**ProjectXYZ - Clinical Trials Biomarker Testing - CompanyABC**

WEBVTT

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<v Penny Southworth>Mind if you could start with an overview of your professional expertise and background that will be great to get us started and then we can go from there.</v>

00:00:09.250 --> 00:00:13.520

Matt Thomas Yeah. So yeah, I have been informed industry.</v>

00:00:13.640 --> 00:00:19.040

Matt Thomas The principle almost about 30 years now and.</v>

00:00:20.280 --> 00:00:30.530

Matt Thomas Spent quite a significant amount of time in research for the past 15 years or half of the career has been in translation medicine, focus in oncology.</v>

00:00:31.920 --> 00:00:35.070

Matt Thomas Which means that in this role.</v>

00:00:35.970 --> 00:01:05.860

Matt Thomas And I have been working with three companies now that approach I am overseeing, in particular file market strategies for our clinical assets or also to be identified clinical assets starting in research and all the way through towards the approval of a compound should it make it there. So and that includes the difference in the definition. There is of course.</v>

00:01:05.960 --> 00:01:35.850

Matt Thomas Exclusion of what type of biomarkers are we interested? Are we are we required to test for and what what is the the the the sampling frequency where the obstacles and what should they let's say give us a feedback. You know typically interested in finding predictive biomarkers that help us guiding the best patient for the therapy.</v>

00:01:36.850 --> 00:01:55.070

Matt Thomas And in that respect, uh, been part of a couple of new drug application. So I went through the very end to the authorities and know what they actually want to see and that includes also experience with companion diagnostic, which is a particular part of our business here.</v>

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<v Penny Southworth>OK, yeah, perfect overview and that. Thank you for that. A couple specific questions that will help guide our discussion today. So curious to know across a few different high level categories if you have experience with these types of biomarkers or testing solutions. So this would be there's four categories, genomics, proteomics, immune monitoring and histopathology.</v>

00:02:22.680 --> 00:02:38.420

Matt Thomas Yes, uh yeah, actually, all all four of them do play a role. So especially now colegi, we do have a lot of reasons to look into genomics proteomics. Mr. Pathology, of course.</v>

00:02:39.550 --> 00:02:43.160

Matt Thomas Literally component of our strategies.</v>

00:02:56.360 --> 00:02:56.970

Matt Thomas No.</v>

00:02:45.130 --> 00:02:58.310

<v Penny Southworth>OK. And then in terms of where you have been involved in the clinical research, is it just like US and North America or is sometimes, you know, Europe cites involved or APAC?</v>

00:02:58.410 --> 00:03:06.910

Matt Thomas Yeah, yeah, yeah, it's it's OK. So you what you can imagine, I would say the largest majority of our trials are global.</v>

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Matt Thomas What, whether that includes China, so market or not, it's a little bit contingent to the individual program. I would say the majority included China as a market with all the complexities that we are facing with specially for our biomarker programs. But we're not not necessarily focused on one region only simply because sometimes these are rare diseases and that's why we have to get every patient.</v>

00:03:37.420 --> 00:03:38.820

Matt Thomas Others existing on the world.</v>

00:03:40.980 --> 00:04:07.260

<v Penny Southworth>OK, excellent. Very helpful. And then last question in terms of different modalities that you have experienced with within the oncology space, the view that we have on our radar are selling gene therapies, a biologics, which would be things like monoclonal antibodies, obviously cancer vaccines and then basically all other types. So whether it's a small molecule or or really anything else.</v>

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Matt Thomas Yeah. Well, what's the first one, please again.</v>

00:04:11.000 --> 00:04:12.210

<v Penny Southworth>Cell and gene therapy.</v>

00:04:11.670 --> 00:04:12.400

Matt Thomas The the the.</v>

00:04:13.260 --> 00:04:43.590

Matt Thomas Ohh. OK, well, yeah, let's let's put it this way. The I I will be able to cover everything except the cell therapy space because that's something at least the companies I worked with are not yet fully exploiting. We do have very early programs, of course, as you can imagine, but they're not yet in the realm of my work. So therefore I won't be able to give you a lot of details. Of course, I can't speak to some of the obstacles.</v>

00:04:43.670 --> 00:04:51.060

Matt Thomas But you're facing there as well. Yeah, but everything else can to work shines, actually.</v>

00:04:51.330 --> 00:04:55.420

Matt Thomas When you know Dash on critic wirelesses small molecules.</v>

00:04:55.900 --> 00:04:59.620

Matt Thomas More biologics in general, that's all what we do, what we are doing.</v>

00:05:00.770 --> 00:05:06.920

<v Penny Southworth>Got it. OK, excellent. OK. So this is super helpful. It's going to help focus our.</v>

00:05:36.910 --> 00:05:37.280

Matt Thomas Yes.</v>

00:05:08.110 --> 00:05:40.490

<v Penny Southworth>Our discussion here, so I'm curious to know, maybe before we really get into the nitty gritty questions in terms of the, you know biomarker field and I know that you have a a pretty high level perspective on it. So it would be great to understand in oncology what are maybe the two or three most important trends that you're following related to the use of biomarkers. I mean it seems like these are only going to become more and more important as time goes on. But I'm just I'm kind of curious to hear what are the two or three most important things that you're following?</v>

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Matt Thomas Yeah, I guess there are a little bit related to each other, but since we have seen a very strong growth in agent.</v>

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Matt Thomas That work on the immune system kind of immunomodulatory activity.</v>

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Matt Thomas That obviously our strategy is complemented by looking at the involvement of immune cells in the tech to the cancer cells and that's the high level. And in terms of platforms, obviously the.</v>

00:06:18.850 --> 00:06:46.990

Matt Thomas The the classical platforms of transcriptomics and genomics that we've been using the past ten years or no longer sufficient, and I would say there's still a little bit of debate, proteomics space well, we can translate it like that. But I would simplify by going into what we call spatial analysis. That's something that trend that is going let's say going up.</v>

00:06:48.430 --> 00:07:17.620

Matt Thomas Concomitantly, we're trying to establish more and more know how using single cell approaches which also allow you to get subpopulations of cells, in particular also immune cells analyzed with the variant or variable techniques that we apply. And lastly, in terms of the proteomic field, we are seeing a trend towards.</v>

