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

0:0:0.0 --> 0:0:0.920  
Harry Graham  
As for many.

0:0:13.320 --> 0:0:13.580  
Harry Graham  
Sure.

0:0:7.580 --> 0:0:19.640  
Angela Angle  
OK, the recording has been started. It'd be helpful. Yeah, you could just continue starting out the call with just a brief description of your background and your role in selecting ceros for biomarker related testing services.

0:0:20.590 --> 0:0:28.0  
Harry Graham  
Yeah. So I think some sort of industry for 23 actually almost 24 years.

0:0:29.200 --> 0:0:33.730  
Harry Graham  
And most of my career, I was in big pharmaceutical company.

0:0:35.350 --> 0:0:43.250  
Harry Graham  
And my current role is I'm the senior VP of Translation Medicine and the clinical Obama Care, which is precision medicine.

0:0:44.510 --> 0:1:5.920  
Harry Graham  
You have midsize company I mentioned before. We have over 2000 employees on and we use analytical essays to support the drug discovery and the development specifically on the biomarker. I'll I'll provide more detailed information when you ask your questions.

0:1:7.220 --> 0:1:11.310  
Harry Graham  
Is that sufficient for your introduction, or you want me to get into more details?

0:1:21.390 --> 0:1:21.800  
Harry Graham  
Still.

0:1:27.820 --> 0:1:28.410  
Harry Graham  
Yep, Yep.

0:1:12.800 --> 0:1:28.880  
Angela Angle  
That's helpful. And I think it also be helpful to know what your previous roles in current role, what types of therapeutic modalities you've been, you've been working on and are there specific therapeutic areas like oncology, immunology and infectious disease that you've been focused on?

0:1:29.780 --> 0:1:46.100  
Harry Graham  
Yeah. I think focus on primarily on on topology and autoimmune diseases in both drug discovery and development. And I am in charge of selecting the vendors to support our.

0:1:46.470 --> 0:2:5.300  
Harry Graham  
I'm early and the later development programs and including the analytical lab as well, I used to be responsible for the clinical development programs in my previous company and also holds the primary decision maker for select clinical seattles.

0:2:7.870 --> 0:2:13.300  
Angela Angle  
And have you been focused on small molecules or antibody drugs or other types of biologics?

0:2:14.620 --> 0:2:24.980  
Harry Graham  
Oppose. I'm adding, you know my current company. We are working on both small molecule as well as the biologics that the antibody so critics.

0:2:26.540 --> 0:2:27.690  
Angela Angle  
OK. That's helpful.

0:2:29.370 --> 0:3:0.540  
Angela Angle  
So I guess I just want to understand what sorts of biomarker testing services you typically deal with in the programs that you've been involved with. And one of the ways that we're thinking about kind of segmenting the spaces, there's immune monitoring, testing, which could be looking at cellular phenotypes, flow cytometry assays, proteomics, this could be amino assays as well as mass spectrometry and other analysis genomics, which includes sequencing and PCR.

0:3:0.610 --> 0:3:1.990  
Angela Angle  
And then histopathology.

0:3:10.180 --> 0:3:10.580  
Harry Graham  
Yep.

0:3:12.250 --> 0:3:12.850  
Harry Graham  
Yep.

0:3:3.690 --> 0:3:14.130  
Angela Angle  
Which contains a variety of different tests there as well. This is segmentation makes sense to you, and are there any other major categories that we're missing?

0:3:15.190 --> 0:3:40.260  
Harry Graham  
Yeah, it might totally makes the sense you actually you know what you listed is quite inclusive. So first I'll start with what how we use about markets in supporting drug discovery and development by market actually gives talk at conferences before colors, the continuing of drug discovery and development, it starts from.

0:3:40.990 --> 0:3:59.890  
Harry Graham  
You target identification when we select a the the new target we wanted to use oncology as example. We normally looking for major oncogenic driver pathways. The target on those pathways and we profile use.

