the patients; sometimes they'll even stop their cancer treatment because of it. So clearly we want to do whatever we can to mitigate that not only in head and neck cancer, but more broadly ideally at the end of the day.

And so that's really what we're targeting. But at the moment there's actually no approved drug for treating oral mucositis in any solid tumor cancer setting – breast cancer, colon cancer, it doesn't matter; none of those settings is there really any treatments, any drug approved for treating oral mucositis. So it's really an unmet medical need and we're really excited that our drug, at least in our phase 2 studies, showed that it was able to really reduce the amount of suffering that these patients experienced just by taking this drug at the same time as they're doing the rest of their normal therapy. So that's sort of the approach we're taking, and so we really think that it'll improve patients' quality of life.

Taren: That's wonderful. Congratulations. Keeping fingers crossed for positive future results. That's great. It certainly is an unmet need. Well, talk to me about your work in biodefense.

Dr. Donini: So like our work in specialized biotherapeutics, we also do have a public health solution segment and we focus that segment on unmet medical needs again, but in this case in the context of emerging infectious disease and biodefense. We have a number of different approaches here. We do have our ricin toxin vaccine where we're the world leader in the development of this vaccine, and we've been able to show really good potency with this vaccine in animal models. So we're very pleased because the vaccine is based on a protein technology,

which really is the gold standard for safety in vaccine platforms and we're using a proven alum adjuvant.

So we think that this vaccine could be very broadly applicable obviously in the biodefense context, and we're also very focused on the fact that we have a thermal stabilization platform that allows this vaccine to be exposed to temperatures as high as 40 degrees Celsius and still maintain its potency. We think that's really important for vaccines that may need to be stockpiled or distributed worldwide. We've been sort of using that platform as a jumping off point and we've been expanding on this technology with our colleagues at the University of Hawaii where we're using different adjuvants which have the ability to stimulate more immune responses but still maintain our ability to thermal stabilize the resulting product.

So this work has also been shown to be very efficacious in animal models of Filovirus infection, so I'm thinking of Ebola or its cousin Marburg viral disease. The vaccine is very clinically convenient for use in endemic regions because it can be shipped sort of at a variety of conditions. It doesn't need to be kept frozen and it can be reconstituted with water for injection immediately prior to use. This same technology actually is also very relevant in the context of our COVID-19 vaccine effort as well. Because the antigen for COVID-19 is a glycoprotein just like the antigens that are in our Filovirus effort, many of the processes, procedures and findings from our Filovirus work are directly applicable and we've recently conducted some proof of concept studies that we find really promising in that space.

Finally, of course, outside the world of vaccines we are also continuing to develop our innate defense regulators again in the context of infectious disease and antibiotic resistant bacteria and we continue this research with the support of government funding.

Taren: Well, it's an exciting time, especially now in the midst of COVID-19 and all the work that you've been doing leading up to this. How has the pandemic impacted some of your clinical trials in terms of COVID-19 and your other vaccine work?

Dr. Donini: That's a really good question. I think a lot of people in industry obviously would tell you that just like with many other aspects of our society, there has been a significant impact on clinical trials in general with COVID-19. In the context of our cutaneous T-cell lymphoma program, the timing just worked out and the study – the main part of the study actually wrapped up prior to COVID really being a strong effect, especially in the United States. So we're very pleased about that. In the context of our oral mucositis program, again, we're very close to the end and so what we decided to do was just take a little bit of time and make sure that there hasn't been any adverse impact on the study, but at the moment we're still projecting wrapping that up this year.

Taren: You all also are working in the areas, as you said, inflammation, oncology, as well as biodefense. How do you manage all of those different maybe competing areas and set the strategic direction as the chief scientific officer?

Dr. Donini: Right. It does have like a lot of diverse areas, but what we need to understand is Soligenix's focus is really on addressing rare disease and unmet medical need, so we really look to those niche indications often orphan designated where patients really don't have adequate alternatives for treatment. And so our goal really is to address those needs as efficiently as possible. Soligenix has a really core group and core skill set that understands the non-clinical, clinical and regulatory requirements to operate specifically in these orphan indication spaces.

So our goal is to identify technologies that we can rapidly deploy our expertise in, including running those clinical trials from within our own organization, not contracting them out, and this enables us to really develop earlier stage assets to later stage clinical trials rapidly and efficiently. So obviously we have the two phase 3 programs we're working on right now – one in cutaneous T-cell lymphoma and one in the oral mucositis we just discussed. So that really characterizes our R&D strategy. We want to clearly define our understanding of the core technology and how it can be applied and then understand the clinical realities of the situation and marry those two concepts up to produce a very efficient clinical development program with the hope, really, of aiding patients who otherwise don't have many alternatives.

Taren: And as we discussed earlier, you really mapped out a purposeful career leading to your current role in the C-suite. Is there anything you know now that you wish you had known as you were moving up the ranks?

Dr. Donini: I think the key to advancing in biotech is to never be afraid to take on new challenges. So if you see something that needs doing and sort of that step in and step up philosophy, and then as you develop new skills and new contacts of course, you continue to advance. So it's important not to be afraid to share your ideas, to speak up, to be confident in your own knowledge and your own understanding of the data. I think it's also really important to take the challenging path, the one that interests you as opposed to perhaps the safe path.

Obviously I think that what comes with experience is a more nuanced judgment of those situations, and it would certainly have been nice to have had that judgment much earlier in my career. That being said, I don't think there's any way to achieve that without living the experience.

Taren: Well said. And finally, can you tell me about an accomplishment or a wow moment that shaped your career?

Dr. Donini: So back when we were first working in Inimex Pharmaceuticals developing those innate defense regulators we were speaking about, we had a really young team and we were all so focused on trying to help patients, and I don't think any of us really understood how long that road really is – well probably our C-suite did, but I think they were probably wise in not laying that out too clearly for us at the time.

I remember that when Soligenix we first got that phase 2 study result with SGX94, it was the first biological proof in humans that the drugs could help people and it was a really novel

mechanism of action, so there had been some doubters. It was the first proof that things worked the way we thought they did, and that was really mind blowing. Like I said, oral mucositis is a really terrible side effect, and we were so pleased that SGX94 was able to reduce their suffering and hopefully make the cancer treatment more tolerable.

So when we got that result, I remember thinking how long the list of people who contributed to that outcome was, not just at Soligenix but also at Inimex and at the University of British Columbia. So we were all so pleased that all that hard work had translated into real benefit for real patients, and I think that is the moment that I always remember.

Taren: Congratulations. As I said earlier, I mean this is great work that you're doing and we couldn't wish you more heartfelt good wishes on your continued success. Oreola, thank you so much for being part of our WoW podcast program. Thank you for sharing your story and thank you for some really great insights. Appreciate your time.

Dr. Donini: Well, I appreciate your time as well. Thanks for asking the questions. They made me think about things differently.

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