Novel Cohorts
Podcast Series

Dan Housman, Chief Technology Officer of Graticule, and Omer Saka from Roland Berger discuss

Dan Housman:

This is Dan Housman here, and I'm here with Omer Saka from Roland Berger. We're here with the Novel Cohorts podcast with Graticule. We're to talk about some exciting stuff relating to Target Product Profiles and some new work we're doing together with Roland Berger to come up with a way to help clients sort through this question of Digital. So I want to introduce Omer. We've worked together in the past, and we were colleagues when I was at Deloitte, and we've stayed connected throughout some of the years. I will let Omer introduce himself and what Roland Berger is and then will get into the topic of Digital Target Product Profile.

Omer Saka:

My name is Omer, I'm a physician by background, education and I've been in advisory, professional advisory services for the past 15+ years. As you rightfully said, we met at Deloitte. Before we called it anything real world data, when we just named it data. I had the chance to work in the real world data space since the early 2000s in chronic disease, particularly deploying non-clinical trial data to understand effectiveness of clinical pathways. For the past 15-16 years after academia, together with most of you at least 14-15 years together we have been designing value propositions for new treatments - new modalities or even medical devices. They can even be digital solutions themselves to enhance the provision of care. We've been struggling to get efficient ways of real-world data to actually support the pathways for our clients.

In our opinion, If you allow me to say, I know you contradict me. That's one of the most exciting things about working with you guys. You know, you've got a very good dialectic, contradiction based improvement system. That's what I call, you know, R&D in real time. So, but you know, we are going through a really, I'm gonna say difficult times, but it's actually beyond difficult for the pharma industry especially. There has been a major increase in different types of innovation. There's a lot of new drugs coming in. And I guess, recently also with the increasing discussions in the US healthcare system, are we paying too much for drugs? Do we have the right methodology to understand the value of drugs? And do they actually create, are they able to convert? What they claim as their efficacy and safety endpoints, are they able to convert those to effectiveness? So I think there is an agreement that the best way to prove that any treatment modality, be the drug, be it a medical device, either supplementary clinical pathway. The best way to demonstrate this is via data. And you know, of course we need clinical trials, but we also need anything that we can get our hands on within the construct of evidence-based medicine to support the enhancement of value. And I think it would be fair to say that this is where we've been challenged and battling, many battles in several different areas and disease areas.

Dan Housman:

Back to this, contrary view, I'd say we've had a lot of success. It's not all battles. And I think when you look back in time, the drug industry started in an era where there was nothing digital, like there really was, like, you made a drug and you got to market, and sometime in the 70's or 80's, whenever it was the wave of drugs that came out. Then they designed how the drug industry works. Maybe they designed it in the 50's, right? And the rest of the world's been moving at this big, accelerated pace to adopt new things. For example, when I grew up and I was just watching Super Friends, which I watch now with my kids, you have these cartoons that were made with who knows what kind of technology. It was what was high tech in the 70's with Hanna Barbera where analog television transmitted images across the wire. We were mostly doing everything on paper back then, probably running clinical trials on paper back then.

Well, we're living in a world where everyone's got a mobile supercomputer in their pocket and multiple mobile supercomputers all over their body, right? And on top of that, everything is completely networked and has been for a long time. And the result is we have this new world which wasn't how the pharma industry was originally designed, and we've been slowly building ways to electronify the old pharma industry.

And there's this big opportunity that everybody knows about, which is how to make the new pharma industry that's truly digital. We're not there yet, we're like this is a slow-moving industry. I will agree that there's challenges, but we keep taking advantage, though, and I think this is where we're getting to this discussion here about, you know, when we thought of our original products, we thought about them living in this analog world. It's a pill you take at the right time of day with your, you know, non-digital watch with the hands clicking around.

Omer Saka:

I recall, this was some 15-16 years ago. One of our clients in Switzerland, you had flown from Boston, and I was there together with you. We organized that big workshop to demonstrate what digital health can do, and we made them build these pill boxes, which were linked when it was time for the patient to take it. At the time, people were getting into the mobile phones, into the super computers in their pockets, but still, digital was a bit of a toy, you know, you really needed to think beyond what could be capable to understand one of these solutions could actually then pave any path for through the journey of a drug.

It was 15 years ago we needed to do this with, you know, demonstrations and with, actually, tools that, if you remember, we built, like it involved electronic engineer, you know, they kind of added bits, and we made the people build those, those little tubes, and we built spoons that if the dose of a drug was too much, the poured syrup was too much, then the school nurse would give a little notification blink that the patient is taking too much of our drugs. So that of course, moved on from that.

And it is not to say the pharma industry isn't looking at all of the benefits of their drugs holistically. Especially if we think about the way we design economic models, we try to understand the clinical benefits, the economic benefits, the benefits to the health care system. And look at the intangible benefits of something that is a treatment pattern that would enable the next of kin to have maybe an

easier life because the drug would improve mobility, or it wouldn't necessitate a patient to see a physician every so often, so on and so forth.

So we've been working in these areas with Target Product Profiling. I think the entire regulatory landscape needs to thank the FDA for coming up with the concept of Target Product Profile. It really made it easier to visualize and understand how value transforms into something that could be commercialized and be articulated across all the specialty areas from R&D and clinical development to medical affairs to marketing to health economics to market access to commercial teams. It helps develop concepts that can then be adapted to different countries' health policies, and there you go.

You got a value proposition. But I think it's my view, and when I used the word backline this time, I hope you'll agree with me, it's not that it's been a battle that people are in blood or anything.

It's a battle because both you and I are exposed to various different digital enablement, let me call it that way, that could become an integral part of a drug provision, either at the follow up stage, at the provision stage, at this stage of obtaining outcomes, be it patient reported outcomes, be it technology reported outcomes that could actually enhance this value.