00:07:17.820 --> 00:07:48.730

Matt Thomas It increased or significantly increase multiplexing to complement the transcriptomic and genomic space. So those are the three major transit I'm seeing right now evolving significantly. Obviously they are linked with what we call artificial intelligence approaches to come up with a prediction of algorithms that try to predict certain features. All that is a little bit going together, but technically wise.</v>

00:07:48.820 --> 00:07:53.730

Matt Thomas I think I I would would remain to the three things that I met just a minute ago.</v>

00:07:54.830 --> 00:08:26.220

<v Penny Southworth>OK, excellent. And a lot of those are on our radar as well. So I'm glad to see where we're pretty aligned there. I wanted to talk a little bit about some of the implications that are associated with those development. So as I mentioned, you know, we kind of have these four areas of, you know testing that we're curious to understand. So if we drill down into like immuno oncology types of treatments specifically you know biologic treatments that are.</v>

00:08:26.310 --> 00:08:31.800

<v Penny Southworth>You know, monoclonal antibodies and other similar products for immuno oncology.</v>

00:08:52.870 --> 00:08:53.630

Matt Thomas Yeah.</v>

00:08:33.220 --> 00:08:56.120

<v Penny Southworth>Walk us through sort of the development path of a a typical molecule and how the needs related to genomics, proteomics, immune monitoring, and histopathology kind of a change and evolve over that development pathway. So you know, starting with preclinical and then getting all the way to to face three, what what role do the biomarkers play in the research?</v>

00:08:57.090 --> 00:08:58.030

Matt Thomas Yeah, I guess.</v>

00:08:59.590 --> 00:09:28.120

Matt Thomas I guess we we have an established understanding of the genomic market setting. I guess here our understanding is robust enough that it will run systematically with every trial to to let's say exclude it into the analysis. The transcriptomic space is something which has seen some evolution in terms of going into the single cell approaches. Now what what I can say.</v>

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Matt Thomas Is that?</v>

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Matt Thomas In terms of the the progress from research to the clinical development.</v>

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Matt Thomas We see the biggest obstacle in the absence of reliable number of preclinical models, especially for the immune oncology space. There's only a couple of mouse models available to that is immunocompetent still the most of them are compromised or immunity efficient and so that that's the problem. When you take in account the complexity of.</v>

00:10:08.040 --> 00:10:37.610

Matt Thomas I mean it it it doesn't really. So so the the result of course you can apply all those techniques like I said genomics transcriptomics space or single cell activity, everything can be done nicely with these mice models. However, the biggest problem is does that mean anything? So in other words, every finding that you get out of that is not necessarily a reflecting the complexity that we see that the human patient now.</v>

00:10:37.670 --> 00:10:43.780

Matt Thomas That is now the big playground where we all slotted that means the.</v>

00:10:44.940 --> 00:11:02.300

Matt Thomas The the the early clinical development in in phase one is actually now the scenario where you generate the most important data which includes you know for the, for the modalities the dosage, scheduled dosing strength, all of these.</v>

00:11:03.780 --> 00:11:34.450

Matt Thomas Let's say parameters that are relevant for your efficacy and safety, and we need to undermine that with the appropriate biomarker data. So you can very well understand that, especially when you go into the human being with a compound where you're pretty confident that it has worked nicely in the mouse that is not guaranteed when you switch over to human beings. And that's where actually we all see quite a number of companies failing in the moment.</v>

00:11:34.700 --> 00:11:44.390

Matt Thomas I have because they don't have the the runway to really extensively study the different.</v>

00:11:45.650 --> 00:11:48.640

Matt Thomas Let's just do the variable set unnecessary to be studied.</v>

00:11:55.280 --> 00:12:03.380

<v Penny Southworth>OK. So it sounds like there's definitely a need for additional support in the preclinical space.</v>

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<v Penny Southworth>But then yeah, how? How are things kind of evolving from there? You know, once you have?</v>

00:12:09.590 --> 00:12:12.300

<v Penny Southworth>Products in the clinic. So I guess like you know for example.</v>

00:12:27.640 --> 00:12:28.320

Matt Thomas Yeah.</v>

00:12:12.940 --> 00:12:33.220

<v Penny Southworth>Are you know when we get to the phase three clinical trials, are we starting to see a lot more need for you know kind of like repeated immune monitoring types of tests, maybe longer longer clinical trials and and those types of things or is it kind of the same across all the different phases, just trying to get a little bit better sense of that?</v>

00:12:33.700 --> 00:12:36.670

Matt Thomas Yeah, I I guess the way the way how these.</v>

00:12:36.770 --> 00:13:06.800

Matt Thomas A development plans are organized is actually starting off with what we call proof of clinical principles. So we define actually some quantitative matrices that allow you to really assess under the conditions tested whether you you see the effect that you wanna see. So the phase three to be honest is.</v>

00:13:06.880 --> 00:13:11.200

Matt Thomas Finally, the controlled way to determine.</v>

00:13:12.480 --> 00:13:36.910

Matt Thomas You know the final efficacy, the these, those clinical endpoints they have typically compared to the current standard of care. So you don't really have time anymore to understand what you need to change and optimize to get there. So therefore I would say in principle there's a lot of front loading in the clinical development towards the phase one.</v>

00:13:37.930 --> 00:13:46.020

Matt Thomas And phase two, so actually pretty much at a confirmation of the selected dose, you will still have some.</v>

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Matt Thomas It biomarker testing, but keep in mind when you go to the final stage with the phase three program which may have several hundred of patient, your biomarker program by itself needs to be completed. It could be and that's something that is of course.</v>

00:14:04.520 --> 00:14:28.830

Matt Thomas Pretty frequent case that you may have a patient's election marker that you have identified. You know just, you know, take the new checkpoint inhibitors that are measuring the PDL one expression levels on tumor cells to check if the patient may be eligible because you have seen if you can see for those.</v>

00:14:29.790 --> 00:14:39.910

Matt Thomas For those sparkers when they are, you know higher expense. So that's something that has evolved in the early stages of development, but you're not doing it anymore later stage so.</v>

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Matt Thomas The playground for all those new technologies is in the phase one. It's also just for ethical reasons.</v>

