Embracing Innovation: How Today's Tech is Transforming Translational Medicine for Patients with Cancer

Gary Karr: Hi, I'm Gary Karr. I'm a senior group director at Real Chemistry, and we're here at Takeda with Chris Ward and Julie Dixon to talk about data, digital and technology. Thank you both for being here.

Julie Dixon: Great to be here. Thanks very much for engaging in this dialogue; it's a great and exciting topic. I'm Julie Dixon. I head up the Global Regulatory oncology team here at Takeda and have been here several years. But, you know, it's a really passionate topic of ours and looking forward to the discussion.

Christine Ward: Thank you. And I'm Chris Ward. I'm in the Oncology Therapeutic Area unit, and I head up the Oncology and Cell Therapy Precision and Translational Medicine Group. This is a timely topic because my team and I are actually spending a lot of time digging into ways where we can leverage data in the work that we do every day. So very interested to have this dialogue today.

Gary Karr: Thank you. And we're really excited to be here today to talk about this. Both of you have a wealth of experience going back to when data and digital were probably not a major factor, certainly not the digital, the technology part of it. So, if you could just tell me a little bit about how you think things have changed over the past 10, 15, 20 years. Julie, I'll start with you.

Julie Dixon: Yeah, thanks. You know, I think it encompasses almost every part of our daily lives, but also from the science, I think about the oncology aspects, even how we do our simple health; the rate that we can actually diagnose disease, the way we can treat disease, the way we can detect the disease, has, I think, made tremendous improvements in the last few years. And with cancer, the sooner you can detect it and as soon as you can try to treat it, the better prognosis for patients. So, you know, I just I look back on the technologies that we have now, and things are very different for patients. And that's a great thing.

Gary Karr: So if 10 years ago you, or 15 years ago you, woke up, Chris, and realized what you can do today, how amazed would you be?

Christine Ward: Wow. In my space, in precision and translational medicine, the improvements and advancements have been mind-blowing. Nowadays we have the ability, if we want, to look at the expression of certain target pathways or biomarkers rather than just being limited to the small number of patients in our trials. There are now real-world databases where we can go and search and understand the distribution and the prevalence of certain biomarkers. 10, 15 years ago this was a wish and now the wish is becoming a reality. And then I also think about clinical trials, how we conduct them and how we find patients in clinical trials. We're right on the cusp now of being able to, as we design a trial, being able to go to databases and say, where are these patients? And making sure that we're bringing in patients into these studies in a way to ensure success and ultimately bring the treatments to patients sooner.

Gary Karr: So what does that mean? I want to follow up with that for just a second. What does that mean to be able to find what is essentially new patients that you wouldn't have known out there? What does that mean in terms of the innovation and in terms of the speed of that innovation to getting to the marketplace?

Christine Ward: I think in oncology, we have a lot of targeted therapies. I think our drug, is a good example. It targets EGFR exon 20 and lung cancer and it's a relatively small population. And I think knowing and being able to go out there and see where those patients are now that many patients are getting next gen sequencing to detect that mutation, I think that's a good example. I think the challenge for us is how do we do this for the immunotherapies that are emerging? How do we go out there and find patient subsets that have particular target pathways? And now the tools are finally becoming available.

Julie Dixon: And maybe I would add from the regulatory perspective, making sure you have the right representation of patients. So, this is allowing us to reach underserved populations; different demographics that aren't always included in clinical trials but have been a focus of ours now. So, I think these tools and the ability to access those patients, to invite them in, is a really huge advancement. And you know, in other aspects of the clinical trials, with some of the remote monitoring, technology is really enabling us to do some things decentralized instead of having the burden on patients to go to centers and do things. They can do things more digitally now.

Gary Karr: So this is decreasing the patient burden at the beginning, not just the end where you're getting the treatment, but at the beginning part of the equation. That must be one of the biggest impacts on getting a more diverse base of patients for a clinical trial.

Julie Dixon: Absolutely.

Gary Karr: They can't get there. They can't go to the trial. Well, now they can. I mean, it's got to be just an amazing advancement for people who are rural black Americans, Hispanic Americans. There are people that are traditionally underrepresented, right? Any other particular groups that you think of that we're really looking at?

Julie Dixon: I think back to Chris's point of figuring out technologies, allowing us to figure out the population we should be studying. So, we have a much more focused approach instead of having to study 500 people, we might be able to actually narrow it down to a smaller patient population so that we can actually target the clinical trials more precisely and of course increase, hopefully, the clinical benefit for patients. So, things just go quicker, quite frankly, and that's a benefit to patients.