And I think the backlog was that we were always trying to sneak in these ideas and demonstrate to our colleagues in the industry to say, you know, there is a return on investment here. Not only is there a return on investment for patients, because they're going to have a base of compliance, they're going to be able to monitor their stages of their disease better. It's going to give feedback. This creates feedback loops to the physicians, to the healthcare system, so they can actually trace down the line how their patients are doing and when they need a little warning sign, or when they need a little pat on the back, you know you're doing really good. You're going to come to the hospital again, so on, so forth.

I think the battle has been to systematically be able to integrate these little micro-chips, little elements, into the pathway, into Target Product Profiles. I think that's what we're going to talk about today, because we've got a methodology now we can somewhat integrate them all in a holistic question.

Dan Housman:

I think that the thing that's been interesting and is fun for us, I think, is that the digital world is not stable meaning there's always new things happening. In the biology world, where things are pretty stable. Human biology may be evolving, but at a very, very slow pace. And the things that are changing, or maybe what drugs we're putting into our body and what we're eating, and there's things that are maybe changing our biology a little bit. As you can see, we're getting more obese. So things obviously are happening, but at the same time, you know, if you look at a drug, that's a molecule, it's an API, it's maybe formulated differently. Most of that stuff that's the core product profile type components, they're nice and stable, so you can even count on them.

The digital world just keeps changing, look at AI where suddenly chat GPT lands on the scene, and everyone's brain is exploding trying to understand it. What does that mean for what we can do to observe things and learn things, right? And that's something people usually point out. But then there's

all these behind the scene things, seeing things that happen in digital like mergers and acquisitions driven by private equity in industries who have this very fragmented universe, and now you have this very consolidated universe with these digital opportunities that you didn't have before.

So I think one thing is, we can landscape a lot with digital whereas you don't do as much landscaping with biology, except at the beginning and middle in pre-clinical to understand, you know, how does a pathway work? But thinking about how the pathway works for a human being in a digital world, wandering through the universe, that's really dynamic and it's a gap, because it's going to be the way to differentiate, for example, among 20 GLP drugs, or whatever it's going to be. Every drug is going to have competition. If there was no competition, you might not care, but you do care. And certainly, if there's no reimbursement, you're not going to be able to have a drug, and reimbursement is going to depend on proving it achieves intended benefits. And achieving benefits requires behavioral factors. The number one thing, I think, in improving medicine is human behavior. Digital is how you change human behavior. You look at things like social networks. There have been recent bans on social network apps for kids, because they have such a huge effect on their behavior. So, absolutely need to figure out how to take advantage of the best in medicine.

Omer Saka:

We've seen all three stages. I think you know when we were referring to those workshops we used to run 15-16 years ago, that was the time we were trying to introduce what digital technologies are and what they can do. So this was more like an eye opener for several of our colleagues that we work together with. In my opinion. And I again, I hope you agree we are in a state right now. I mean, work with clients. It is more like, reminds me of kids in a big Christmas market, you know, there's a lot of things around and should I just purchase this? That? Would it actually work with my drug?

Here's a blood glucose monitoring application example that comes to mind. If you can actually monitor people's speech patterns, would we be able to understand how Alzheimer's or multiple sclerosis may be evolving better? Would we be able to catch people that are in the prodromal stage of a nervous disease, central nervous diseases?

It's a bit like going to that Christmas market, you know, you may actually purchase a lot of things you don't need. You don't know how it's actually going to work with your patients exactly because of the way you said, because its patients behavior, it's a major determinant on how these drugs actually work.

Also, how do patients think that they work whether or not it's good for them, also how the physicians think that they work whether they're good for the patient. So I think in this stage we are now, we should really get out of the Christmas market approach. And, you know, buy a lot of trinkets that we may not use. You know, we realized a few days after Christmas break is like, why did I buy that little, you know, holiday wine mug when I had about 25 of them already and they aren't that great. They don't keep the coffee hot enough, or I can't take them with me wherever I want to go.

So I think this is the third stage where we need to start talking about, how do you enable your already existing value proven Target Product Profile by using digital technologies. That doesn't mean looking for

trinkets that are already available in the market, that is with a broad mind, understanding your value proposition, understanding your evidence gap in its entirety, and even going back to the market.

Yes, there could be things you can plug in. Some of the variables could work for you, some of the patient platforms you may want to build that are great and very valuable, both in terms of educating patients and physicians, but also giving feedback to the system.

