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*In this episode, Taren Grom, Editor of PharmaVOICE magazine meets with Karmen Trzupek, Director, Clinical Trial Services and Rare Disease Programs at InformedDNA.*

**Taren:** Karmen, welcome to the PharmaVOICE WoW podcast program.

**Karmen:** Thank you. It is such a pleasure to be here.

**Taren:** It's our pleasure to have you. I find your background to be really interesting. I understand you have a degree in genetic counseling. Talk to me about how this experience has influenced your career and what is genetic counseling?

**Karmen:** Maybe that's the better place to start – what is genetic counseling? Genetic counseling is really the process of talking with patients and families about their genetic disease, and in some cases a disease that they want to know whether or not may be genetic. It's helping them to navigate clinical genetics, so helping to navigate the process of obtaining an accurate diagnosis, of determining the most appropriate genetic testing and then interpreting the results of genetic testing, which is getting increasingly more complex and really providing support to patients and families as they navigate the impact of that disease for their own health and what that risk means to their family members.

So I think for me – so I guess I answered them in backwards order – but for me when you say how has that impacted my career, to me genetic counseling is really the core of what I do. It's my center. Over the years I've been practicing as a clinical genetic counselor for over 18 years and in some ways you would say that what I do today is not genetic counseling, but I think genetic counselors have this strong feeling that once a genetic counselor always a genetic counselor, you're just doing other things with those skills. So over the years I've counseled literally thousands of patients, and those conversations are really vulnerable.

People really open up about what this disease means to them, what it could mean to them about their fears and their losses. They go through a grief period about what that means for their future in comparison to what they had believed it would mean or for their child's future. And so I think those kinds of conversations, those experiences, really profoundly affects the way I now think about developing and implementing programs in support of clinical trials because all of it is very patient focused.

**Taren:** I would have to imagine that those conversations have to be very difficult at times. Where do you find the strength when you have to counsel somebody who's been delivered devastating news about a rare disease?

**Karmen:** I think there's hope in almost everything. That's probably the number one answer. For many, many years I specialized in inherited retinal diseases for which there were no meaningful treatments for any of them. People didn't die from these diseases, but we'd be talking maybe to a 12 year old about a disease for which he would likely go completely blind. That's a hard, hard conversation – or even a 30 year old who's looking at the loss of their career that they worked so hard for and they're really just getting started in, and what does this mean if they're no longer going to be able to see.

But there's always this hope about maybe being involved in the research and what's happening in the research. There's hope about what they can really do and how they can change their expectations. I think that's part of life. Like we all have this picture of what our future is going to look like but you don't know what's going to happen. It's a fine balance because I don't want to hold out unrealistic hope, but there are ways in everything to try to help people navigate while thinking about where is the gratitude and how can you find something to work toward.

**Taren:** It takes a really unique person to be able to do that, so kudos to you. And when we look at genetic testing it's come – I would imagine again, come a long way since you started 17 or 18 years ago.

**Karmen:** Yeah.

**Taren:** So how has technology helped you in your role?

**Karmen:** The primary way technology has changed the field of clinical genetics is when I think about genetic testing because 18 years ago whenever I was working in clinic and we had patients who we thought might have a particular genetic disease, if we wanted to do genetic testing – first of all, we didn't know a lot of the genes that cause those diseases, so for some diseases we would – all we could offer them was to participate in research studies to help us try to find the genes. In other cases, maybe we knew some of the genes but not all. So we would say well we know a couple of genes that cause this condition, let's go ahead and order testing, but the likelihood of finding an answer might be 20%, 10% and that doesn't mean you don't have the disease; it just means we just don't know enough about the genetics of it yet.

And today that's just dramatically flipped. So the good news is that genetic testing has gotten so much better. It's gotten so much cheaper. It has completely changed the way that we can utilize genetic testing to help obtain really accurate diagnosis for patients. But the downside is that we often get so much information back because we've gone from doing maybe genetic

testing where we were testing for two genes because that's what we knew to doing testing routinely of like 300 genes at once and you get back a lot of noise, frankly what a lot of people call noise. Like there's just a few just test report with all these variants and what does that mean, so it's a lot to navigate.

So I think that genetic counseling, while the core of it is still about being in those vulnerable moments with patients and families and helping them to navigate that whole process, it has shifted to being a whole lot of genetic variant interpretation and really helping to try to sort of dig in to the meaning of genetic test results.

**Taren:** It sounds hugely complicated and complex and as you said, there's so much information coming at not only you as a geneticist, but as to the patients. So how do you kind of break through some of that noise and help focus the communication for patients?