0:4:0.570 --> 0:4:20.260  
Harry Graham  
Look at the by market data to make sure that we pick the target that play important role in cancer cell transformation. But it doesn't, you know express very low level or doesn't express in normal tissues. Try this type of target normally can give us.

0:4:20.350 --> 0:4:34.910  
Harry Graham  
A good therapeutic window because it it doesn't. The drug target doesn't express the at the high level in in normal cells, so it's easy for us to find the index the window.

0:4:35.580 --> 0:4:39.190  
Harry Graham  
And then once we started a program, we look at the.

0:4:39.270 --> 0:4:50.920  
Harry Graham  
The the individual individual activity of a lead compound so you know from you type the identification then regardless you you use the small molecule.

0:4:51.0 --> 0:5:3.310  
Harry Graham  
A bit or anybody you know, the biologics, you will do the lead identification and then lead optimization. So once we have optimized the molecule.

0:5:4.150 --> 0:5:35.430  
Harry Graham  
And then we look at it, the PDF fact that somehow dynamic effect which can serve as a bull market for the later study and also in clinical development, basically we look at how the drug works is the drug acting as it supposed to do when it engages the target and that's where the PR bond market comes into play. And then we would for translation medicine, we know there's a big window.

0:5:35.520 --> 0:5:39.30  
Harry Graham  
The gap between the drug discovery and the developments.

0:5:39.820 --> 0:5:59.390  
Harry Graham  
Because oftentimes what we see in the preclinical setting doesn't translate into a canonical to human. So we as a bridge we perform biomarker study to make sure the preclinical observation of the biomarker PDX will be translated into human.

0:6:0.130 --> 0:6:11.40  
Harry Graham  
And also we make a good efforts to identify if there any predictive biomarker we can use to predict.

0:6:11.830 --> 0:6:28.100  
Harry Graham  
Didn't come in a call which patients may be likely benefit from the drug treatment, and we develop such essays or work with CRO to leverage their development assays to address all those questions.

0:6:29.710 --> 0:6:45.960  
Angela Angle  
And I guess in what stage of the development process do you start looking at individual model or individual biomarkers, do you have an idea when you start the project and identify your specific target or does that come later in the development stage when you look to move to preclinical?

0:6:46.900 --> 0:7:8.340  
Harry Graham  
It it depends. For certain targets, we know that we should biomarker to look into from the get go but for certain target if it's a very novel target not much information in the literature in the public domain then we have to design discovery biomarker discovery study to identify those.

0:7:15.440 --> 0:7:15.720  
Angela Angle  
Umm.

0:7:8.430 --> 0:7:17.460  
Harry Graham  
The target and then now I'm getting to your next question regarding to the technology platforms, what kind of platform we use?

0:7:17.580 --> 0:7:40.810  
Harry Graham  
I'm for many of the, you know, oncology targets especially immuno oncology targets. The history IIRC, even though Histochemistry as they offload cytometry, you know important platforms we adopt plus ELISA type of study like MSD.

0:7:40.890 --> 0:8:12.580  
Harry Graham  
And the the soma, you know some of the highest sensitivity ELISA assays used widely to measure, you know Skype token, current level, the flow cytometry, you can do the immune cell phenotyping and then for ICC can look at the the protein biomarkers on the the sample, the sections on the slides to look at the morphology and expression and also for IHC, you can run Multiplex.

0:8:12.660 --> 0:8:33.630  
Harry Graham  
If you see, you can look at a different cell cell interaction by standing multiple biomarkers at the same time, and then we also use the molecular technologies such as eggs. You can do the sequence of sorted tumor as well as liquid biopsy.

0:8:34.290 --> 0:8:34.570  
Angela Angle  
Mm-hmm.

0:8:34.520 --> 0:9:0.110  
Harry Graham  
The plasma samples you look at the circulating tumor DNA RNA. By doing sequencing, you can look at the the, the gene, you know the mutation and the insertion, deletion of gene fusion or structure variations. So you can get a lot of information from the NGS testing and they are large validated.