00:14:51.740 --> 00:15:00.430

Matt Thomas These are typically patients where they're tolerate, you know, heavy sampling collection or sample collection.</v>

00:15:00.510 --> 00:15:02.900

Matt Thomas Umm it eventually if you wish.</v>

00:15:03.800 --> 00:15:06.290

Matt Thomas Because they are pretty much anyway.</v>

00:15:08.410 --> 00:15:27.010

Matt Thomas In the end of their therapy. So you know that's that's where often they are willing to to support our trials for that. I hope it. I I drove you to the direction but I wanna say late stage trials are not the playground for new biomarkers. Yes they can confirm if you need it.</v>

00:15:45.840 --> 00:15:46.400

Matt Thomas Yeah.</v>

00:15:47.910 --> 00:15:49.310

Matt Thomas Yeah, but.</v>

00:15:29.510 --> 00:15:50.140

<v Penny Southworth>Yep, that's helpful. Is there any differences between the needs and immuno oncology versus other types of products and oncology like for example if you happen to be involved in any therapeutic vaccines that are targeting oncology conditions or you know small molecule types of on oncology programs?</v>

00:15:49.550 --> 00:15:55.220

Matt Thomas And and and and in principle in in in. Well, yeah, in principle.</v>

00:15:56.950 --> 00:16:05.880

Matt Thomas This scenario is slightly different, so if you have let's say an immuno oncology space. So I guess the the main.</v>

00:16:07.110 --> 00:16:22.140

Matt Thomas The the the main question is, I mean the that's no I have to step back. So the first generation immune checkpoint inhibitors like pembrolizumab, model map acting on PD1 and blocking PD one.</v>

00:16:23.140 --> 00:16:52.970

Matt Thomas On on this, on the cell, on the on the immune cell. So those those, those are gone. Now we combine with those first generation and the markers we don't really know and I think the cancer of exceed also trying to stimulate the immune system to act on the immune self to finally attack these cancer cells with you know surface markers.</v>

00:16:53.210 --> 00:17:12.100

Matt Thomas That you've activated against and so you'll recover them from the from the tumor cells and and then in the patient's. But that's a little bit early. There's not a lot, not a lot of cancer vaccines that finally went to the approval. So small molecule typically start off with a different approach. They have a hypothesis.</v>

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Matt Thomas Especially when you when you're working on a signaling pathway, you typically have a pretty good understanding and the big difference here is here the preparing to world, he's much better off to support the identification of biomarkers, be it for patients election also for pharmacodynamic reason. So classical small molecules out of the immunology conscious space are still very actively sought after.</v>

00:17:44.450 --> 00:18:14.340

Matt Thomas And they're easier to find this strategies as compared to the IO. Now that leaves us with the IO itself. And as I said, we do have certain hypotheses, but we never the less need to confirm then and the quickest place isn't able to do so. So we either do that in the phase one, the typically technically speaking this is done by multiple biopsy type of approach where we get two more samples from the same patient at different time.</v>

00:18:42.230 --> 00:18:42.770

Matt Thomas Yeah.</v>

00:18:19.470 --> 00:18:50.960

<v Penny Southworth>OK, that's helpful. Then that makes sense covering the the different modality types there, what about the technologies to actually assess the biomarkers? I'm curious to hear if there are any particular trends that you're following and you know in terms of the, you know the different platforms or the technology to actually assess the biomarker, what would you say, you know if you were to look forward a couple years, the two or three most important technologies for any service provider to?</v>

00:18:51.220 --> 00:18:55.500

<v Penny Southworth>Make sure that they have to, you know, be able to meet the needs of where the markets going.</v>

00:18:56.650 --> 00:18:57.860

Matt Thomas Yeah, well.</v>

00:18:56.350 --> 00:18:59.880

<v Penny Southworth>And if needed, I can, you know, throw out a few examples, but go ahead.</v>

00:19:04.970 --> 00:19:05.220

<v Penny Southworth>Umm.</v>

00:19:00.540 --> 00:19:30.430

Matt Thomas Yeah, let me let me try to give you my perspective. So what we are seeing right now is the rise of, as I mentioned, single cell approaches. So it is a, let's say, most officated way to study two more or stronger environment from samples that you collect and get a sense of more quantitative representation of cell types.</v>

00:19:30.540 --> 00:20:00.470

Matt Thomas Whether they are dynamically remaining stable or moving a combined with that is actually the other thing that is to some extent evolving a lot, but I'm not seeing overlap. It's the spatial analysis, the approaches where you do single cell in a spatial environment. It's not really a defined resolution because it is still pretty quiet of large quadrants that you look after so.</v>

00:20:00.650 --> 00:20:30.510

Matt Thomas But but that's the two top of the of out of the head of approaches that are going after now the the leftover question is there's a hot topic liquid biopsy approaches and biomarkers out of the bloodstream. I think one thing is clear, if you have a therapy that is, you know expected to work, you may go after liquid pipes, yeah.</v>

00:20:30.560 --> 00:21:01.080

Matt Thomas Coaches, but that is more or less in the direction to go for minimal residual disease. So that means you try to monitor your your patient. So it's not necessarily in the realm of of product development only that goes also outside of farmer in towards the classical patient cancer screening and monitoring approaches. Now I think the two top are the ones that I've just mentioned.</v>

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Matt Thomas Channel mixes stable. I mean when I speak about single cell, the single cell is of course a mix of a chronic analysis. So you do sequencing of single cells, you do transcriptomic analysis of single cells and you do some limited proteomics as well. So it's just not taking bulk tumor anymore rather than dissociating the tumor cells into individual ones to submit to really identify those subpopulations that is present in your.</v>

00:21:31.900 --> 00:21:32.300

Matt Thomas I meant.</v>

00:21:57.660 --> 00:21:58.640

Matt Thomas Yeah.</v>

00:21:33.440 --> 00:22:02.930

<v Penny Southworth>OK, yeah, great overview of maybe a few specific questions. So within the world of immune monitoring, I don't think you touched on us in too much yet, but I'm curious to know about the your thoughts and the evolving role of really three different areas, so flow cytometry versus spectral flow cytometry versus side top and then maybe there are some other ones as well. But if you had to kind of predict the utility of those 3 going forward, you know, how would you, how would you place it?</v>