Christine Ward: And then I want to add something to that – I think one of the things Takeda is doing that I see as an industry leader in this space is really going out and understanding how potential patients that could become part of our clinical trials, actually look and learn about clinical trials. And so, I think understanding the social media aspects, the local community aspects and as a company now we're starting to take a very active role in leveraging those communication pathways. And I think it will only benefit patients in the end.

Gary Karr: Where is it that Takeda you think is out in front of the rest of the industry? Not just from a competitive standpoint, but also in ways that you might be able to kind of educate the rest of the industry.

Julie Dixon: We're trying to take a holistic view across the whole organization. I think it's been very clear we're committed to data and digital to help all facets of our development. Again, we're looking into decentralized clinical trials. We're working with consortia. I'm in regulatory with organizations trying to innovate of how we can do things from a cloud-based instead of paper or electronic with other health authorities to expedite reviews. So, we're doing it from an operations perspective, we're doing it from clinical trial perspective, we're doing it, as Chris mentioned, identification of patients. Our science is rooted in it as well as, again, trying to enhance the patient experience with trying to understand a digital footprint for a patient to see how

technology can enhance our marketed agents and how they feel and what we can do to make them better. So, I think we have a very holistic view and how we're looking at the science.

Christine Ward: What I would add is building on the consortium theme. So, one of the things that's very powerful in our space in oncology is that many of us generate biomarker data in our clinical trials in relatively small populations. What winds up happening is if we can aggregate our data with that from other pharma companies around drugs with common mechanisms, we can find ways and paths forward to validate new biomarkers for different uses, perhaps monitoring treatment response or predictive biomarkers. One of the consortia that we're involved with right now is Friends of Cancer Research, which has a consortia called CT Monitor. It's looking at ctDNA and the impact following tyrosine kinase inhibitors – is one part where we're contributing data. And then they're also looking at it for checkpoint inhibitors. And we were able to participate in the tyrosine kinase inhibitor arm. That group is coming together to bring all the companies together that have data. And together, by aggregating our data, we can see trends that perhaps no one of us could look at because our population is, you know, it's fewer numbers of patients. This, to me, is the future, and we need to continue to partner in this way to move the field forward for patients.

Gary Karr: So, one of the big questions that I have when it comes to data and digital technology advancements is whether our reimbursement and regulatory systems are keeping up with that. One of the most important things in health care is: can you get the medicines to the patients? Can you get the innovations to the patients, and can they begin to have access to them in the ways that they can take them? So I guess this is more your purview, Julie, than yours, Chris, but how are we helping the regulatory and reimbursement systems, the payers and the regulators keep up with these advancements?

Julie Dixon: That's a great question, and you know science is always ahead of the regulators and the policies. How do we play that catch up and help bridge that gap? We have a really great policy team that is working very diligently too with external bodies to talk through things, and to influence where we can. The regulators have committed to this. So has the FDA – it's very much on their agenda to be bringing in real world evidence and how can we use data and digital decentralized trials to really reduce burden. And it's not just FDA – you have something from European Union, we have Japan, so you're having definitely the global health authorities around the world putting out guidelines as to what do they need to see? In this space, a lot of it is about the input of the data. So how can we standardize the data well enough that we can use it? That's where the real advancements need to come – how can we work amongst all the stakeholders to collect the data when we talk about having electronic health records? If we don't standardize how those health records are put in, you can't aggregate them across the world.

Gary Karr: Ultimately, Chris, what matters with data, digital and technology is the impact it makes on someone who has cancer. It ultimately never matters unless you can make it impact the person who needs to take that medicine, who needs to have access to that medicine. How are you seeing that impact translate?

Christine Ward: The obvious answer is speed to patient. Right? We have medicines that we're studying in our clinical trials. We're always aiming to study it in the right patient population, build these hypotheses – robust hypotheses – for where these drugs are going to work at the very beginning, and then recruiting the trials as quickly as possible. It's not a one-stop. It's not like if we inject data in digital one part of this process, it's going to be across the continuum. And one of the things that I'm seeing now that I find very inspiring and encouraging is the embracing of the digital mindset. Digital is not a place that can just sit in one part in an org like up in the high tower, and then people throw like, "Hey, use this digital tool." At the end, as a drug development organization that cares about bringing our medicines to patients as quickly as possible, we need to all embrace digital every step along the way. And in my space – the precision and translational

medicine space – we believe within our core, our deepest hope is really that our approach will help accelerate our treatments to patients because we're developing these hypotheses early on that allow us to generate compelling data, work with terrific partners like Julie and our regulatory group and get the data in front of the agencies as quickly as possible so they can also see what we see in the data.