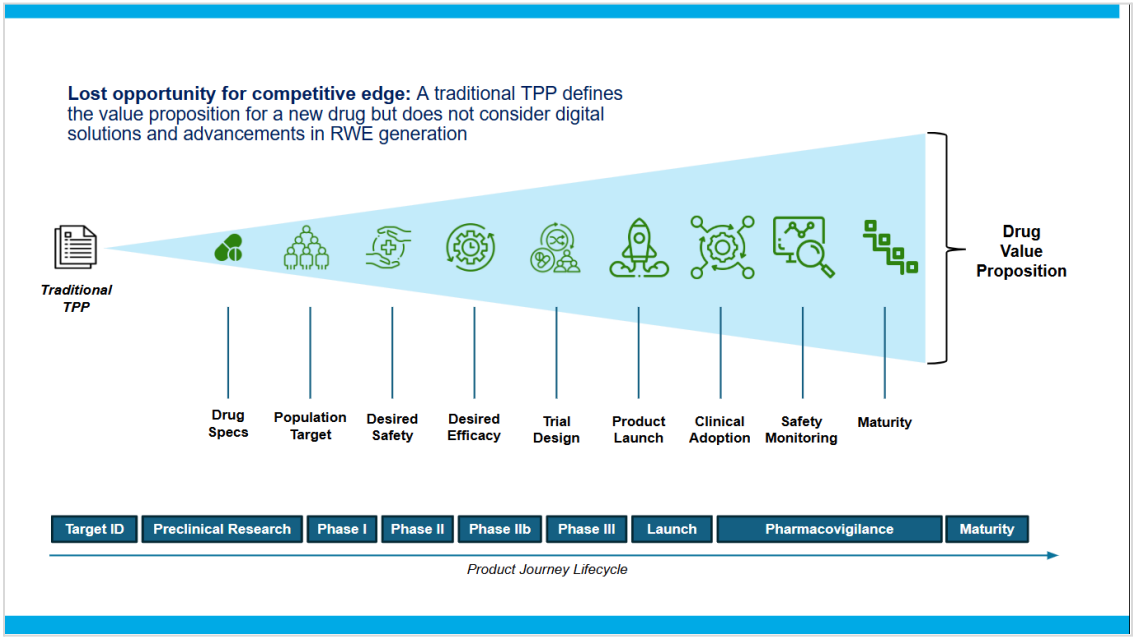
This can improve the pathways of how drugs should be used and help enable the creation of new technologies when there are actually gaps in your Target Product Profile, in your clinical pathway that you introduce a drug to a patient. I think that's where we know, that's where we come to our concept of Digitally-Enabled Target Product Profiles.

And that's why we kind of in a fashion that was iterative, you know, we realized, you know, throwing technologies here and there. when we work on a value design for one of our clients may not work. They may not have the budget. It needs to be systematically done. It needs to be attached to an evidence plan. And it needs to be understood and planned for upfront, with very tactical budgets created and very tactical return investment ideas explored so that it becomes a part of that investment package. It becomes a part of this solution, at the core of it. But what that solution would achieve in the market with patients with that healthcare system, that's, I think that's why we are and that's why we want to talk about Digitally-Enabled Target Product Profiles.

Dan Housman:

We should show a couple of slides just so the people who are watching, they kind of know what we're talking about- from a what's the difference between a traditional target product profile and a digitally enabled target product profile?

Target Product Profile



Here we are in pre-clinical land. We are in target identification land and we're thinking about a drug and trying to figure out how to make a drug that's going to fit some new need in the market. And that means we're looking at what's going to be the receptor, it's targeting, what's going to be the mechanism of action of that drug. All the things you want to know in the specs, including the formulation, the frequency of dosing. Many of those pieces usually go into the drug specs at the level of the early target product profile, but the smart companies think about it all the way over to looking at what's going to be the commercial outcome of that drug.

When I launch this product, we ask ourselves, what's the TAM (total addressable market) for the new drug? How many people do we expect, and what do we predict is going to be the cost of the drug per dose. What's going to be the expected level of adoption, and which segments will adopt. Because you need to know that, because you're going to make $ 100 million to a billion-dollar investment. And on top of that, you're looking at segmentation of the population. It's got some genetic marker now you've cut it down. Is it going to be an orphan drug, looking at some of the structures of how it's going to get moved through the regulatory processes, and oftentimes, safety and efficacy become the most important pieces to defining how it's going to be positioned long term.

Is it more effective than the existing drug, or is it just safer than the existing drug with the same efficacy and part of the product profile then goes down to, how can we design and measure these things with the trial? Go launch it. Go figure out how to get it adopted, assuming we actually have reimbursement.

Now, we still have the problem of, how do we communicate the right evidence back to the clinicians we're going to prescribe and the patients who are going to take the drug and the safety and the other pieces to be able to move that thing into a mature drug that, you know, eventually goes off patent and goes into generic land.

So people are looking at the target part profile from the perspective of all these phases, and it's going to keep increasing the level of information attached to it as it goes down, because from drug spec all the way to maturity, but the early drug specs almost defines the product profile to begin with, and as you go forward, you're always looking at, well, how do we do real world evidence generation? It's a great framework, and we still use it all the time. But you think here, it doesn't, it doesn't look at the digital world, right? It's very traditional. We could have drawn this graph in 1975 Absolutely, pretty similar,

Omer Saka:

As the slide title says, there is a competitive edge in this timeline, we all are trying to create commercially competitive drugs that will generate interest from patients and also generate sufficient usage. But beyond that in a traditional TPP, we do not consider, or really integrate what you mentioned, the most important element: the patient behavior. There's not a feedback loop with a traditional TPP between the healthcare system, the interactions are carried up by the pharma industry, by employees in countries and regions, in hospitals, and tracking of how patients actually interact with the system.

But there's nothing that is digitally enabled, even in this information age, that does this in an automated fashion, or doesn't even necessarily in a systemic fashion integrate technology enablement, No

mechanism that integrates elements that could actually cater to patient behavior, caters physician decisions and choice, caters to the learnings captured as the drug is used in the market. If this does occur, the digital mechanisms are certainly not effectively deployed and , even though we have been seeing regulation recently around the use of digital technologies, for industry does talk about their drugs to be digitally enabled, the industry as a whole, this is still an ad hoc modality of plugging in some of the solutions on the drug. And it's a nice to have, a market attraction and not really part of the fundamental value proposition of a drug, or treatment modality or a medical device.

Dan Housman:

I think we also see this impedance, that's already built into the process that we see today.,We do a lot of work in R&D. What's one major R&D challenge in drug development that I've seen is recruiting patients for clinical trials . And if you break down why it's so hard to recruit patients in a clinical trial, there's a novel treatment that's going to solve a problem that no one solved before. There's a bunch of digital problems and a bunch of human behavioral problems in patient identification and working through enrollment into a study. That's a small model of what it's going to look like when you're trying to prescribe it. You don't know the diagnostic process, because you are introducing a new intervention that didn't exist before, and it's disrupting this whole digital universe. And it could be that we don't have a diagnostic for this new drug. We don't do this genetic test, and we never had to do this genetic test, because why do we do this genetic test? There's no drug for it, right? So what's the pathway and workflow in the digital world to get to that genetic test? What's going to be the identification process, what's going to be the documentation process?