0:9:1.800 --> 0:9:30.270  
Harry Graham  
Approved the CD XS is using the the NGS platform and for the certain you know target you you know your target of interest. You don't always need to use the big's panel. You can use the PCR based testing. That's you know that those type of assay is relatively fast and quick to you know quick and inexpensive to develop and it.

0:9:30.350 --> 0:9:40.600  
Harry Graham  
If if your paper so when you have a specific gene or genes in mind and and also you know there are the platforms.

0:9:41.720 --> 0:9:57.950  
Harry Graham  
You know, came from and she has like you can look at the minimum residual disease using the NGS platform. You can also use the flow for MRG testing as well. And now the for eggs, another big area is the.

0:9:58.680 --> 0:10:4.630  
Harry Graham  
It's the single cell analysis and then combine with the the genomic and proteomic.

0:10:4.880 --> 0:10:9.750  
Harry Graham  
Uh technologies Special Genomics has been used.

0:10:9.830 --> 0:10:10.160  
Harry Graham  
The.

0:10:11.340 --> 0:10:15.140  
Harry Graham  
It in the recent years and they become a very useful tool.

0:10:16.910 --> 0:10:45.0  
Angela Angle  
Great. That was really helpful. Review the different technologies and I'll have some follow up on each and a few of the different technologies that you mentioned. But first I wanted to understand the process of developing your biomarker assays. Is this something that your companies have typically done in house or when would you look to outsource the development of the essay in the 1st place and if this varies between the large company that you worked at in the mid to smaller size companies, that would be helpful to know as well.

0:10:46.30 --> 0:11:16.20  
Harry Graham  
Yeah, yeah. So this is the. Yeah, it varies it depending on the. It depends on the target. So for power market, you know just go through the discovery and development process for any new target is started from new target identification and then you need to validate the new target and then you know once you get a a validated target that you can get the official approval from the organization to initiate the formal program.

0:11:16.100 --> 0:11:19.830  
Harry Graham  
To, you know, get a endorsement for resource allocation.

0:11:20.620 --> 0:11:50.510  
Harry Graham  
And then you if it's small, Molly to you, you know, you work with your chemist to, you know, either do high throughput screening or do some structure based drug design to generate the small molecule for for recall the lead identification or, you know, high throughput screening and that to identify the the lead compound and then your work with your tenants or crawls to do the hit to lead optimization.

0:11:50.680 --> 0:12:20.570  
Harry Graham  
And then you continue, you know, work with your chemist to optimize the molecule and you have a lead compound, which would, you know, people call preclinical candidate PC and then you work with you know, TMK scientists, the safety scientists, make sure the molecule has a preferred physical property and have a good preclinical talks profile. And if everything lines up then you can.

0:12:21.250 --> 0:12:51.900  
Harry Graham  
File ID to get the drug into chemical development and for small for big molecules is the same. First you identify the target, validate the target and then you work with your biologist who can help you to to, you know, generate the lead antibody and then do the optimization of the lead antibody, make it drug like and then profile the physical property and also safety profile.

0:12:52.240 --> 0:13:10.160  
Harry Graham  
Uh, profile that toxicity profile and then when the molecules ready you, you file aren't D so it's, you know it's a very similar whether that's a small molecule or big molecule. And in terms of biomarker, as I mentioned in the early new target identification phase, you can.

0:13:11.80 --> 0:13:41.180  
Harry Graham  
User by marking formation that genomics data the proteomics data to make sure that you select a target that's you know it's it's relevant to your to your interests of you know disease indication and also has a specific expression differential expression in the disease versus normal tissue. And then after you you know the.

0:13:41.330 --> 0:13:48.850  
Harry Graham  
You have the lead molecule. You wanted to make sure you have the pharmacodynamic biomarker which can measure.