**Karmen:** So we might get a test report back and there could be say six different genetic variants in the test report and the laboratory does a really amazing of filtering out most of the noise because there might be hundreds that they initially look at but the algorithms will filter most of it out as normal variation because there's like ton of normal variation in our genome, way more than we thought there was when the human genome sequence was completed. So the laboratory does some of that and then we get a test report back and it still got a number of these on there and so part of what we'll do is we'll look at the patient's phenotype for their clinical diagnosis or symptoms and try to determine how likely is it that the variants that we reported in this test report really matched the phenotype of this patient, what I see in front of me.

Does it match the family history because they can be inherited in different ways? So part of it is a little bit of puzzling, just puzzle together and then if there is a variant or if there are a couple of variants that seem strongly associated with that patient's disease we can sometimes provide additional information back to the lab, so it's a collaborative process sometimes, that will help them to do further filtering. We can sometimes do additional family member testing that will help to see oh how are these genetic variants being inherited in the family and does that fit with what we would expect for this disease. So sometimes it's easy. Sometimes you get a test report back and it's like clearly positive, right at the top, very easy answer. Sometimes it's not. It takes time.

**Taren:** Thank you for that. I appreciate that explanation. And as you think about the future, how do you see the role of genetic testing changing in the future? Is it going to be that, maybe that silver bullet that could help predict future disease?

**Karmen:** I think there's an in between. I think right now what we're seeing is we are really rapidly approaching a time when genetic testing is no longer just being used for classic genetic diseases. We already see this in cancer. So we see this all the time for tumor profiling where

genetic testing is done on a tumor itself to determine what were the genetic drivers of that tumor and that's utilized to help guide treatment decisions. It's part of the overall hype about precision medicine. It's hyped for a reason where treatment is based on the underlying cause of disease or at least one of the drivers of that disease.

We're seeing that very consistently in cancer, but we're also starting to see that much more common multi-factorial diseases. Diseases like Parkinson's disease, for example is the common adult onset, neurodegenerative disease. Everybody knows of Parkinson's diseases, but there are multiple underlying genetic risk factors where those genetic risk factors in combination with environmental and lifestyle factors are what ultimately lead to the disease. So we're starting to see lots of pharma and small biotech companies developing and testing therapies that are based on that underlying genetic risk trying to get at not just thinking about treating Parkinson's disease as one big disease, but what's driving that disease and is there a different drivers for it.

Let's think about how we can approach treatment in those different avenues, those different drivers. So I think that's where it's going in the short term. That's what we're seeing. The longer term which you got out in your question is are we going to get to a point where everybody gets a test, everybody gets whole genome sequencing and it's going to tell us what we're at risk for and how we should modify our lifestyle. I think we're still a lot further away from that than it seems to a lot of people. We can do the testing, but right now it's super complicated to dive into the test results from a 300 gene panel, imagine what that's going to be like if you're testing all 22,000 genes and trying to work with that. We just don't have enough data for the interpretation to do that well.

**Taren:** Fascinating and agreed and we also have that human component. Are people going to be willing to know what they're at risk for?

**Karmen:** Well and then beyond what they're willing to know there's been a lot of really interesting questions and research studies looking at how do people really change behaviors. Do people change behaviors based on something they know they're at risk for if that risk isn't something they're already personally familiar with? So if you have a parent who died young of cancer and you find out that you carry a genetic risk factor that predisposes you to that will you make different decisions in your medical management? Yes, the vast majority of people will.

But if you find out an incidental finding that you're at risk for say early onset cardiomyopathy and no one in your family has ever gotten that, you don't really know much about it, you feel really healthy, will you change your medical management? Will you do anything differently? And most of the studies say people don't, so we also have to get to the point where we think about what are we going to do with all of that information and when people have so much of it will it actually change behaviors.

**Taren:** Interesting. It's fascinating and the future is going to be even more interesting and fascinating. It's going to be a whole new – it just it opens up a whole new world of well everything, behavior change, testing, drug development, everything. It's quite interesting. I would imagine that fuels your passion for what you do on a daily basis and I know you came from an academic medical research center and then you joined InformedDNA, what drew you to the company?

**Karmen:** That's actually easy. I was working in academia. I working at really, really significant clinical research center and people came to us from like an eight-state radius. It was really an amazing experience to work there and to develop the expertise there in that center for me, but there were so many patients who never got to our clinic and it wouldn't be at all uncommon for us to diagnose someone and enroll them in our clinical research studies and then that patient might call me later and say 'My sister, I think she has the same thing and I was telling her about my appointment and she just wants to participate in the research, can she do that?' Yes, of course. Let's make her an appointment. No, no, she lives in Illinois. Well no, she has to come to our center. She has to be evaluated and we have to do all these tests before she can be part of research. Well, she can't.