Solving these types of things are what's happening in the digital world, not saying it can be magically fixed immediately. But, if you can't figure out how to recruit patient and trials, I can predict you have a problem getting patients to prescribe or physicians to prescribe the drug, for the same reasons you're having trouble getting into the studies, right, because you don't understand the pathway by which the patient ends up on that drug. And then, similarly, there's other issues that are on the back side, which is you design clinical trials thinking that's how the real-world works, because you can do whatever you want in clinical trials. You can define any measurement vector you want, and you'll rapidly run into the problem that that's not what people really do. So you end up with this impedance of practice change at scale. You have something the clinical trials showed that if you had this nice measure that academics wrote down as a way to collect how someone feels, depression scale, I don't know, but a new depression scale that works well for your drug. Guess what? That depression scale doesn't exist in the real world. Now you have a global problem of having people adopt that depression scale so that someone can use your drug. And so there are connected problems that you're breaking the system when you introduce new interventions.

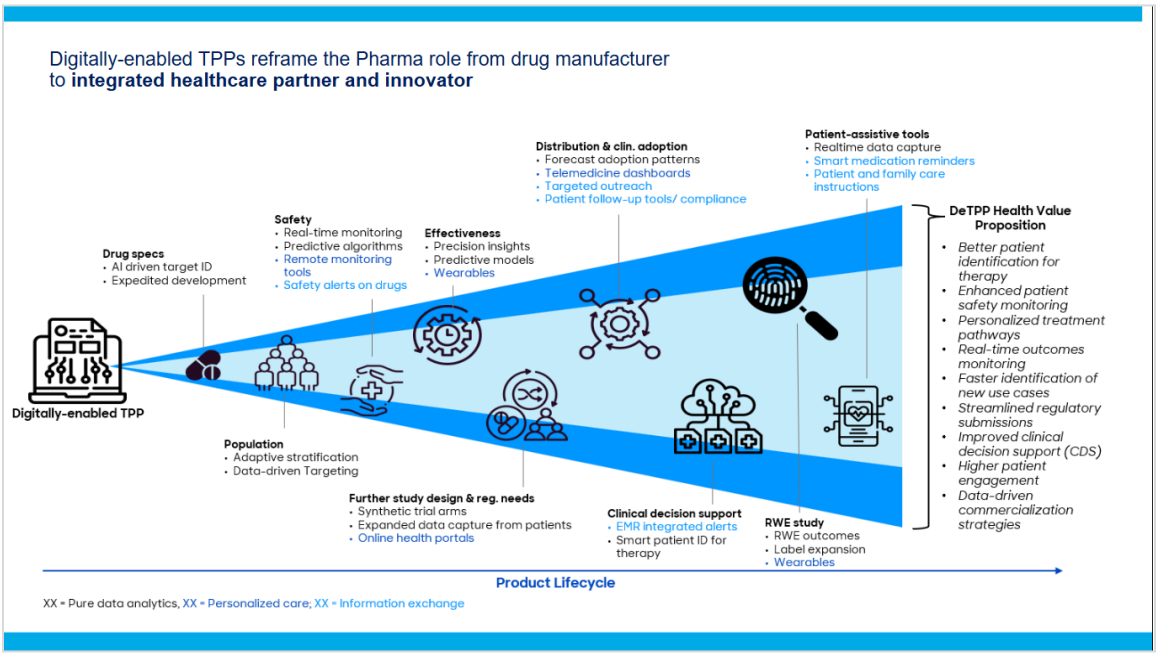
And if you're not thinking about how the system works and how those things are going to be translated, even in your trial implementation, you're going to run into problems later when you try and do product launch and adoption and things like that. So you always want to be moving backwards. I think if you're in strategy with inside life sciences companies,of : how can I fix these before it becomes, you know, a $100 billion problem when it finally went approved and built a forecast, and people aren't using the drug and adopting the speed I expected because of something we could have fixed. And I'd say there's big

I'll call them pregnancy problems, right. You can't just throw money at some of these problems,you need time.

Omer Saka:

As you said you need time in advance, so maybe let's move to the new slide.

DeTPP



We're discussing the need to develop new metrics to accurately measure treatment outcomes and effectiveness as treatments reach a larger patient population in the market.

How do we understand if the patient complies with the drug? How do we understand that the right tests would need to be done? How do we follow up on what the patients would need to or what the patients are actually doing during their time of treatment, what sort of outcomes, what sort of pain, what sort of side effects they are experiencing.

And I think all of these, as you said, all need to be planned in advance. These need to be planned within and integrated into the evidence plan into the longer-term achievements that a certain drug would like to have, certain levels of efficacy and victims and safety that they would like to, they would like to get to. The secret to this recipe lies in thinking about this in advance. But the complicated thing, perhaps, is to integrate these technologies. Some of them may exist, as you rightfully said, some of them may not yet exist.

But alongside the product life cycle, we need to plan for wherever we may have, perhaps in our variable composition, wherever our clinical trial has not been able to collect sufficient data, wherever we need further emphasis, you know, especially in the cases where some of the genetic tests, some of the you know, you know, biolab tests, may not even be available, like in the case of new drugs that will come to

the market serving cardiovascular diseases that will require a healthy little late test, for example, how would they actually what would they mean?

