EPISODE THREE:

Moving Diagnostics to the Forefront of Precision Medicine

Dr. Hannah Mamuska, Alva10 | December 28, 2018

Welcome to The Precision Medicine Podcast, where experts come to discuss the problems oncologists, reference labs, and payers face as precision medicine grows, and consider solutions for advancing the quality of patient-centered cancer care.

Jerome Madison: I'm Jerome Madison, Vice President of Provider Relations at Trapelo and one of the hosts of the Precision Medicine Podcasts, and today, I have Hannah Mamuzka, founder of Alva10, and we'll be talking about how to improve the perceived market value of diagnostics and truly move it to the forefront of Precision Medicine. Hannah, thanks for being a guest, and welcome to the Precision Medicine Podcast.

Hannah Mamuzka: Jerome, thank you so much for having me. It is great to be here.

Jerome Madison: Tell us about your background. I know about your background, we've worked together in the past, even before Precision Medicine, that was not known as Precision Medicine, but share with us your background and what inspired your vision to create your company Alva10.

Hannah Mamuzka: So, my background, I'm a Molecular Biologist by training. I started out in the lab, I worked at NCI, I worked for a couple of small Pharma companies that got acquired by Big Pharma. I worked under a drug called Velcade for a number of years, which is a targeted therapy. I really saw the evolution of what we now think of Precision Medicine, being the ability to use biology to develop drugs that are targeted to specific molecular mechanisms within patients. And, I also saw that we had the technology to identify those patients and that we're not really using it.

And so, I transitioned my career to the business side 12 or 15 years ago to really get a better handle on how we drive technology into our health care system. What I really observed is that one of the biggest hurdles towards getting technology accepted and used for patients within our health care system is reimbursement. And so, I founded Alva10 three years ago to broker better relationships between health insurance companies and diagnostic developers who have the technology that can really impact health care.

Jerome Madison: Yeah. We shared for years diagnostic testing in Oncology has great potential to save patients valuable time and finding a right drug that works for them. Saving money, because, as it has been stated by many health care professionals, the most expensive drug is the one that doesn't work, right? And also saving patients from excessive or unnecessary toxicity. Yet, you express in your writings that payers still undervalue these diagnostic tests. In fact, you make a statement in one of your articles, you call diagnostics a downward cycle of low value leading to poor Precision Medicine. That's a strong statement, so explain a little bit what you mean by that.

Hannah Mamuzka: Sure. You know, I think it's a... I think anytime there's a downward cycle there's an opportunity for growth, and that's really what we're trying to do at Alva10 is show really what the value in diagnostic technology could be. But if you think about it now that you have diagnostic tests that are paid between $100- and $200-dollars guarding access to drugs that are $150,000 to $250,000 dollars, that is enormous disparity in value, when the access to the drug is completely predicated on that diagnostic test. That diagnostic test inherently has value, but is not being paid for in the market, and what this does is this really creates a missed opportunity for additional diagnostic tests to break into the market and impact patient care.

Hannah Mamuzka: Even outside of Oncology, no patient wants to go on a therapy that they're not going to respond to or have such a severe adverse event that the adverse event is worse than the disease they are being treated for. But for the majority of targeted therapy there is on the market today, there are no [inaudible 00:03:49] diagnostic tools to stratify those patients.

Jerome Madison: Yeah, I mean do you think that the lack of peer support kind of discourages innovation of these tests in involving Precision Medicine?

Hannah Mamuzka: Well I think that both parties are at fault, frankly. Diagnostic companies generally approach payers with a fully-baked test, because that was how they were taught to enter the market. Historically, diagnostic companies just in order to apply for a CPT code through the AMA that would allow them to eventually get paid, they had to launch their test onto the market, and that test then had to be used by "many labs."

Hannah Mamuzka: And so, that taught diagnostic developers to rush onto the market as quickly as possible, so that you can apply for your CPT code, so that then you can wait the 18 months it will usually take in order for you get paid on that code. And so, what diagnostic developers have been taught to do is wait to generate robust data until you're on the market fighting for coverage.

Hannah Mamuzka: And so, if you think about that from the payer perspective, what that means is you have all these diagnostic developers essentially beating down your door for payment for something that they would admit isn't fully validated and doesn't have maybe an update behind it to support that. What the diagnostic industry is seeing is that has translated into poor coverage, into low value, and into a fee-for-service reimbursement system that doesn't really allow for innovation. When I say for allow for innovation, it's very difficult to get paid on a cost-plus model, but then be expected to generate the same load of data that Pharma generates when Pharma gets paid on the value that the drugs provide to the market.

Jerome Madison: I've seen you in action when it comes to someone with opposing viewpoints that say, big Pharma companies should have control of developing diagnostics, since after all it's their drug that will ultimately deliver the beneficial outcome. I've not seen many people take on that perspective as well as you have (laughs). So, what do you say to those people who believe that Pharma companies should have control of developing diagnostics, instead of you know, laboratories controlling their own destiny.