Gary Karr: One of the great things that I hear about Takeda, that I hear from people at Takeda, is how often you're partnering with and working with a wide variety of people, in and out of the industry: academics, patient advocacy groups. How often, Chris, is this subject of data, the subject of discussion and how important do you think it is that we at Takeda help lead the people we work with in this data / digital transformation that we're trying to do?

Christine Ward: We are a data and science driven organization and culture. One near-term example that comes to mind is there's a particular clinical study that we're working on right now where we have compelling data that we may be only able to study the effect of the drug in the tumor, not in the blood, which is going to require potentially biopsies being collected from patients. Right? So we could just push ahead, write it in the protocol and then work to get it, and then it becomes difficult, but by showing that data to our investigators. Right? Helping them see what we see, so then as they're interfacing with the potential patients that could come into the trial, they're really vested in the why. That to me is also something that's changing; we're showing that data and helping investigators and patients get as excited about the trials as we are.

Gary Karr: And I was thinking, when it comes to your role, Julie, you can't just do it in your silo. You have to have other partners. Maybe there's academics you talk to, both of you. Maybe there's other people at companion organizations. They might even be, quote on quote, competitors. But you're all working on the same challenge, right?

Julie Dixon: Absolutely. And we touched upon this. This is a full cross functional team, clinical and then the clinical stakeholders. We've got key opinion leaders, as Chris had mentioned. We also have an organization that works very closely to finding these external data sets and data for us. And we work with other institutions that have data collected with outcomes that we can partner with and discuss with and bring that in-house to utilize for hypothesis generating or augmentation of our own clinical data. Our statistics group, in our bio stats there, they're a key functional group. We often have, again, consultants that come in, but absolutely regulators, as we talked about already, and patient advocacy groups are huge.

Gary Karr: And of course they can see the impact, so they understand it. And the policymakers, not just the regulators, but the policymakers, the people making laws in Washington or in the state houses can see the actual impact as well. So, we started off, Chris and Julie, with a discussion about can you imagine yourself ten years ago and where we are now, but let's go forward ten years. Imagine we're sitting here discussing what data digital and technology has done for Takeda, for patients, for the industry overall. What kinds of things have happened? What's your dream scenario for what's happened in the next ten years?

Christine Ward: I'll take that one first. I'll give you my wish list. At the end of the day, we're using database technology and clinical trials – and it's not just Takeda, pretty much most pharma companies – that's very similar to ten or 15 years ago, And it's clunky, right? Any inquiry has to be programmed into the database, right? It becomes very difficult to say, "Oh, I have this question, what about this patient type? What about this?" In the future, what I aspire and look forward to is when I get that idea, I can go to my computer, type the query, and I'm able to search my own internal clinical trial data. And so, I think within the ethical confines, being able to mine our own data in real time is something that I look forward to.

Julie Dixon: We talk a lot about a tumor. Oftentimes you need to have a biopsy of your actual solid tumor. That takes time – to sequence, to send it out. In the future, it would be great to be able to take some blood-based, noninvasive biomarker samples that you can get a diagnosis of sequencing in a matter of days rather than three weeks. I think that will help the speed of diagnosis. I hope we have many more therapies that are more effective to specific targets; we have areas of cancer that we still haven't been able to make a strong headway like pancreatic cancer and things like that. So, my wish is that we would have targets – ways to actually address those unmet needs for patients and really diagnose and bring medicines to patients a lot quicker. I think from a more practical perspective, from a regulatory perspective, we actually submit things at an agency, it's done with lots of PDF documents, and you build it into a backbone that goes in. Here, again, it's a cloud. You just upload your data into the cloud. You know, a regulator can see it on their end, however they want to look at that data, they can send you queries, and you can do it through a cloud base rather than, a backbone and days of submissions and things like that. So, there's a lot of practical stuff going on.

Gary Karr: The simple things can get done more quickly through data, digital and technology to leave the more complicated things to actual human beings. The human being relationships that you need to have, the science expertise that you need to bring, Chris. Now I wonder in a very big picture way, do you think there are some aspects of cancer where we really don't have good answers for now, that ten years from now, because of data, digital and technology, we'll have much better answers for how to treat?