What would they value mean alongside a drug's introduction cycle alongside a drug's life cycle. And how should they be planned in advance? How should these gaps be envisioned in advance? And what would be the tactical and strategic meaning of covering these gaps in advance? This does need to be done at a global level, although certainly starting with a number of base countries, where you can actually create the solutions alongside your product pipeline. And you can go to the agencies, the payer agencies, the insurance agencies, the single payer system gate holders, gatekeepers, and you should be able to actually discuss with them that you're not designing, you're not selling a pill, you're not selling a lollipop to the market. What you're actually trying to introduce is the utmost effectiveness, conversion from efficacy and utmost benefit to patients, that will actually enable the patients to see the outcomes, enable the healthcare system to have an idea on what they should be expecting and course correct, you know, and these expectations are not met, either on the safety side or on the effectiveness side.

So that's, that's, I think, what we're what we're focusing on, both from a drugs or a or a clinical treatment modalities, strategy on how it should be implemented, or a drug, how it should be provided to the market, towards an area where you're actually targeting a healthcare problem, and then you're trying to sort of solve the healthcare problem. This drug, this healthcare modality, treatment modality, could be at the heart of it, still, but actually it is connected to several different enablers, which is the reason why we call this digitally enabled target product.

Some think digital will be the heart of healthcare itself. I personally don't believe that. I think digital enablement is a very important element of the future of care. But we still need to provide care in hospitals, we need physicians. We will still need to see the patients. Patients will still need to get tests done, etc.

What we are saying is: if we were to slice and dice the use of digital technologies, we can basically look at them in three areas. One is the data itself. How do we actually collect, capture and carry-on capturing data digitally so we can do analytics, hopefully in real time, so that we can understand what we are capturing from an individual patient to a population cohort. What is it that we are achieving?

The second element is to enable the personalization of care as much as possible. Technologies that there are, either via wearables or via applications that patients use, would reflect their own experiences, their own outcomes, their own journey, when they're actually on the path of either being diagnosed or they've prevented a certain disease from happening to them or being prevented from things getting any worse. So the second cluster is the technologies we would use to capture that personalization.

And the third group we defined to be information exchange. In the third group, it doesn't have to have technology, and does not need to collect data. It does not need to provide any personalized thoughts or personalized feedback to the patients or to the healthcare system to the healthcare professionals.

What it does is it trains the physicians. It trains the patients. It gives them, you know, information about when they should take their drug. It gives them information about if they're not feeling good, if they are

having any issue with pain, any issue with a headache, or any issue with mobility impairment. You know, what is it that they should do? What is it that they could do, what sort of help could they seek to actually create this immediate response without wasting any time to mobilize whatever needs to be provided to these patients or to healthcare professions. In terms of information? We divide that, you know, we divide the digital enablement in these three groups.

And of course, we'll talk about an example. We aim to offer clients a structured platform, not ad hoc suggestions, to identify key outcome metrics or wearable use cases

Rather than suggest to them a certain monitoring of biologic indicators, we say we need to do this in a systematic fashion. We need to design it as a part of the value proposition, as a part of the data plan, the evidence plan, and then convert the ideas, or create a prioritization of these ideas, so that the companies that will bring these collective solutions to the market, they know how much they need to invest, and they know how much of a benefit they would receive from these technologies in order to avoid, obviously, the deployment of unnecessary trinkets here and there.

Dan Housman:

I think it's great to have a rubric to classify capabilities. You know, data analytics, personalized care, information exchange. The warning, though, is that life sciences come with finite resources. Therefore you can't have 10,000 partnerships to bring a product to market. Many of these elements are interconnected and should be combined, as in the real world—analytics link to information exchange, and personalized care ties into both.

Thinking strategically, how can one somewhat minimize the number of initiatives to do to get these things done, possibly merging those pieces back together, so you can find a way to acquire the data you need at the same time as executing integrated alerts for physicians? So they don't become two different things, they become complimentary in an investment.

When doing DTTP work, we do need to landscape out where’s the best bang for your buck, we must identify the best value areas, as the fragmented landscape presents a significant challenge. The big challenge when we look at a picture like this is that the universe is fragmented and what is special about pharma or med device or diagnostics is whatever you want to look at, is the life sciences world is fragmentation is not how they're inherently built, because they're built on a one product for every one model, right? You know, I make Ozempic. That's what I do. I'm not gonna make 10 million versus Ozempic, so I know how to ship it. If I'm novo, what's going to be my footprint? so I can have a solution for EMR integrated alerts that's universal, which is the hard part, and that means looking for where to scale opportunities and things like that. So just realizing that this, this is not intended as a way to make a million little solutions for every possible problem.

Omer Saka:
Absolutely, I love the fact that we sometimes have these little choreographed conversations. And you throw a seemingly curve ball at me, for me to answer it in the right fashion.

So this is a part of what I was saying at the beginning. We have this dialectic way of trying to improve what we do towards clients. The fundamental idea behind it is exactly what you said. What are the technologies that will properly enable your value proposition in the market, that will enable you to close the potential evidence gaps that you may have. Unless you plan this from the get go, it's always going to be an haphazard deployment of a million different technologies in different countries, in different solutions, that will never become economized. They will never reach scale application, because you haven't been able to actually create a platform that will deploy a lot of these things together in a sense of economies of scale and target the exact point of gap that you have in your value proposition.

So I think this is one of the most important outputs of what we try to achieve when we work with our clients with Digital Enabled Target Product profile design. It is not about blue sky thinking on what they can actually implement into their patient pathways, into the product life cycle. It is exactly deploying the most cost-effective infrastructure of technologies, either the platform or it could be obviously standalone, but in an integrated fashion. So there's conversation between data collection procedures, there's conversation between different healthcare systems and you can deploy them rapidly. There's conversation between the healthcare professional with the patient. There's conversation between the patient and the actual provider of that drug.