00:22:03.140 --> 00:22:10.240

Matt Thomas So yeah, so I I have to, I have to admit to where to English it hometree equired in every study.</v>

00:22:11.560 --> 00:22:16.110

Matt Thomas Obviously there are some some limitations to it.</v>

00:22:17.390 --> 00:22:21.800

Matt Thomas The major limitations being that you need to predetermine.</v>

00:22:22.950 --> 00:22:29.990

Matt Thomas Your Marcus election for the divisional cell lines and tell cell subtypes.</v>

00:22:31.620 --> 00:23:00.480

Matt Thomas The the other major drawback, especially in the clinical world, is that you know we at least need to shift the samples to a 0 which is which is good. So and it's a sophisticated playground for them. The only caveat is that you only have this one shot on goal. Your blood sample has only a limited lifetime, so you predetermine everything from your.</v>

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Matt Thomas First assumption. Nevertheless, your analysis itself is pretty much automated preset, so you know this kind of technical settings in the cytometry field are predetermined to at least cover the major population. It doesn't really allow you to play around to focus on certain subpopulation that you may find interesting, so it is a kind of chance funding and quite honestly.</v>

00:23:30.100 --> 00:23:59.370

Matt Thomas Most of of my peers and myself have found some nice data, but not outstandingly. To really continue these pretty expensive efforts now that's that is classical psychometry it called. It's also the spectral cytometry where as site talk is of course a more proteomic directive approach which is a combination of mass spectrometry and cell sorting.</v>

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Matt Thomas Right now what I can say is that the site off is predominantly tissue based, so in it it's changing a little bit the scope compared to the the other side tell me to be approaches which take peripheral plot that you are now entering the tumors or you're pretty much in this kind of tumor space going. Yeah. Not not the same way but to the directional single cell analysis as well. So that's a little bit.</v>

00:24:30.620 --> 00:24:40.140

Matt Thomas My take here so summary is yes, we do the cytometry. Have we found some outstanding new data, unfortunately not yet.</v>

00:24:41.740 --> 00:24:42.210

<v Penny Southworth>OK.</v>

00:24:53.610 --> 00:24:54.150

Matt Thomas Yeah.</v>

00:24:58.590 --> 00:24:59.110

Matt Thomas Yeah.</v>

00:24:43.480 --> 00:25:00.700

<v Penny Southworth>OK, moving on to proteomics, curious to understand your expectations around the role of mass spectrometry versus immunoassays versus spatial proteomics. And I know you kind of alluded to some of these, but just kind of curious to make sure we cover each of those specifically.</v>

00:25:01.090 --> 00:25:18.310

Matt Thomas Yeah. Yeah, OK, yeah, let me let me start with my spectrometry. I mean, much spectrometry, whenever it started getting involved into complex proteomics, which is quite a long time ago, it was never really able to fulfill the promises.</v>

00:25:19.450 --> 00:25:41.740

Matt Thomas We see high end mass spectrometers which restrict the use to some dedicated and well trained staff people, so it's not a market which will really evolve to, I would say a product that is placed everywhere and simply because you just need highly trained.</v>

00:25:43.000 --> 00:25:51.960

Matt Thomas You know, staff to do, to run the the instruments. The other thing which is a little bit cumbersome is for my spectrometry.</v>

00:25:53.410 --> 00:26:22.840

Matt Thomas You can work a lot with soluble proteins and of course like for cytometry you work with circulating markers. The caveat there is you have a couple of highly abundant species like albumin and globally that require some preprocessing and pre analytical type of proches and it's not true and not known what kind of information do you actually lose there.</v>

00:26:22.960 --> 00:26:52.030

Matt Thomas Uh should, simply because we don't understand the entire priority end of the day, we must spectrometer has resolved. Maybe between 1000 and 3000 protein, but not the entire protein that that people were speculating a long time ago. So that's it. Mass spectrometry is stone, but more or less for research purposes. It's not for routine analysis for the reason that I just mentioned. That brings me to the immune.</v>

00:26:53.430 --> 00:26:57.150

Matt Thomas If you based approaches and here we have seen a lot of evolution.</v>

00:26:58.250 --> 00:27:07.500

Matt Thomas It's all the classically ELISA or, you know, related to that is it's still, let's say, used and predominant.</v>

00:27:08.560 --> 00:27:29.230

Matt Thomas And and variations thereof like Luminex. Or we just get all that is is classically used. What we've seen now is these platforms like Soma Logic or only link that actually go into much higher complexity. The issue there is it's still the same. So you protein.</v>

00:27:32.040 --> 00:27:59.930

Matt Thomas Empire and and the question we have is whether or not we find the response in the circulation or whether or not our response is really local that we restrict ourselves to really look into the tumor itself. So I know that especially colleagues in other therapeutic areas like metabolic PCs or inflammation, they haven't used those.</v>

00:28:00.250 --> 00:28:01.040

Matt Thomas High Plex.</v>

00:28:02.180 --> 00:28:31.270

Matt Thomas Proteomics approaches. We do so as well, but you know there's no outcome yet. I mean you, you measure a lot of things, but you don't. You're not sure whether you can relate your result to a too much specific type of outcome. So therefore, to be shown so far, these markers did not pin out to be going towards the diagnostics. I mean, that's the sign just for you guys, everything that has a chance to go for diagnostics.</v>

00:28:31.470 --> 00:28:44.680

Matt Thomas I like companion diagnostic purpose is something which is highly associated to your therapeutic approach and we don't see that for proteins. We see that for genomics, but not for proteins. So lastly.</v>

00:28:46.170 --> 00:29:16.680

Matt Thomas The tissue pays. The proteomics is something which is still struggling because the the the the context you're working is that we were somehow applies to follow the classical pathology lookup and that restricts us to kind of immune to chemistry, type of approaches and they are not that highest import. So we can do multiplexing, but not to the to the level of three to 5000 different markers.</v>

00:29:19.140 --> 00:29:29.900

<v Penny Southworth>What do you think about the future of multiplexing and how is that going to evolve and is that going to, you know, kind of increase the demand for these types of proteomic services?</v>