And this would happen fairly frequently. And so when I came to InformedDNA, here our entire model is let's take that experience, that experience that people have when they go to a large clinical research center and they can get the best genetic testing to determine the diagnosis and they can enroll in research and they can learn about what's going on in clinical trials, all of that. Let's deliver that on a telemedicine model to break down these economic and logistical barriers that people have because so many people cannot just get on an airplane and fly across the country to get to the best clinical research centers and we shouldn't be delivering that care only to the people who can.

**Taren:** Amen. Absolutely. Yeah. I couldn't agree with you more and for a variety of reasons. So tell me how were you looking to break down those geographic and economic barriers? What are some of the things you all are doing?

**Karmen:** You can tell. Yeah, you can tell I'm totally passionate about this.

**Taren:** I love it.

**Karmen:** Yeah, I am. I think not only can we do better in diagnosing patients who aren't able to travel to those large academic medical centers, but we can also do better in inviting them to participate in clinical research and inviting them to participate in clinical trials. So a lot of what I do comes down to this. So how – how are we doing that? Well, we make genetic counseling appointments available to people utilizing telemedicine. We have EMR systems available today where you don't need to be physically on site at an academic research center in order to be in

the EMR, an electronic medical record. That's just unnecessary. So we deliver that over telemedicine.

We order genetic testing remotely. We have labs, these specialty genetic testing labs send test kits out to people's homes and this is not like direct to consumer genetic testing. We're hoping to determine what is the best test for this patient, what is the most appropriate but then when we order it we're getting it shipped directly to their home. And then where once we get the results and we interpret that and we provide that information to the patient's family, we're also throughout that whole process we're partnering with community physicians because these community physicians don't have the expertise to know what is the best genetic test for this patient today, which might be totally different than it was two years ago and I can't keep up with that.

And they don't have the luxury of time, but thankfully genetic counselors do get. They don't have the luxury of time to sit down and research those genetic variants and then sit with the patient and their family to discuss those findings. So we partner with those community physicians to say you can incorporate this into your medical practice and we'll be your partner because we know that you want to help patients get better diagnosis. We know that you want to screen your patients for these clinical trials, but you don't have the infrastructure in your own clinic to do it, so let's partner together.

And then I think the final piece of all of that is that we can by doing all of that really implement remote clinical trial screening. There are so many clinical trials that fail due to insufficient patient enrollment. There's a huge, huge problem for the entire pharma and biotech industry, but I think it's an even bigger issue for patients because when I think about all of the work that I've done over the years with patients with rare diseases any clinical trial that fails due to any other reason than a lack of efficacy is a total loss to the patient community is real failure.

So let's not do that. Let's screen patients in their home communities, sometimes right in their own home and then we can really talk to them about how could we support you as a clinical trial participant if that's something you wanted to do. What would that take? Where could you travel to given the support? How frequently could you do that? What would we need to implement closer to home to help you to be part of this?

**Taren:** That's excellent and it would obviously solve as you said one of the biggest problems in clinical trials and that's patient recruitment and patient retention and as we look at the dearth of investigators that is predicted to be in the future we really need to start to think about some telehealth and some other ways in which to support clinical trials for the benefit of everybody as you said. So this is exciting. Congratulations.

**Karmen:** Thanks.

**Taren:** Let's switch tracks a little bit and let's talk about you as a leader. I understand that you serve on a couple of boards, I'd love to hear what that experience is like for you and tell me why board service is important to you.

**Karmen:** I do. I serve on two different boards both related to a rare disease called Usher syndrome. Usher syndrome is the leading cause of combined deaf-blindness in the Western world. So many years ago now, gosh I would say like 13, 14 years ago maybe I was in clinic working as a genetic counselor and we had a family come to us and we diagnosed their son with Usher syndrome. He was born deaf. He had cochlear implants at the time that we saw him and was starting to lose his vision. This is a devastating diagnosis and that family left that day and told me later that after lots of crying they pulled it together and decided that they needed to do something.

They just really desperately needed to do something and after doing little research they decided to start a foundation to raise money and awareness to try to help fund treatments, research toward treatments. And I helped them and just volunteered with them for a while and then eventually they asked me to join their board and then I've served on that board for now probably the last 12 years and then at some point a few years into that, and that's a local organization, it's called the Hear See Hope organization in Seattle which is where I live and then a few years into that experience the Usher Syndrome Coalition was born.