So, you know, we can only understand the package of investments if we plan this in advance. When I say in advance, of course, it doesn't have to be done five years before a drug is deployed, but it could be. I think what we recommend is that, you know, you think about that systematic, systematic way of evaluating value when you're designing your value proposition.

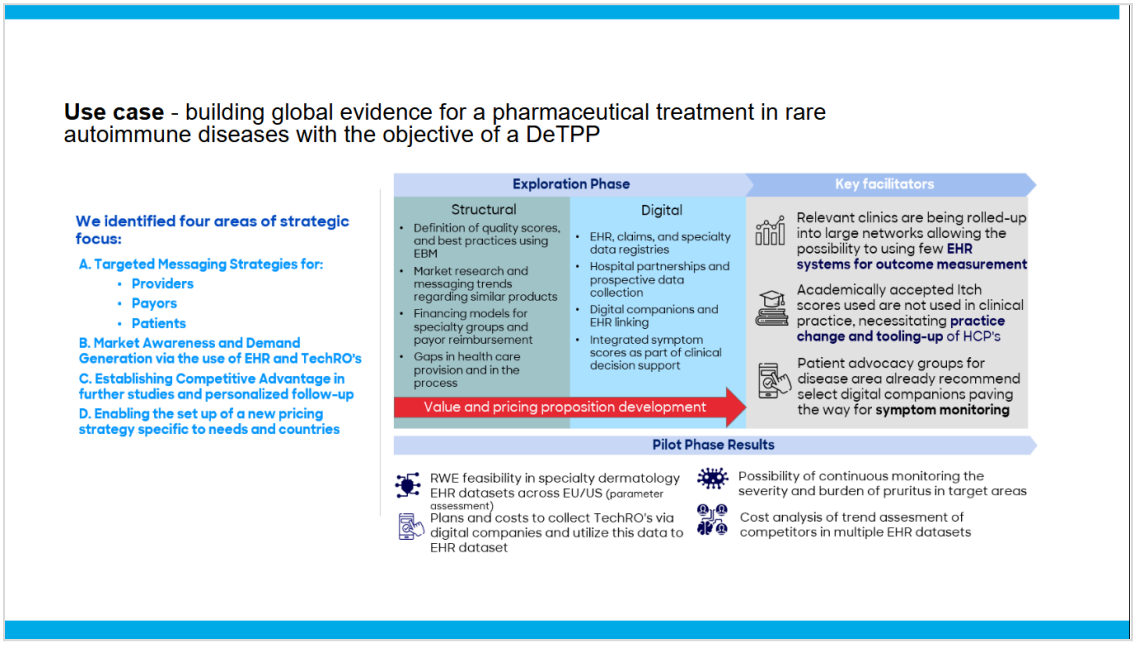
You need Medical Affairs specialists. You certainly need your clinical development teams, but you also need your country teams. You also need your market access teams so that they could be packaged up with the right arguments towards the payers and towards the finance teams that the right investment, with the right packaging, with a right output, could be designated up front.

Dan Housman:

So you had a bunch of value propositions, here I think people can read on the screen. But I'd say the rough summary is, you know, how do you end up solving for, getting a product that's actually going to have the impact you're looking for in the population. That's all the way from getting regulatory submissions, getting reimbursement, getting clinicians in a position to be able to prescribe, because patients have been identified, as well as the patients are activated to solve their medical problems.

So all those pieces come into play. If we get this digital thing right, maybe we can look at the next slide, which I think we've done a little bit to highlight or show an example of how this is done.

Use Case



Omer Saka:
This example was a client that we engaged with. The client has a drug for rare autoimmune disease. And the point where we engaged was the value proposition design —a very common step for most pharma companies and device companies.

A certain amount of time before a drug is launched, they would like to understand: how can they make their case towards the healthcare system, towards the payers and also for their own teams? What's the actual metrics beyond just simple efficacy metrics—how should they be able to find their way into the healthcare system—how should they convince the prescribers that this is the right drug to use, this is the right solution that they would need to deploy.

So we started this particular assignment with, you know, a relatively conventional way. You know, we looked at clusters of value blocks, critical value blocks, economic value blocks, value blocks towards the healthcare system, benefits, value, intangible value—blocks that the patients or the healthcare system will experience—but they may not necessarily be captured by direct metrics.

We looked at the value proposition from a very broad stance and from a structural perspective. Obviously, it wasn't just the definition of value-based standard metrics frameworks such as EQ-5D. We looked at quality scores. We looked at what are the best practices in evidence-based medicine, to demonstrate the very specific benefit this particular drug was bringing to the market.

We did a number of analog assessments. We examined if these metrics could be applied in clinical practice, given that rare disease trials with only 200-300 patients may not be widely generalizable. Will the drug's use in the real world match its clinical trial results? We also create financial models to show healthcare players and payers the cost-outcome equation for this drug.

What would that mean if new treatments were to be if all the treatments were to be replaced, what sort of operation issues they would need to look at what sort of diagnostic metrics they would need to deploy. When we were doing that we came across a few very interesting findings. Some of them were really practical, practical in terms of the deployment of our current measures. Some of them were very operational, in the sense that who actually deals with these patients? Can we find these patients in multitude, in a group that we can actually become worthwhile targeting a number of areas, targeting a number of providers, so that we can actually get the biggest impact for what we'd like to do, and we realized that there are a number of digital solutions that could actually enable us to overcome both. The operational problems and the actual systemic evidence related problems, and we found some key facilitators.

