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In this episode, Taren Grom, Editor-in-Chief of PharmaVOICE Magazine meets with Rebecca Kusko, PhD, Chief Strategy Officer, Immuneering Corp.

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

Dr. Kusko: Thanks for having me, Taren. I'm very excited to be here.

Taren: We're excited to have you here. Becky, I understand you have a love of creative problem solving, which messes with your goal of helping patients. Tell us about this synthesis.

Dr. Kusko: I'd love to. That's a great question. It's true, I do really love solving problems, especially the ones with non-intuitive solutions. I find that when it comes to getting better medicines to patients, the solutions are often non-intuitive. I think it's best if I answer that question if I give an example from what actually happens to be one of my favorite projects and my first project that I worked at Immuneering when I joined.

An interesting puzzle that we got to solve, Teva Pharmaceutical came to us with a really interesting question. At the time, they were developing a drug called pridopidine for Huntington. The drug was meeting some of its secondary endpoints in clinical trials. So it was actually helping patients to feel better. The drug was originally developed to bind to the dopamine receptor. However, when they tested out the binding of this drug to the dopamine receptor, it turns out it actually wasn't binding nearly that strongly at all.

So they were in this really interesting situation where they had a drug that by some metrics was helping patients to feel better, but they weren't sure what the mechanism of action was. It was a really fascinating puzzle.

Immuneering worked together with Teva to use gene expression of pridopidine itself, as well as Huntington animal models and Huntington patient data to solve that mystery. And what we actually found was that pridopidine was acting through the Sigma-1 receptor instead and activating the BDNF pathway. Which in case you're unfamiliar, the BDNF pathway and BDNF itself it's like candy for neurons. That's a really great thing in Huntington. The really fascinating thing was all of those genes that pridopidine through the Sigma-1 receptor was upregulating were actually down-regulated in Huntington animal models, as well as Huntington patients.

So the non-intuitive lesson there was that this drug was working, not just by hitting its target, but through hitting that target, it was reversing disease-associated changes in gene expression. And Immuneering actually saw this pattern across multiple different successful drugs that we've had the pleasure of working on and that inspired us to create a tool called disease-canceling technology.

I'll just pause and see if you have any other questions before I keep going on.

Taren: No, that's fascinating. I think it's so interesting how you unraveled all of that mystery to find the answer. Tell me what that process was like a little bit with your team. How did you lead a team through this?

Dr. Kusko: Great question. There was a lot of back and forth between our side and Teva's side. Immuneering at this point has 12 years of experience in bioinformatics services and Teva is really an expert pharma company. So there was a tremendous amount of back and forth – actually when I first joined that project, we were presenting to them three times a week, because it was really urgent.

What we would do is we would analyze data. We would have these really interesting results and we would turn to them and show our computational results. And then they would turn and go and do experiments in their own labs, and we would look at those results and that would drive further analysis. It actually really helped us sharpen the scale of using bioinformatics to better arrive at actionable insights for pharma and was a fantastic collaboration that actually resulted in four publications. What an interesting story it was.

So when I started that project, I was actually alone on it. By the time that project ended, I was supervising three other people. It was an interesting part of my career transition.

Taren: We're going to get to that career transition in a second. In addition to trying to unravel the mysteries of the earth and the world, you also have a passion around reproducible science. And in fact, you were a founding member and serve as the current deputy board chairman of the FDA-led Massive Analysis and QC Society. Which is an organization committed to promoting reproducible science and best practices for the analysis of massive datasets. Why that as a passion?

Dr. Kusko: I'm so glad you asked about that. Topics like reproducibility, rigorousness, quality control and best practices tend to really kind of put people to sleep. But as you can probably hear from my voice, that's really what keeps me up at night and what gets me excited. I'm an engineer in my heart of hearts, and I'm always looking for ways to improve a system.

So to quote a common statistic, a 2015 study showed that around \$28 billion per year is wasted in the United States on irreproducible research. Patients don't have the time...

Taren: Say that number again for our audience. What was that number?

Dr. Kusko: A 2015 study estimated that \$28 billion per year is wasted in the US on irreproducible research. It's astounding, right?

Taren: Yes, that's a big number.

Dr. Kusko: That, and patients don't have time. They need better medicine now, not irreproducible research. I'm really fortunate to be part of an organization that cares about this as much as me. In all of Immuneering's history we've really cared about getting actionable insights from high throughput data. And the best way to do that is, of course, to be obsessed with these kind of boring seeming topics.

So we found that the key to our success is focusing on these untrendy details. It turns out that while myself, as well as my organization Immuneering is really obsessed with reproducible science, there's other organizations who share our passion. It's really important for drug regulation. So this is a topic that's very important to the FDA also.

The FDA, in collaboration with myself and some other key opinion leaders in the reproducible science space, launched the MAQC Society that you mentioned. The goal there is focus on quality control and analysis of massive data that's coming out of these high throughput technologies and help establish best practices and actionable recommendations for the whole community. So it's something that's really exciting to be a part of.

Taren: That's awesome. What great work you're doing. So thank you for that.

Dr. Kusko: Thank you.