Hannah Mamuzka: So, you know, I'm not anti-Pharma. I think some of the innovation in Pharma—especially over the past decade—has been absolutely incredible. I think that there are new therapies that are extending and changing and improving lives. And I think that, when they work, they're absolutely worth it financially. But I also think that it's not in Pharma's business interest to develop tools to shrink their market, particularly if the regulatory agencies aren't going to require them to. And I think that for there to be a robust diagnostic market, the diagnostic market has to be able to stand on its own feet, develop its own tools, and establish itself in the market that allows diagnostic tests to be paid.

Hannah Mamuzka: You know, the example that I talk about a lot when people talk about companion diagnostics is KRAS and the use of KRAS testing with EGFR therapies. So, if you remember way back, the first targeted therapies in oncology were coming out, the Pharma companies that were developing EGFR therapies submitted their data to the FDA, and the FDA said, "Okay. Looks good. But based on this data, you really need to go and develop a companion diagnostic to identify patients who have mutant ceres." Because it's clear from the state of the patients who have mutant ceres are not going to respond to the EGFR therapies.

Hannah Mamuzka: Okay, the Pharma companies have commissioned two large diagnostic companies, Roche and Qiagen, to develop diagnostic tests to detect the presence of mutant ceres. But the test is pretty small, it's not really comprehensive, it only looks at mutant ceres on codons 12 and 13. If you look at NCCN guidelines, ASCO guidelines, ANT guidelines—pretty much every cancer body that puts out clinical guidelines—you'll see that the guidelines state that you should actually look at four codons on KRAS, four codons on NRAS, as well as BRAF and BI3k. But the Pharma companies are not incentivized for that comprehensive diagnostic test to be a companion diagnostic with their drug, since the FDA didn't require it. This disparity between the KRAS IBD companion diagnostic and the extended RAS testing that's in guidelines means that patients are over treated by about 28% when they are treated with the IBD.

Hannah Mamuzka: It's in the interest of the patients, payers, and the diagnostic companies to have the most robust diagnostic tests. It allows the diagnostic labs to make an argument for value, allows the payers to not pay for therapies that are ineffective and adverse events that are unnecessary, and it allows the patient to have a better shot of going on a better therapy that they're going to benefit from. That may not all be in the interest of the Pharma company.

Jerome Madison: For those who may not know, you write articles, and you speak on the topic of the value of diagnostics and in helping to improve the perceived value of molecular diagnostics. You write for the Journal of Precision Medicine and, you wrote a fascinating article on the role of Pharmacy Benefit Managers or PBMs and the amount of control and, quite frankly, power they have to dictate which drugs were prescribed. But in the era of Precision Medicine in highly specialized drugs, you suggest they're not equipped to serve their customers, and, of course, their companies are the insurance companies and employers. So, why is that? And what is the potential solution for it?

Hannah Mamuzka: So, I think diagnostic companies and PBMs could work well together. You know, right now, PBMs make deals based on pricing and volume discounts that they can get from the manufacturers of drugs that they then bundle and pass on to their customers, which are the insurance companies and large employer groups. And for the most part, especially outside of Oncology, they're looking at all drugs as being equivalent. So, if a drug...if you have a disease like Multiple Sclerosis or Rheumatoid Arthritis for example, where you have a number of drugs, all of them being targeted therapies but none of them having significant superiority over another in terms of clinical efficacy.

Hannah Mamuzka: None of them having any diagnostic tools right now to stratify patients. The PBMs are making deals based on pricing…based on volume discounts that they can get around pricing. And so, if you take Rheumatoid Arthritis for example, what you end up with is Pharma companies making a strategic decision to offer certain discounts for certain drugs, to drive volumes of those drugs into the market. That may have nothing to do with the efficacy of the drug.

Hannah Mamuzka: This has been well published in Rheumatoid Arthritis, patients first-line biologic therapy is an anti-TNF inhibitor at least 90% of the time. Despite the fact that anti-TNF inhibitors, these are drugs like Humira, Enbrel, and Remicade, only work about 32% of the time in patients in which they are prescribed. There are multiple other classes of drugs that have similar response rates, but the PBMs have put anti-TNF inhibitors on the top of the formulary in the absence of tools to stratify.

Hannah Mamuzka: Now, if there were diagnostic tools that would stratify patients for response to each of those classes, that would be a very different conversation both for the PBMs and the insurance companies with regard to which of those patients received drugs.

Jerome Madison: Yeah, you made a powerful statement in that Precision Medicine is more than just cancer care, it involves many different diseases. And your conversations with payers, how are they responding to that? Because you just mentioned anti-TNF therapy, you know, what are the other diseases that you see that they're interested in or innovation coming down the pipeline to expand Precision Medicine to other disease states?