That organization is a national organization that really works to try to provide kind of a single home for patients and families affected by Usher syndrome sort of a one place to go and get support information, but also they work really, really hard to try to insure that researchers are actually talking to each other and sharing data and thinking about what is the roadmap toward meaningful therapies and how can we ensure that we have people doing different parts of it and not overlapping and doing all the same things. So this can be difficult to manage, but they've done a great job with it so I started serving on their board as well because they asked me to come on board and do that and it's been a really rewarding experience.

**Taren:** I think it's wonderful that you are serving for organizations that are so dedicated to these underserved patient population specifically this one Usher's disease and it is so devastating and I have to say I had not heard of it before, so thank you for sharing information about this. And I find it so fascinating that so many of these rare disease organizations spring up from grief as you say, grief and then into hope because at the end of the day what else can these parents do. They need to do something and this is their way of doing something, so your support is very admirable.

**Karmen:** I think most people who get into the field are very passionate about it. They believe in it strongly, so here at Informed DNA I have other colleagues who serve on boards as well and they didn't go out searching for a board position. They just said, 'Hey, for the last three years I participated in a Susan Komen walk for breast cancer, but there is a local organization that's

doing some work as well and maybe I'll just volunteer locally for them.' And then one thing leads to another and they end up serving on their board because that board realizes, that organization realizes oh having a genetic counselor experience, that perspective on our board would be really valuable and so it's pretty organic, but I think anybody who's interested in serving on a board it just usually starts from offering to help, really just offering.

**Taren:** I know so many of our listeners are looking for ways to pay it forward to provide service and give back based on their career experiences and it's hard, let's face it it's hard to get on to a board especially on a big public board so one of the ways to get your feet wet is through a local board where they have an affinity or a passion for it because I think it makes it easier also.

**Karmen:** Absolutely. And the smaller ones often really need help and so having that perspective, having that help – I've told my kids, my teenagers who have these volunteer requirements make sure that what you're doing when you're volunteering is something that you're passionate about, but it's also something that fills a need. Don't go out and volunteer to check a box on a form. Make sure it actually fulfills a need, so ask what they need. Don't say this is what I'm going to do for you.

**Taren:** Also great advice. Thank you. Talk to me about how you lead your teams. How would you describe your leadership style?

**Karmen:** I guess I hope that the members of my team would say that I am a leader who looks for the strength in others. I think that's certainly what I try to do. Some of the genetic counselors – and I'm going to speak mostly about genetic counselors because InformedDNA is a company that is built on genetic counselors. I don't know. I might get in trouble for showing up this number, but I'm going to guess that like 75% of our workforce is genetic counselors who do a variety of jobs. They don't all do clinical genetic counseling, but most of my experience as a leader has been in leading groups of genetic counselors so I'll speak from that.

But some of the genetic counselors that I work with are clearly natural leaders who we try to find opportunities to help them to develop any of those skills, but not everyone was meant to lead. I think that's clear. So I really try to look for other strengths and other interests because ultimately I want every one of them to feel fulfilled. I want them to stay with us, so I want them to feel like this is a place that listens to who I am, what are my interests. I recently promoted someone to work with me who is incredibly detail oriented, so so much more so than I am which is such a great balance to me and to my own strength, but I very much talk to her about that when I hired her, when I promoted her on the team.

That was a huge part of why I chose her and promoted her and wanted to ensure that she agreed with that strength and it's something that she actually enjoys doing because I end up giving her a bunch of tasks that are very detail-oriented and she loves it. Hallelujah. Yeah, hallelujah and it's probably worth pointing out that some of our genetic counselors here are

amazing counselors and we're so lucky to have them doing exactly that and they're not looking to do anything different. They love being in those vulnerable moments with patients and doing that work and so it's important to recognize that, too.

**Taren:** Talking about those individuals who have to work with patients in those vulnerable moments and as I alluded to earlier it really takes a special kind of person to be able to do that work. How do you keep your teams inspired and motivated when often they're dealing with really difficult conversations and it could become I would think quite weighty on someone?

**Karmen:** It can become weighty on someone and I think over time there is a little bit of compassion fatigue that happens to some people and I don't mean that like they stop caring.