00:29:31.730 --> 00:29:33.620

Matt Thomas You mean my speak committee? Was that the question?</v>

00:29:35.490 --> 00:29:39.820

<v Penny Southworth>Uh, just multiplexing. Yeah, associated with any of the technology.</v>

00:29:38.850 --> 00:29:49.630

Matt Thomas I'm going to testing. Yeah. Yeah. OK. I'm Multiplex. Well, yeah, I I guess multiplexing is the method of choice. I I can only say my own experience is that.</v>

00:29:50.690 --> 00:30:01.640

Matt Thomas You often find some results that you can't explain. If you're multiplexing because you are abandoning a biased.</v>

00:30:02.970 --> 00:30:15.830

Matt Thomas Individual or whatever selection approach. So for instance, if you if you have a molecule and you don't really know what what you're looking after, you may select I'll limited number of markers.</v>

00:30:17.200 --> 00:30:45.950

Matt Thomas Main often you find some modulation of these markers, but my experience and you published a lot of that is that the best case you end up with some kind of prognostic impact under, that's not really the objective of our work. Now the multiplexing allows you to go out of a predefined space. You say I'm not interested in only looking at a small number of cytokines of growth factors.</v>

00:30:46.000 --> 00:31:08.270

Matt Thomas Blah, blah blah. Let's go. Everything that is able to be tested you of course generate a lot of data, but with the help of client formatic, bioinformatic worker, you can then be convolute this data and come to a result that is often pretty surprising. So the future is that definitely in the multiplexing.</v>

00:31:11.280 --> 00:31:11.680

<v Penny Southworth>OK.</v>

00:31:12.330 --> 00:31:29.590

<v Penny Southworth>Very helpful. Yeah. And that aligns with our expectations as well. Moving on to genomics, curious to hear a little bit about your expectations around the evolving roles of digital PCR, quantitative PCR and end GS as well as spatial genomics.</v>

00:31:30.880 --> 00:31:39.330

Matt Thomas Yeah. So I I think let's, let's speak about the digital PCR or let it PCR based approach in general.</v>

00:31:40.270 --> 00:31:47.060

Matt Thomas I guess these are relatively low cost approaches. I don't think they will disappear.</v>

00:31:48.170 --> 00:31:53.050

Matt Thomas But the the downside is that in fact your.</v>

00:31:54.890 --> 00:32:25.960

Matt Thomas Let's say you're intended use is quite dominantly limited to a scenario where you have your marker identify and you only want to go after your markup. So that means mutation and you only monitor that, but that's actually pretty much the outlier, because keep in mind, especially these days with the understanding of comprehensive genomic profiling.</v>

00:32:26.140 --> 00:32:30.050

Matt Thomas Uh, you will get a pretty comprehensive picture of the tumor.</v>

00:32:30.980 --> 00:33:00.840

Matt Thomas Especially for for the patient's electric criterium, that if your market is not in your sample or let's say or you're too but doesn't carry the marker, you make that convolute or you may reveal other markets for which there are therapies out there. So all in a setting that genomic profiling will definitely help you to identify actionable targets for which there may be drugs out there. So that's something which.</v>

00:33:00.920 --> 00:33:30.230

Matt Thomas And the the other side note is, as I said, if your marker is not on the panel, something else will pop up, so you only do it once and cover good number of different therapeutic options for a patient. So that's really something where I see a strong growth in the in the next few years and then we see it already in some regions that those tests are now becoming reimbursed rather than going into small panels. So because they all realize.</v>

00:33:31.000 --> 00:33:53.940

Matt Thomas That the reimbursement allows, uh, the physicians, if that is not the appropriate patient for that treatment intended, there may be others available and so that means a PCR based is too limited. I think it will not grow a lot. Now lastly to the spatial genomics, I mean to be honest with you.</v>

00:33:54.940 --> 00:34:16.650

Matt Thomas And I I I struggle a little bit with the with the, with the use of that you know if it's spatial transcriptomics, that's something where I can understand we do see differences, different cells, but genomics to be honest, it's something which is nice to have, but nothing really on the critical path for our work.</v>

00:34:21.670 --> 00:34:22.230

<v Penny Southworth>OK.</v>

00:34:23.050 --> 00:34:33.640

<v Penny Southworth>So that's a good a good summary. Probably the most exciting man and sort of the NGO space, it sounds like, although PCR will still have a role spatial generics, it's it's kind of hard to tell exactly how that's going to.</v>

00:34:34.690 --> 00:34:35.330

<v Penny Southworth>Fit in.</v>

00:34:36.030 --> 00:34:49.230

<v Penny Southworth>Umm, what category is that Hiphop? Excuse me, histopathology types of applications, curious to understand your expectations are around the evolving roles at different technologies there.</v>

00:34:49.770 --> 00:34:51.920

<v Penny Southworth>Uh, in that oncology space?</v>

00:34:51.520 --> 00:34:52.000

Matt Thomas Yeah.</v>

00:34:53.770 --> 00:35:04.510

Matt Thomas Yeah. I mean, as you can, as you can imagine based pathology especially in oncology has always been one of those.</v>

00:35:04.590 --> 00:35:05.120

Matt Thomas The.</v>

00:35:06.300 --> 00:35:17.530

Matt Thomas Let's say crucial diagnostic steps just to identify the disease, to undertake that. What we what we see there is a couple of.</v>

00:35:17.660 --> 00:35:28.920

Matt Thomas Umm couple of streams that are evolving from here. As you know, one of the classical steps in the histopathology work up is.</v>

00:35:30.570 --> 00:35:33.230

Matt Thomas In 18 each day, which is this blue stain.</v>

00:35:33.310 --> 00:35:53.680

Matt Thomas The microscope slide that you typically see in the future. What what we have seen now is that artificial intelligence is trying to identify with the help of their algorithms, certain biomarkers without doing any of those genomic goal.</v>

00:35:53.920 --> 00:36:19.290

Matt Thomas Ohh English to chemistry types of analysis. So I see I see the potential that we see artificial challenge, intelligence, space image analysis progressing here in order to let's say identify further whatever markers without going into a very specific.</v>