Hannah Mamuzka: I think it has really been eye-opening for them, and they really see it as a potential opportunity. Because we all talk about Precision Medicine in Oncology for a variety of reasons, but Precision Medicine exists in every disease. Every drug that has been developed over the past 30 years is a rationally designed molecule that hits a specific pathway within a specific disease [inaudible 00:12:11] And so, there's enormous opportunity to use diagnostic technology to stratify patients for response, prediction…for adverse event-prediction across virtually all diseases.

Hannah Mamuzka: If you look at Multiple Sclerosis, and you look at all the different drugs that are approved in each class of Multiple Sclerosis, patients can start out with nine options at the beginning of their disease journey. Physicians really don't have any tools to determine which drug the patient should start with. So, patients are treated with an initial therapy, and they don't response more than 60% or 70% of the time, so then they move on to another therapy, and if they don't respond to that drug, they move on to another therapy.

Hannah Mamuzka: This is extraordinarily expensive. Not just in terms of dollars, but in terms of disease progression, because if you have a progressive disease like MS or Rheumatoid Arthritis where your body or your immune system is attacking your joints, or where you're seeing deterioration in your muscles, you don't have time to waste on ineffective therapies. Which is why we need more diagnostic tools in the market to be able to assist physicians in determining what patient should go on which therapies.

Jerome Madison: Here at Trapelo, we're leading the conversation to greater access and scale of Precision Medicine by eliminating financial and administrative burdens like prior authorization. You work with payers in your conversation with insurance companies. What are their concerns with paying for genomic tests, and do they see a future where diagnostic companies are reimbursed consistently at profitable rates to encourage innovation and new development?

Hannah Mamuzka: They do. I think the conversation is changing. I think there is starting to be an understanding that diagnostics provide opportunity for payers to see better outcomes in their patients. One of the things they are concerned about—which I think is why Trapelo is such a fascinating company—is the ability for insurance companies to see that a test is used, see what the data from that test provides, and then see how the physician uses that data in the management of their patients. Because, you know, in our work with the payers, we have heard it's such a challenge for them to understand that they're paying for certain diagnostic tests, and then they don't know how that data is being used or if that data is being used correctly. I think there have been some assumptions that, you know, all patients are getting treated up to guideline standards.

Hannah Mamuzka: All physicians are following the testing that they should be following. And then, when they get into the data, they find that that's really not true, and part of this is physician education, part of it is access to diagnostic testing, part of it is turn-around time when a patient needs to be treated. But the ability to follow the continuum of care and managing that data and understand how diagnostic testing is actually impacting their patients is really critical for the uptake and utilization of diagnostics.

Jerome Madison: You have been in the Precision Medicine industry for a long time. You remember, I mean, those were the earlier days, where we had to take fresh tumor specimens from surgery. In vitro assays, and I distinctly remember physicians calling it snake oil, like...you know, this is [inaudible 00:15:34] marketed therapy. That's crazy. If it was anything special, we would have done it years ago (laughs). It's a tough business to say the least, but another reason why I have a great respect for you is because you are a college athlete, specifically you ran track, which to me is one of the toughest sports. So, how has your competitive spirit helped you stick it out in this business?

Hannah Mamuzka: Well, now I'm a marathon runner, which I guess means I like to just constantly pursing things and I have the ability to stick to it. You know, running really clears my head, it helps me think, and it keeps me sharp. Both physically and mentally. It's a long road, especially starting a company. You have to have the endurance and the mental fortitude to just put your head down and keep going, and I think that has actually helped me tremendously over the past three years.

Jerome Madison: Outstanding! For those out there who want to connect with you, do you have any social media platforms, whether it's LinkedIn or other. Give them your website, so they can connect with you.

Hannah Mamuzka: Sure, absolutely. We are on LinkedIn and Twitter. Our website is Alva10dx.com, and we are actively working with both payers and diagnostic companies, and we would love to hear from you.

Jerome Madison: Absolutely. We thank Hannah Mamuzka of Alva10, and of course, all of our listeners for joining today. We hope you'll tune in for the next episode of the Precision Medicine Podcast, and don't forget you can download full transcripts of today's episode at PrecisionMedicinePodcast.com. If you enjoyed this episode, you probably would know someone who would too, so please tell them! They'll thank you, and so will we. Hannah, thank you for delivering good stuff and being on the podcast today.

Hannah Mamuzka: Thank you so much, Jerome. (song)

About Our Guest: Hannah Mamuska, Ph.D.

Hannah Mamuszka, Founder and CEO of Alva10

Dr. Mamuszka is a senior executive in the Cambridge, MA biotech community, with extensive experience in both drug and diagnostic development, validation, and commercialization. With more than 20 years of experience in healthcare from the bench to the business side, she believes that diagnostics are the key to Precision Medicine. Her thorough command of cutting-edge science compliments her business acumen when evaluating the complex diagnostics deals that shape this industry. She is a well-respected voice for diagnostics in the industry, and a natural choice to bring change to this field.

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