**Taren:** No, of course not.

**Karmen:** But it's like – no, of course not, but there are some people who get to a point like wow, this is just really hard to continue to do day after day and so those are the people who we try to look for other opportunities and wait for them to grow and develop other skills. But I think for the genetic counselors who genuinely love what they're doing, but do still get sometimes a little weighted down by the difficulty of some of those conversations and by just the weight of what this means for patients and families I think the number one thing that I probably can do to help inspire and motivate them is just help them to realize how much we are making a difference. That we are helping people through these really difficult times and we get patient feedback that's just, it's amazing.

I said before it's like a drug to hear people say so frequently oh my gosh, that was just incredibly helpful to me at a really difficult time in my life, thank you for what you do. But then beyond that on the kind of bigger picture beyond one family, beyond one patient I try to help them to remember our team. I try to help them remember like what we're doing we're enrolling more patients in clinical trials. That's leading to therapies. We have been really entrepreneurially involved in helping to support clinical trial screening for programs that have led to FDA-approved therapies that have completely changed the landscape for patients with multiple different rare genetic diseases. That's incredible. So it's pretty great to have those, to have the perspective of what you're doing on an individual patient basis but then on a bigger picture scale.

**Taren:** That's awesome. And so how do you measure those successes because that has to feel great when you are able to change a disease paradigm? That's incredibly intoxicating I would think.

**Karmen:** It is. I mean I can't really measure what we do based on whether or not a drug gets approved, right.

**Taren:** No.

**Karmen:** That's pretty far out of my control, but I think when I came to InformedDNA it was really with a singular purpose, which was to deliver that same level of specialty care that I did previously in an academic research clinic here on a telemedicine model and I think 10 years later when I'm here directing clinical trial services I think that purpose still guides me and it really still guides our success. So I guess what I'm saying is in everything that we do are we increasing access to care. Because of our programs, are more patients accessing and understanding genetic testing? Are more patients with rare diseases choosing to participate in clinical research because the studies have become more available to them? So if the answers to those questions are yes, I think we're succeeding.

**Taren:** Fantastic. Now, if you had to wind back, go back in the way back machine and think about a piece of an advice that you would give to your younger self, what would that be?

**Karmen:** I think embrace change. I actually loved my job in academia. The only reason I left was that my family and I moved. So when I worked in an academic medical institution that was in Portland we moved to Seattle so I couldn't quite continue working for them for really long. That wasn't going to work and saying that at this job at InformedDNA, that was not an obvious choice. At that time, InformedDNA was very small, really just getting their feet wet and I was not at all sure this company would be successful. But I believed in the mission and I was really impressed with the people so I thought well, I'm going to here. I'll just be, I'm going to be here. That was 10 years ago.

And today, InformedDNA is the nation's largest provider of genetic counseling and genetics benefit management services. I never would have dreamed that would happen and if my family and I hadn't moved for other reasons I never would have had that experience and all of the roles and experiences that have happened as a result of that, so I just think there's so much to be gained by just embracing change.

**Taren:** Love it. Can you identify one wow moment in your career that either changed the trajectory of your career or provided you with a lasting impression?

**Karmen:** Yeah. This is actually another really easy one for me to answer. You might think it's going to be a patient story and it's actually it's not a singular patient story. I have so many of those, but for me so I had this incredible opportunity in the fall of 2017, a couple of years ago. I was invited to serve as an expert responder for Spark Therapeutics' presentation to the FDA Advisory Panel when they were going to review their data on gene therapy for RPE65-related retinal dystrophy and that was such an honor. It was a really cool thing to be a part of and for others there, listening to Kathy High and others at Spark present their clinical trial data and listening to the FDA's response and then in the afternoon patients and families got up and spoke

about their experience and how the same therapy had completely changed their lives. I was so incredibly emotional. It's really emotional.

And then at the end of the day, this whole day long experience, at the end of the day the Advisory Panel voted right there, right there in front of us they voted 16 to 0 in favor of approval and that represented the first gene therapy for any genetic disease in history that went on to get approval by the FDA, and I got to be there. That was pretty awesome.

**Taren:** So cool. I had chills. That is like, that's a whole *woop woop* moment, right?

**Karmen:** Yeah, yeah. And you know after so many years of being in that room, diagnosing patients and talking to families where there's nothing, no treatment and there's nothing we can do. I think I mentioned that, but there's no meaningful treatment and then they have the first one and it's like here we go, here we go, we are going to treat these diseases.

**Taren:** That's fantastic. Thank you so much for sharing that. That's great. What a great story. Karmen I'm looking forward to what you do next in terms of genetic testing and the progress you make in making sure that more patients get enrolled in clinical trials so that we can develop better medicines to treat these rare diseases, so thank you so much for your passion and your dedication to the industry.

**Karmen:** Thank you so much. It's great to be here.

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