00:36:20.700 --> 00:36:22.520

Matt Thomas Type of staining protocols.</v>

00:36:23.630 --> 00:36:29.590

Matt Thomas The other workstream is as a is. Is is multiplexing on?</v>

00:36:29.710 --> 00:36:34.080

Matt Thomas No, no, no, no tissue using.</v>

00:36:36.140 --> 00:36:46.140

Matt Thomas Are you using a mono fluorescent approaches and there is a quite a number of those coming up here together with subsequent.</v>

00:36:46.480 --> 00:37:03.520

Matt Thomas Ohh spatial image analysis type of approach. So that means the pathological workup at least as long as it is in a research type of scenario in the clinical development will allow you to learn more on the tumor itself.</v>

00:37:04.660 --> 00:37:34.490

Matt Thomas Be that the baseline composition or longitudinally while the patient is under treatment. So the changes that you may observe, So what we see here is of course quite significant automation with respect to the workup of samples, but also with the image analysis by itself, algorithms that are applied for these multiplexing.</v>

00:37:35.310 --> 00:37:38.690

Matt Thomas Tissue based type of analysis so.</v>

00:37:39.930 --> 00:38:04.840

Matt Thomas The only concern I have is that a pathologist is a species of very conservative scientist, so my I'm not certain how quickly such a product would make it to the real world market. So as long as we're going into our very specific clinical development world and empire, we can do many things.</v>

00:38:05.240 --> 00:38:05.850

Matt Thomas Uh.</v>

00:38:05.940 --> 00:38:10.630

Matt Thomas People, it's still unclear when it goes to the channel.</v>

00:38:12.070 --> 00:38:16.250

Matt Thomas Science market that every pathology lab is going to use that.</v>

00:38:17.650 --> 00:38:30.200

Matt Thomas Lastly, I think we see some combinations. You know that spatial type of imaging is is a mix of this multiplexing as well. So yeah, so that's a little bit.</v>

00:38:31.840 --> 00:38:49.610

Matt Thomas Uh, do you match and alysis or chemists or Histology? Kind of of biomarker analysis, but it's it's it's crucial. It is definitely something where we see some progress here in terms of platforms that are involved.</v>

00:38:52.380 --> 00:39:05.830

<v Penny Southworth>OK, got it. Very helpful. So thank you for walking through all those different technologies. I'm curious to ask kind of a few high level questions and in particular related to you know decisions around working with partners on these.</v>

00:39:32.280 --> 00:39:33.160

Matt Thomas Yep.</v>

00:39:05.910 --> 00:39:36.180

<v Penny Southworth>Yeah. And and my partner is really like vendors with for these different types of technologies. When you're thinking about a clinical development program and and kind of the plan for it, to what degree is it valuable to get all these different technologies and biomarker service needs from the same vendor versus going to a different vendor for maybe different geographies, different stages of development or different, you know, technology needs, could you kind of speak to the the value or lack of value of having all this in one spot?</v>

00:39:36.260 --> 00:39:36.750

<v Penny Southworth>There is not.</v>

00:39:34.300 --> 00:39:43.600

Matt Thomas Yeah. Yeah, yeah. Yeah. One thing that I I I can I speak to that very quickly. So we need to.</v>

00:39:43.700 --> 00:40:14.180

Matt Thomas Umm, we need to disseminate or not to to do dissect the world into China and rest of the world. So for many reasons our clinical activities in China are extremely restrictive for us. Samples cannot go out. So just Long story short, we need to have two types of partners for whatever we want to do and there's only a real question that these partners.</v>

00:40:14.270 --> 00:40:15.010

Matt Thomas What percent?</v>

00:40:16.310 --> 00:40:30.440

Matt Thomas Across the different regions. Otherwise we face a scenario that we identify partners that are actually represented all over the world and.</v>

00:40:31.640 --> 00:40:40.300

Matt Thomas So we we're not necessarily looking into very regional type of partnerships and.</v>

00:40:41.340 --> 00:41:10.600

Matt Thomas And, and let's say from a logistic point of view for the clinical trials space, that was never a problem. I mean, we have sample stability for the shipment even for whole blood samples that are worked up with cytometry. So that's not a problem. So next question is is, is is our intention to have a one stop shop or not. So my experience here is that.</v>

00:41:10.700 --> 00:41:19.800

Matt Thomas This is virtually impossible, so if we take these large companies like covens like urea and estell called.</v>

00:41:21.630 --> 00:41:37.270

Matt Thomas You know they are good for a good number of of of of biomarker analysis but the caveat always is that they've never been in the export market. So they they try to get into it.</v>

00:41:38.420 --> 00:42:07.960

Matt Thomas And you can do quite a good number of of analysis, but in the end of the day they're they're all limitations. And so that means to go into various kind of like crucial technologies. And I have to outline those or highlight those so that the two most prominent ones that were we rely on special market is that genomics and the immunohistochemistry.</v>

00:42:08.040 --> 00:42:23.850

Matt Thomas Let's tell you why our it it is, it is not so surprising. We see the largest number of companion diagnostic development, either the genomic market or using immunohistochemistry.</v>

00:42:24.650 --> 00:42:26.360

Matt Thomas So now that all in there something.</v>

00:42:27.810 --> 00:42:30.460

Matt Thomas Drives you to a complete different corner.</v>

00:42:31.630 --> 00:42:41.360

Matt Thomas Where you need to have the certain specialized expertise from a regulatory perspective, all the essay validation.</v>

00:42:42.520 --> 00:43:03.010

Matt Thomas Timelines and requirement the local requirements for submitting a company diagnostic application that is not possible with a large 0. So therefore we are going to specialize. Then the next thing is please speak about those you know.</v>

00:43:03.530 --> 00:43:04.310

Matt Thomas Uh.</v>

00:43:06.130 --> 00:43:30.910

Matt Thomas New upcoming platforms like single cell like Spatial, these big companies are too slow, fast, too slow to establish them as a routine. So that means the end of the day our objective is to identify those specialized companies that have focused on a certain subset of markers and distribute our samples to those and get the data back.</v>

00:43:36.640 --> 00:43:50.020

<v Penny Southworth>OK, so there's a few areas where you really need to have the specialized capabilities and so therefore you know you're going to a certain provider and then other areas where maybe it's not quite as as critical.</v>