Dan Housman:

To make it a bit more specific, of the different rare autoimmune diseases one of which is various forms of psoriasis and the particular project we were trying to deal with was in the dermatology and dermatology is an interesting space. Dermatology is unique as it exists both within health systems and in specialized practices. This segment has been going through big change, a roll up from private equity firms. And the impact of the roll up of dermatology and private equity firms means you now have these mega dermatology providers which is an opportunity to establish some kind of scale capability for practice change within those groups.

And I think we're seeing a lot more of that in the last 10 years, because independent groups have become a target for PE firms, not just in dermatology. It could be anything. It's been in ambulances, emergency department groups. There's been roll ups in almost every specialty of some sort, where the specialties can live sort of partially in the health system, partially as an independent group, because they're trying to consolidate. Using digital all that knowledge, expertise and automation that's hard to do when you're just a practice inside of a health system where the innovation gets blocked, and then the result of all that, in the case of dermatology, is also that they now use integrated electronic health records. So you know, there's a dermatology specific electronic health record that is connected to these large, rolled up dermatology practices.

Omer Saka:

During our investigation, this was one of the outputs of our investigation, wasn't it?

Dan Housman:

Yes. In connecting with that group, they're open to injecting new digital tools on top of it. So a new digital tool in the case of this particular product, if we go back to the original target product profile, you know, they've been measuring certain factors of dermatology that were differentiated from the drugs of the market. So if you look at problems in dermatology, will you have, you know, How comfortable is the patient? What is the size of their psoriasis? How long does it last after treatment? How bad is their Itch? And these sorts of factors aren't tracked in traditional systems. They keep things at a very high level.

And so if you tried to compare their clinical trial that was designed off their traditional target product profile, there's no representation in the EHR to track the patient's progress relative to those specialized improvements in the drug versus other psoriasis drugs in which patients are the best targets, based on the differentiated properties the drug. And so the opportunity there was to introduce new workflows and forms to collect that data, both from the patient—keeping in mind, measuring Itch at a visit, for example, once every year for the dermatology visit isn't going to be as effective as adding a patient reported system that's a digital app they can use to track their own experience

So that's something that they're going to see and most likely want integrated into their electronic medical record. You can try and make something that's totally independent, but the patient themselves thinks of it as part of their engagement with their healthcare provider. So you know, for those of us who use Epic MyChart, that's where I get my lab values, that's where I get a survey before my visit, that's where I'm expecting to see things that are connected to my point-of-care visit, and therefore thinking about the digital wrapper around a psoriasis drug is, well, how do we do that?

And so one way to do it is through those EHRs. Another way is that the patient advocacy groups for psoriasis, which are the places where we can find these specialized patients with specialized needs, already engaged them pretty effectively. They're already engaged in providing tools for those patients as a support function that they think is core to their mission. And therefore again, there's another window of opportunity to partner with the advocacy groups that are providing Mypsoriasis app, to plug in the kind of things that are necessary for this product to be differentiated in the app. And it's a win-win for the advocacy group, because it's new funding for them to improve their application. And furthermore, it's not like you're marketing a drug. You're helping patients to track some of their symptoms. And if the drug is the right drug, that'll go through, the drug is a different drug. You know, you obviously have to have good medical ethics when you're doing digital products, and it can sometimes be a blocker, and you have to think through all this, right? Because, because you can't just implement advertisements in the middle of the care providers, the advocates workflow. But they don't have the resources. They don't have a big pile of money that comes in, either from healthcare providers or from the patients themselves to improve these products. They're all strapped for resources so that the design of a sort of pilot through implementation is, well, how can you translate? How can you translate these opportunities into practice within those healthcare provider groups that are dealing with those special patients, those advocacy groups are dealing with special patients, and the existing infrastructure they use, which in this case is the EHR system that specialized for dermatology and the advocacy group for psoriasis is an app that the patients already used to track their disease.

And so now you end up with a nice package, and on the backside of that, from the analytics perspective, forming these partnerships can also get into: now we can look at long term outcomes, now we can look at the patient journey and understand what other digital tools could be added.

And it's funny because, like, we started off talking about, like, well, think about all these IoT devices, right, which was the big hot thing when we're me and Omer, were assembling pill boxes. IoT isn't at the center of almost everything, maybe it's just, you know, cellular phones and EHRs. But it could be more, if it's a different disease, right? It could be that you could take some of the burden away from that

patient by taking devices that are doing measurements that are natural, off of whatever the specific device does.

Omer Saka:

I guess one of the practical points we need to mention, number one, all of these things that we found, the three main points that are mentioned on the key facilitators, was a result of that investigation of that project. They were also cost and the return investment assessment was provided, and of course, they found their way into the payer documents. So they were used in enhancing the pricing argumentation, because they would be a part of a whole package, not just a single pill value story and the solution is provided together

In this kind of slightly less mainstream rare disease, it may be a bit easier to to find these types of game changing parameters for the launch of a particular treatment modality. Because without those elements the argumentation on the value of a drug becomes very difficult to be reflected upon. In broader areas. If you talk about Ozempic/GLP-1's, the scope of what you can achieve is a lot broader. We're looking at more than long term outcomes, maybe even looking at issues around mental health. We're looking at satisfaction of daily activities, of daily living. So we're looking at broader concepts as had been pinpointed in this particular example that we are looking here

Dan Housman:
In a GLP one, sure, Ozempic, and Zepbound, the Novo Nordisk vs Eli Lilly world, it's a trillion-dollar product space. But there's 30 companies that are making GLP-1 drugs that are in phase 2 and phase 3 clinical trials. So they're going to be exactly in this same set of problems everyone will be. Oh, I designed a drug that reduces my nausea with GLP-1 drugs. Well, how are you tracking that? How are you going to show that that is actually better? How will you show the patient's quality of life is better? Why are you charging $1,000 more per year because you lower people's nausea? Can you prove it? Because that's going to be hard to prove.