Taren: Let's go back to the transition now. You joined the company as a consultant, which then led to your current role as Chief Strategy Officer. Tell me about this transition for you and what led you to take the lead. And then we'll do a follow on as to what your role as Chief Strategy Officer entails.

Dr. Kusko: Yeah, my career transition to Immuneering was actually, I would call, highly unusual. So I'm pretty prone to having strong opinions and sticking with them. And basically starting when I was around 14 years old, I decided that I was going to be an academic purist; I was going to go on to do a PhD and a post doc and go and be a professor because I wanted to impact patient lives, and that seemed like the best way for me to do it.

While I was in this career in academia, I heard about this interesting opportunity to work a couple of hours a week as a consultant at this company which was local to me. They were looking for me to do this kind of analysis that I was not terribly familiar with but I thought maybe by doing this work, I can improve my skill in this analysis and it will help with my grant writing and then I can get more grants funded. That was originally my plan. I saw it as only furthering my academic goals.

The more time I spent around Immuneering – I think I started out as three hours a week, but I felt like I was having more of an impact on patient lives and doing more exciting research in my three hours a week at Immuneering than my whole academic career. I was at a school of medicine at that time. My lab mates were medical doctors who were seeing patients. So I increased my hours bit by bit and that was mutually agreeable to Immuneering. They increased my hours, and the hours just kept increasing and increasing. And once it was like 30 hours a week, I just switched to full time and abandoned what I was doing in academia.

That's how I ended up at Immuneering. I never did the normal interview thing, because once you've been consulting that intensely for that long, it's actually a very natural career transition.

Taren: Pretty seamless then, right?

Dr. Kusko: Yeah. It was very natural.

Taren: Tell me about your role as Chief Strategy Officer.

Dr. Kusko: Yeah, let me tell you how I ended up in that role. And I know the title Chief Strategy Officer is a bit uncommon; not every organization has one. When I joined Immuneering, I really like working on hard problems, as we discussed. So I said to my CEO, 'look, I really want to work on whatever is the largest, was driving imperative for Immuneering right now.' So it means that within my first couple of years at Immuneering, I had contributed to bioinformatics services. I had helped to develop some of our platforms. I contributed to our drug discovery pipelines. I had worked in oncology and CNS. I had written code. I had written papers. I had written grants. I drafted two year budgets. I had been an individual contributor. I had managed teams. I led client engagements. I had done business development. I helped raise our Series A.

So Immuneering, as a company, went from being just a bioinformatics services business to also having some of our own proprietary tools that accelerate drug discovery, as well as having three separate pipelines – one in oncology, one in immuno oncology, and one in Alzheimer.

Some companies talk about having multiple shots on goal. Immuneering had multiple hockey games. So the company really needed someone who could be forward looking and making sure that Immuneering is moving in a good direction, but also make sure that our strategic initiatives get buy-in across all the different business units and sectors of what we're doing.

So it turns out I was actually very qualified for that appointment because I have worn pretty much every hat at Immuneering, and at some point sat in every single department. So that's more or less what I do as Immuneering's Chief Strategy Officer, is I make sure that all of our initiatives are coordinated and synchronized, but I also make sure that we're forward looking and thinking about our future.

Taren: That's exciting. I love that you carved out that space for yourself using your experience and figuring out where your best value was. That's highly unusual, that's wonderful.

Dr. Kusko: It was a lot of fun.

Taren: When you're leading these teams and you're thinking about the future what is your vision for the company?

Dr. Kusko: As a company I'm really excited, especially about our newest initiatives, which are our three pipelines. So, like I said, we have a pipeline in oncology, we have a pipeline in neurodegeneration and we have a pipeline in immuno oncology. In the oncology space we're actually working on a pan-KRAS inhibitor, so this is something which could treat all KRAS-driven cancers, not just the ones with the G12C mutation.

In the Alzheimer's space we actually have a program where we've discovered subsets of Alzheimer's that have totally different molecular biology and we think will respond to totally different targets.

As I look to the future of Immuneering I'm so excited to see these existing pipelines grow. And given the technologies that we have, I'm excited about the new pipelines that we're going to add in addition to continuing to maintain fantastic bioinformatics services for our clients in that space.

Taren: That's exciting. Thank you so much for sharing. In addition to the hats you wear at Immuneering you also serve as a mentor to graduate women at MIT, which is your alma mater. Why is mentoring important to you?

Dr. Kusko: Mentoring is very important to me because I really believe that I'm successful because of a lifetime of fantastic mentors. If my career is a baseball game, I was effectively born on third base, if we're being really honest. Both my mother and father are electrical engineers by training. It took me until I was 14 to realize that there are some professions that have more of one gender than the other. By the time I was 16 my chemical engineer aunt had convinced me that I should consider doing a PhD and my uncle with an MBA had already explained to me what company stock was. I could go on, but I think you get the picture. I've had tremendous mentoring from a very young age up to the current point.