00:43:50.740 --> 00:43:51.160

<v Penny Southworth>Umm.</v>

00:43:52.280 --> 00:44:13.700

<v Penny Southworth>I noticed that you had indicated that you had worked with a couple different service providers and I'm just kind of curious to hear, you know, high level what you think of in terms of like the the differentiation for those different service providers. And it's I notice you put cell Carta precision for medicine and quanterix.</v>

00:44:14.780 --> 00:44:15.430

Matt Thomas Yeah.</v>

00:44:15.550 --> 00:44:15.990

Matt Thomas Yeah.</v>

00:44:14.480 --> 00:44:19.010

<v Penny Southworth>Any thoughts on go to the differentiation between the what are they each known for?</v>

00:44:21.230 --> 00:44:28.100

Matt Thomas So what I can say is we finally have retained cell Carta.</v>

00:44:28.180 --> 00:44:32.940

Matt Thomas Uh, and I mean, there's there's a couple of components.</v>

00:44:34.310 --> 00:44:48.690

Matt Thomas These organizations that teachers named are all all good now. The second the second component that we have to bring in here is it is very slow for us as a pharma company.</v>

00:44:49.810 --> 00:45:14.510

Matt Thomas To move on with these contractual paperwork, So what we typically do is that we run some small pilot experiments to screen whether or not the company is is acceptable, and if that is positive, then in a second round we we build up all the contractual framework and then run experiment. So what?</v>

00:45:14.630 --> 00:45:19.000

Matt Thomas What? Uh, what came out of that is that in fact.</v>

00:45:20.200 --> 00:45:37.790

Matt Thomas Self Carta for us right now is the partner of choice for many of our exploratory file markers. The other one that you mentioned, precision for medicine, is a partner for tissue acquisition. So why we're not using their services, so they have a pretty good.</v>

00:45:39.280 --> 00:46:09.570

Matt Thomas Sample inventory where we can get too much tissue from and lastly carries is a partner which we also use, but we're not. We're using them in the context of the clinical trial recruitment. So they have a patient referral system, but we're not necessarily using them although they are good. I'm not saying they, they are specialized, they're good in what they do. I would say it's good, but what we have already.</v>

00:46:09.640 --> 00:46:10.160

Matt Thomas Interesting.</v>

00:46:11.240 --> 00:46:22.460

Matt Thomas Contract and and it's very cumbersome for us to open new ones if we're not required to. So therefore I think that's a little bit slightly that you will hear more often in pharma.</v>

00:46:23.240 --> 00:46:28.570

Matt Thomas You're not going after everyone that is out there, so you have your partners and work with them.</v>

00:46:32.910 --> 00:46:34.020

<v Penny Southworth>Across each of these.</v>

00:46:34.760 --> 00:46:36.220

<v Penny Southworth>Uh vendors?</v>

00:46:38.120 --> 00:46:41.230

<v Penny Southworth>I how would you think about kind of potentially?</v>

00:46:42.020 --> 00:46:43.970

<v Penny Southworth>Expanding your.</v>

00:46:45.060 --> 00:46:50.540

<v Penny Southworth>Use of them. What what like additional services? Would it make sense for each of them to?</v>

00:46:51.300 --> 00:46:53.020

<v Penny Southworth>Offer and and why?</v>

00:46:54.650 --> 00:46:59.060

Matt Thomas Yeah, I guess so. What I can say, as I said.</v>

00:47:02.660 --> 00:47:29.080

Matt Thomas Because I need to, I need to be a little bit open here. So cell Carta is a company which we use for quite a good number of different services such as site telemetry such as immunohistochemistry. You know, kind of exploratory market analysis. And I don't remember what was the that was the 3rd broad scope of of why we are using cell Carta, because they are actually pretty good in doing all that.</v>

00:47:29.740 --> 00:47:36.220

Matt Thomas And I are the other ones worse. I would not necessarily say so. What would it take?</v>

00:47:37.480 --> 00:48:06.530

Matt Thomas So we, we know carries for instance, it's pretty strong in the genomic analysis. I thought they they do receive samples from hospitals directly. So all that is well established. Now why are we going to specialized labs like foundation medicine for eggs, you know the metric driver is the track record for all those programs.</v>

00:48:06.600 --> 00:48:26.840

Matt Thomas For which we are obliged to run companion diagnostic development, we have seen if you don't use the same, if you don't see use the provider with the experience of such a specialized company, you run into obstacles over and over again. So in the end of the day, the decision to go to.</v>

00:48:27.480 --> 00:48:36.010

Matt Thomas You know, the top scoring company for that purpose is is wise, because even if it's not a cheap exercise, at least it is.</v>

00:48:36.290 --> 00:49:08.200

Matt Thomas Umm it is a Safeway and Karras doesn't have that track record. They do standard genomic testing so they have a brilliant database for that purpose. We are using them but unfortunately for our precious samples we rely on who's there. So and I'm not expecting that a company like like carries is is trying to expand by the 12 expanding the companion diagnostic but they have their difficulties exactly.</v>

00:49:08.270 --> 00:49:37.730

Matt Thomas For the reasons that I've just mentioned, and lastly, Karras has one problem. They are pretty US centric, so that's of course unlike Pradesh medicine where we get one program running all around the world except China with carriers, we won't be able to do that even in Europe. So we need to go somewhere for the submission somewhere else anyway. So precision for medicine as I said.</v>

00:49:38.530 --> 00:50:09.260

Matt Thomas It's it's, it's for me. More tissue provider. That's OK, but not necessarily the same testing level Tory because we have already identified cell Carta. Now, why aren't we using cell Carta for diagnostic development again, same story. They are very good in the standard testing, but not necessarily with all the nitty gritty details for compact diagnostics. So therefore we can go to wash molecular diagnostics which have the.</v>

00:50:09.340 --> 00:50:13.990

Matt Thomas On the day that the know how and the expertise. So it was a bit lengthy.</v>

00:50:14.010 --> 00:50:30.880

<v Penny Southworth>Yeah. Call yeah on them, building out the capabilities around getting, you know, kind of the nitty gritties with containing diagnostics, your perception of how difficult something like that is. And if you know cell Carta, like for example, came to you and said we could start doing that now.</v>