Where is the volume of nausea measurement in the data that flows in from your real-world data system. It doesn't exist. I guarantee it. I'm sure of it. I'm sure if nausea is the problem list or not, which tells you crap about whether your drug is better than others. I'm pretty sure. So if I'm in one of these drug companies, I'm thinking about that, or I'm thinking about the other problem, which is reimbursement. The big barrier to adoption from the provider side is they're completely burnt out filling out prior authorizations where they get rejected all the time. Can you make it easier for them? So your digital tool might just be a reimbursement automation framework that helps them to collect the data they need to be able to communicate things back, and doesn't have everybody frustrated when they can't get access to these drugs. This would definitely be good for companies like Novo Nordisk, Eli Lilly .There are lots of pieces here

Omer Saka:

And I think, I mean, I think so I presented this concept in a few places, at the recent EU access forum in Barcelona as you know. Since you mentioned reimbursement, while there one of the payers actually rolls his hand, and he said, Can I say something about this concept that you're presenting? And he said

he's one of the experts in a top payer agency in Europe. And he said that a case, a value case, came in front of them, and one of the recent psychosomatic drugs, that there was a lot of doubt about the value proposition. This particular drug was packaged with patient outcome measurements, actually a patient's progression and safety measurement tool. They were not convinced of the clinical trial results of the particular product, but they actually love the technology, the digital technology that was discussed that was packaged as a part of the drug, and with the condition that this would be provided with the drug itself. They said, under that condition, it could be this particular drug could be included as a reimbursement case. I think these cases are still ad hoc. You know the reason why? As Graticule. On the data side, I'm a partner at Roland Berger. Roland Berger is a strategy consulting firm, 70 years old formed in Europe initially but it's all across the world. Graticule is one of the most innovative, in my opinion, one of the most interesting real world data companies that has partnerships all across the world, which is the reason you know why it brings us together, because obviously work together with these things several times before, but also because we can understand and we can deep dive into the reimbursement requirements in each country. We can deep dive with our partnerships, whether or not these agencies will be willing to deploy, obviously enabled by us that we can actually create the platforms for them to easily deploy these technologies.

The difficulty we're finding, not necessarily just in GLP-1 space but in any other innovative treatment modality space, is the need to think about TPPs in a digitally enabled fashion. They need to think about it as a part of their main value proposition, and they need to equip themselves to go to payers with their pricing proposition, with those tools that are actually surrounding including the benefit that they expect to have for patients in the healthcare systems.

Dan Housman:

I think the good news here is drug development is really, really expensive. It costs a billion dollars to bring a new drug to market, you'll hear some ridiculously large numbers.

Digital Development isn't as bad, which means you get a lot of bang for your buck. If you think about it and come up with a good strategy. Obviously, some folks might be concerned and said, now you're kind of tethered down to needing a digital companion to your API to make it work. But at the same time, you can build all these digital barriers that are things that you're going to want in the future, and at a fraction of the cost that it takes to develop the actual clinical development process around the drug itself, with human trials and other things. And at some level, depending on the level of investment the group wants to take to bring it all to the point to which these are medical devices, they become something that's really hard to replicate, and allows for a way to carve out larger market segments and give greater benefits to the patient.

So, if we take out even outside of the digital world, you look at REMS (Risk Evaluation and Mitigation Strategy) programs, the first people would like curse themselves about REMS programs, yet at the same time, drug makers started using REMS programs to extend their patent life, essentially by saying, well, you can't make the REMS program to your small generic manufacturer, so it's not equivalent, so you can't get in the market and just held on to the same market share. And I'm not saying that that's ethical. What I'm saying is things that go outside of the drug can be a positive, and they can be

strategically built out as a positive. And they can be done cost effectively. So it's a much smaller side car investment that has great value, if people have their eyes open for profit.

Omer Saka:

I think that's an amazing message. I mean, we keep on having these conversations with our colleagues, clients, and friends in the industry. What I would like to say as a last note is that, you know, we don't just come with these concepts. When we talk with our clients, we actually create a pathway on where the digital technologies can enable their value proposition before we even start, just as a kind of showcasing what we can do. And we start the journey together with an exploration phase, and then we carry on with a piloting phase. We also involve them with feasibility analysis. We look at how much this data could immediately be collected. So, you know, we don't want to give exactly as you said, the drug development takes a long time. It's very expensive. We want these solutions to be immediately available as much as possible, and this data to be immediately captured with the right healthcare system. Both in terms of publications, in terms of evidence that systematically, you know, brought back to the world of science, but also to be shared immediately as proof of concepts to payers, so it could be integrated within the pricing proposition of drugs. Because they are increasing, they are having an impact on the effectiveness and the safety of drugs in the market. So that's, I think, what we've tried to do.

Dan Housman

I'd say on the Graticule side, you know, we love working with Omer and his team. They're smart. They understand strategy. They understand commercial strategy. They understand medical evidence strategy. I just love data. I love technical approaches, but I like the problems I can solve.

And, you know, we like to think about, can we make research networks, or can we use existing networks, whether it's IDNs or it's EMRs or it's something that forms a scale opportunity, to make these things real, because it's exciting to think about them. It's much more exciting to do them, even though it's very painful sometimes to sort of go through that process from early concept to the value that has been found even in a small scale. That's the fun stuff for us. We like to get involved in the early stages of planning because then we can try and fit things that might actually be connected to them.

Omer Saka:

So I think that's great. I think we've given it up, but we'd like to talk to people, and we'd love to have, you know, fireside chats. We'd love to have lunches, dinners, get togethers with anyone who would like to understand this a little bit and discuss further. Thank you, it has been a pleasure chatting.

Dan Housman:
Thank you as well, it has been a great discussion. And thank you for listening.