I think rather than just looking up my own career ladder I really want to mentor the next generation. One of my favorite programs is actually called Graduate Women at MIT, so it partners women who are in graduate school at MIT with mentors out there in industry, academia. I've been meeting with the same group for I think three or four years. We meet once a month. I actually sometimes bring special guests to those meetings. My friends who have taken various different career paths and can comment on what its like. The goal there is to help build their professional network and expose them to different careers. I hope that everybody

out there mentors. No matter where you are in your career stage you have something to give to the next generation.

Taren: Very true. Very, very true. You touched on something there, is that professional network and how important that is in your career journey. Can you comment about your professional network?

Dr. Kusko: Oh my gosh, networking is so incredibly important. I'm lucky that I'm – as you might have guessed by now I'm a pretty big extrovert, so if there's someone that I want to talk to I'll just march up to them at a conference and say hi. One thing that I've been very fortunate about in my current job is because Immuneering has a client services business and is client facing I'm actually exposed to people at a lot of different pharma companies. Even when those client engagements end I tend to maintain those contacts.

I'm also still in touch with a lot of people that I got to know at MIT while I was an undergraduate there who are now spread out all across the country doing very fantastic and exciting things.

Taren: Excellent. As you outlined, you have mapped out a very purposeful career for yourself. But not all people, especially women, have that same clarity, let's say. What advice do you have for other women who look to you as a role model, who may someday want to aspire to the C-suite?

Dr. Kusko: I think two pieces of advice there that I've seen really challenge women, especially the ones that I mentor. I think women are very afraid to advocate for themselves, because if we go out and tell everybody about how we're great we feel like we're being arrogant and putting a big flashing billboard in Times Square that's blinking and says Becky is great. That's not really what advocating for yourself means.

For women who are looking to grow their career within their own organization it's really easy once a month, just write up a little, short email with bullets and summarize the value that you've brought to your company that month. Then sometime later when you go to ask for that promotion you have a nice history of emails that you've sent to your supervisor describing the value that you've brought to that company.

For women, people in general, who are looking to do career transitions outside of their organization it's really easy to get hung up on not being qualified for certain jobs. For example, a lot of positions, especially C-suite positions, require previous C-suite experience. Which is kind of like a circular logic. How do you ever get a C-suite position if you've never had C-suite experience? How do you break into that?

I think what a lot of people don't know is you don't necessarily have to have that previous C-suite job title on your résumé if you see that as a requirement. But you can maybe argue about how you have all of the experience that you've had the equivalent of a C-suite job, or are very qualified for that job. So those are two pieces of advice that I would give.

Taren: I think those are really valuable pieces of advice, and I particularly love the one about knowing your value and being able to speak to your value. Really important in today's environment. Also, being an advocate for one's self. I agree that women don't stand up and they don't speak up and want to tick off all the boxes before they move up, and that's not necessary. Excellent pieces of advice.

Dr. Kusko: Thank you.

Taren: I'm going to ask this question. I'm not sure how you're going to answer it. Is there anything you wish you know now that you didn't know as you were moving up the ranks? You were provided with a lot of great mentoring and you really did start your career on third base. But is there anything that you maybe wish you knew then that you know now?

Dr. Kusko: Yeah, oh my gosh. This advice about being your own advocate I really wish I could give to myself. I learned that lesson relatively recently. I was able to advance in my career through academia and in industry through other people really believing in me and championing for me. At Immuneering people within my organization really believed in me and pushed for me, and even people on the client side really believed in me and pushed for me. That helped advance my early career tremendously.

I wish at the time I'd been brave enough to advocate for myself instead of relying on all of these other fantastic humans who really helped to push me and my career forward.

Taren: Well, we think Becky is great so I'm just saying.

Dr. Kusko: Thank you.

Taren: You're welcome. Finally, tell me about an accomplishment or a wow moment that either shaped your career or that has left a lasting impression on you.

Dr. Kusko: I actually have a recurring annual wow moment. Is that okay?

Taren: Sure.

Dr. Kusko: Okay. So every September I go back to MIT and I give a guest lecture for a class of biological engineering sophomores. It's a career exploration class. So undergrad can be a lot of technical stuff. How is it all relevant? At least that's what I remember thinking when I was sitting there as a sophomore in biological engineering at MIT.

When I go and give that guest lecture it's my job to tell these undergraduates about my job and all the exciting stuff that I'm doing to help them think about their own careers. It really makes me feel so great to be able to talk about how Immuneering is using these really cool

technologies, including our disease cancelling technology, to create drug pipelines. It just helps make all of it real.

When I was a sophomore the technology to do what we're doing now just simply didn't exist. The tricky problems that I'm able to tackle now we're nearly so tractable. Every time I go and I give that lecture I'm excited to have something happy to share with them and I'm double excited to see what the next generation of scientists and engineers is going to do with the technologies that are being born right now.

Taren: Becky, thank you so much. Those lucky MIT sophomores, I hope they realize how lucky they are.

Dr. Kusko: Thank you so much, Taren.

Taren: Thank you so much for being part of our WoW podcast program. Loved hearing about what you're doing and how you're progressing drug discovery, drug translation, all of that great stuff that is going to help build the pipelines of the future as well as sharing some great tips on how to progress one's career. Thank you so much.

Dr. Kusko: Taren, thank you for your time, your questions and for the opportunity.

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