Christine Ward: Oh yes. Where do I begin? There's a subset of colorectal cancer called microsatellite stable, CRC, MSS stable. Graphically, when you think of all colorectal cancer it's the patients that are below the waterline. There are more patients that have this MSS stable than the microsatellite high. Many people think of these as, oh, MSS-CRC is one cancer – no, it's probably 80 cancers. So, what I wish for is someday, we take all the data that is available, from Takeda, consortia, external partners, published data, and we can feed it through the digital and AI approach and then phenotypes spit out of what those segments really are. And then we can study it and say "Oh, well this segment is driven by this mechanism, these treatments are what we should study there," and then it would generate new hypotheses for us, for both our discovery team who are coming up with new drugs and new ways of targeting as well as positioning drugs that might be ready for the clinic now, but maybe we weren't thinking of positioning them in that indication, so bringing it back to the patient. At the end these digital approaches will help us accelerate the advancement of cancer treatment for patients.

Gary Karr: So, we'll have a better chance of solving these problems and then maybe giving people longer life?

Christine Ward: Yes, that's what it's all about – extending the life and quality of life for patients so they can do more and more productive things.

Julie Dixon: Yeah, and to add, I think for cancer, we start looking more at the functional cure. We've already made huge headways where the regulators are already more interested in making therapies more tolerable. Because patients are living with cancer longer – it's becoming a disease they're living with versus a disease they're dying from. And so, I think that's really important to reflect on when we start talking about what are going to be the new modalities, the new types of drugs that are going to come. Data and digital is allowing us to do new drugs that we've never done before. We've heard about CAR Ts for a while but now you're having in vivo CAR Ts, you're talking about gene editing, all sorts of things that without data and technology, we would not be able to implement. So, again, I think it's also going to lend itself to novel therapies that we don't have today to hopefully help us get closer to functionally curing cancer rather than just living with the disease.

Gary Karr: One of the great things about this talk we're having today and the series we're doing here is that it will get to all sorts of different people at Takeda. If I'm an early-level to mid-level Takeda employee why is the

subject of digital, data and technology so important to our company?

Julie Dixon: I think each of us, no matter what position you're in, because as we discussed, this is so far reaching, there are a lot of pragmatic things. If you're doing a routine exercise, can you have a bot do that? Do you need to do that? You can even ask yourself very simple documentation things. Everybody, we all have an opportunity to step back and say, is there a more efficient way to do this? Can it be automated? And then from the science perspective thinking out of the box, about "Okay, if I wanted to have a real-world evidence strategy or a synthetic control for this, what do I need? And how do I go about getting that data?" because this takes planning. So, everybody needs to think about this early, there's going to be resources of course, but what are you going to need? Is this practical? And really put it into action and start to think about it. So, I think we need to emphasize to all our team members within Takeda, there's probably something all of us can do that would make our lives better by using data, digital and technology.

Christine Ward: I agree with Julie 100%. What I would encourage all levels of Takeda to do is when new technology and new ways of doing things come your way in the space of data, digital, AI, be curious. Ask questions. Don't shun it. Say, "Hey! I'm open to learning more, how is this going to help me do my job better? Writing first drafts-is something that has always been a struggle for me, so I embrace a world when bots will come and write that first draft and then I can just edit. So that's kind of a simple, cheeky example, but I think that at the end of the day, if everybody embraces and is curious about what data and digital can do to their day-to-day, then I think we'll win as an org.

Gary Karr: Is there something, that we haven't covered that you would really like to talk about when it comes to data, digital and technology?

Christine Ward: I've had the opportunity to work at a couple of other large organizations, but what I really like about Takeda is that, as an enterprise, we are embracing this. We're embracing the gray zone and the uncertainty of it. We're not sure how it's going to play out, but we are going to take a step forward and evaluate and do it with quality, with rigor, with ethics, all of that. And I think that this is something that distinguishes Takeda from many other similar organizations. We really are kind of taking the bull by the horns and going all in with it and it's one of the reasons why I'm excited to be here at Takeda.

Julie Dixon: Yeah, I couldn't agree more. And again back to this ethics part, that's a strong part of the Takeda organization and I think that's great. It's holistic, it's embraced, its encouraged, there's tools, there's education, so I think absolutely Takeda is doing an amazing job with the emphasis on that and it's going to help move the needle.

Christine Ward: Patient, trust, reputation, and business: PTRB, we live it and breathe it every day here. This is a good example.

Gary Karr: Julie and Chris, thank you so much for the time that you've devoted to communicating about the importance of data, digital and technology. It's such an important topic, not just for Takeda, not just for science, but for the people that we're all trying to help, which is the people with cancer. Very much thank you for the time you devoted to this and I think it'll be a really beneficial thing for everybody.

Julie Dixon: Thank you. Great to be here.

Christine Ward: Thank you so much. This was such a great conversation; it was great to be a part of it.