00:50:31.700 --> 00:50:36.470

<v Penny Southworth>What would they have to show? What would they have to do or show you to convince you that they would be a preferred partner there?</v>

00:50:37.840 --> 00:50:39.070

Matt Thomas Yeah, I I guess.</v>

00:50:41.140 --> 00:50:44.460

Matt Thomas I think the most important piece is the.</v>

00:50:45.820 --> 00:50:47.000

Matt Thomas The entire.</v>

00:50:49.180 --> 00:51:16.630

Matt Thomas How should I say work package from starting a program through the analytical and clinical validation to the statistical analysis plan towards the registration of path forward? They would need to show that they have the expertise. I can tell you we in the company have different partners for the genomic testing to go for CX.</v>

00:51:16.780 --> 00:51:42.040

Matt Thomas And I can only report back that the only company where we do not force where we did not experience problems is foundation medicine. All the others they came with the same argument. Yes, we are able to do blah blah blah in the end of the day we are seeing obstacles by obstacle or after obstacle because there is a lack of experience. So Long story short is.</v>

00:51:42.980 --> 00:51:54.220

Matt Thomas At some point, cell Carta, or any company needs to have a need to generate a track record and and and our company is not the one that will do the linear pick here.</v>

00:51:56.920 --> 00:51:58.450

<v Penny Southworth>Interesting. OK, OK.</v>

00:52:01.740 --> 00:52:06.980

<v Penny Southworth>You're and sorry to kind of focus on cell Carta, but it's interesting to hear how you're using them so.</v>

00:52:08.040 --> 00:52:13.310

<v Penny Southworth>What your perception of the the different services they offer today and.</v>

00:52:14.150 --> 00:52:14.820

<v Penny Southworth>Your.</v>

00:52:37.090 --> 00:52:37.710

Matt Thomas Yeah.</v>

00:52:15.540 --> 00:52:40.330

<v Penny Southworth>Utilization of of them are so like are you setting up? I guess you could call like redundancies with other similar types of services that cell Carta. Or is it like anything related to your biomarker clinical development needs, you're you're going to sell Carta? I'm just trying to understand sort of how you would rate how like penetrated they are into the the company today?</v>

00:52:41.640 --> 00:52:47.800

Matt Thomas Yeah, I mean, the reason why why we are heavily using cell Carta?</v>

00:52:49.400 --> 00:53:07.310

Matt Thomas It's of is is pretty much a A history. So we have of course used other companies as well and in the end of the day, we're movie became a little bit annoyed was when we were relying on resource.</v>

00:53:07.390 --> 00:53:14.520

Matt Thomas Ohm, using validated assays, we discover that other players.</v>

00:53:16.010 --> 00:53:24.610

Matt Thomas In this in this in this world, are not really able to come up with as decent as a validation.</v>

00:53:24.850 --> 00:53:55.660

Matt Thomas Ohm program and so we discovered that while while we had originally actually we switched quite recently completely through cell Carta, before that we had a couple of companies, but then we decided we're not taking the risk anymore because we have experience that cell Carta is for us, the most reliable source to validate all these biomarker assays and and that's why and they have the capacity to do so. So that's that's the two things we can.</v>

00:53:55.880 --> 00:54:19.190

Matt Thomas Check them heavy workload and they were able to to to deliver. So that is where we stand now. Obviously this goes only to this kind of prototype asset format. When it goes to a product type of assay then there are no longer the best place to go. Then we need to shift gears and go somewhere else to Ventana or back home or whoever. So therefore.</v>

00:54:20.450 --> 00:54:36.260

Matt Thomas Yes, it it's kind of experience based why we are doing that and and we are so much positively let's say surprised with the way how it works out now that we're not changing our hoses again.</v>

00:54:39.160 --> 00:54:40.510

<v Penny Southworth>Yeah. Interesting. OK.</v>

00:54:52.910 --> 00:54:53.800

Matt Thomas Yeah.</v>

00:54:42.370 --> 00:54:59.320

<v Penny Southworth>So let's see. Last couple minutes. I'm just kind of curious to know if there's anything in this space that's really important that we haven't talked about your your, you know your perception or if you were to, you know, offer advice to any company that's trying to be successful.</v>

00:55:00.040 --> 00:55:02.400

Matt Thomas Yeah, absolutely, yeah.</v>

00:55:00.020 --> 00:55:02.690

<v Penny Southworth>Uh, you know it's successful vendor. What would you tell them?</v>

00:55:03.880 --> 00:55:34.040

Matt Thomas Yeah. So I guess we spoke a lot about all those modern technologies like spatial and so on imaging, you know, single cell sequencing and what what what I did not go into detail is there are black boxes in the sample strategy itself. So I think it's easy to matching collection of blood is all established and straightforward. I think agree with you that there we don't have to work. But when it comes to especially for college.</v>

00:55:34.130 --> 00:56:04.220

Matt Thomas He to tissue based analysis, in particular with the aim to come into the single cell market, you need to dissociate the tumor. The tumor may not be put into formaldehyde, so the classical pathological worker needs to be disrupted. Now, that said, requires a certain freshness of sample and all those protocols are still in its infancy. So what I'd like to see from those companies, not only the.</v>

00:56:04.310 --> 00:56:28.880

Matt Thomas Data generation but also the pre processing analysis or or pre analysis processing of samples that there is a proposal how we can make this an approach that is not impacted by timeline such as you know you have to ship your sample within 24 hours or so. So we need a robust.</v>

00:56:30.510 --> 00:56:38.760

Matt Thomas Pre analysis processing step procedure that allows us to to implement such a platform widely into our clinical.</v>

00:56:39.150 --> 00:56:49.010

Matt Thomas Uh, uh. Let's say procedure. That's my main hope that we get into the protocols that allow us to have a sample partners of a couple of days.</v>

00:56:51.560 --> 00:56:52.080

<v Penny Southworth>OK.</v>

00:56:53.570 --> 00:56:54.750

<v Penny Southworth>Very helpful. Anything else?</v>

00:56:56.380 --> 00:56:58.230

Matt Thomas No, I think that's that's pretty much it.</v>