0:13:49.740 --> 0:14:11.200  
Harry Graham  
The target engagement basically wanted to have about market to tell you whether the drug is acting as what is supposed to be based on the mechanism of action and that biomarker can be used to clinical trial and this for big pharmaceutical companies they have.

0:14:12.220 --> 0:14:25.960  
Harry Graham  
You know the infrastructure to do most of those pretend unical works themselves, they they may or may not outsourcing the work to to see O, but for small and mid size.

0:14:27.280 --> 0:14:28.640  
Harry Graham  
Biotech or biopharma?

0:14:28.720 --> 0:14:59.50  
Harry Graham  
Umm it depending on whether they have resource oftentime they would consider outsourcing the work to Seattle especially you know when some of the Obama platforms, you know, requires special, maybe more expensive equipment or requires special expertise. They may not have it in house. So they probably, you know, choose to use the CRO another.

0:14:59.150 --> 0:15:0.800  
Harry Graham  
The reason for.

0:15:26.170 --> 0:15:26.440  
Angela Angle  
Mm-hmm.

0:15:1.540 --> 0:15:31.330  
Harry Graham  
All the family and the biotech to use Co is when they enter in the clinical trials stage because they are regulation regarding to what labs can perform. Some of the testing to support the clinical trials. For example, if you are using Obama market to identify patient for enrollment by the definition you have to work with the clear CAP lab.

0:15:32.200 --> 0:15:38.610  
Harry Graham  
To perform the testing according to the regulatory requirements and the most of the.

0:15:39.600 --> 0:15:51.520  
Harry Graham  
Find my including big farmers. They don't have their own clear lab in the in, you know, within their company they have to rely on the CIO's to perform the testing for them.

0:15:52.320 --> 0:15:57.750  
Angela Angle  
Umm. And a couple follow up questions for the.

0:16:7.870 --> 0:16:8.130  
Harry Graham  
So.

0:15:58.750 --> 0:16:11.310  
Angela Angle  
The the assays that require specific expertise or expensive pieces of equipment that a company doesn't have, could you provide some examples of that? Like what, what types of tests would would need the CRO assistance?

0:16:12.320 --> 0:16:42.90  
Harry Graham  
Yeah, you know, like I said, if this involves clinical study, it is the essays useful for patients election. They're actually there are three criteria in in US. One is you know whether the the testing results is used for medical decision. The second is whether the testing result that need to be signed to clinical sites. The third criteria is whether the.

0:16:42.270 --> 0:16:56.470  
Harry Graham  
Sampling method is invasive if the answer is yes, then you have to use a clear lab. So like I said, most of the farmers, they don't have their, you know, their own clear lab to do such testing.

0:16:57.400 --> 0:17:25.260  
Harry Graham  
So regardless, this is a complicated, expensive. You know, the essay require expensive uh category investment farmers or biotech about pharmacy or need to work with the the the CEO's. But if if you know this is the for retrospective analysis the testing results are not used for medical intervention then the farmer can do it in house.

0:17:40.390 --> 0:17:40.640  
Angela Angle  
Umm.

0:17:26.320 --> 0:17:43.760  
Harry Graham  
They May 4 big farmers, they have expensive equipment like, you know. For example, if you talk about NGS, you know you may need to have a nice next week high sick or Nova seek, right? This is the enormous system which are quite expensive.

0:18:6.230 --> 0:18:6.510  
Angela Angle  
Umm.

0:17:44.760 --> 0:18:8.170  
Harry Graham  
Did they investment now or, you know, use something like some officials. TGM, you know the protocol and the the genetics is that's the newest automated sequencing system. I'm just using examples of the two leader the technology platform companies in the NGS area.

0:18:9.280 --> 0:18:14.850  
Harry Graham  
And but if you are gonna do proteomics type of essay for example.

0:18:15.640 --> 0:18:45.690  
Harry Graham  
If you need to do some special general mix or or single cell sequencing, you know special genomics Courier system is is quite expensive. It probably cost anywhere from 300K to half minute right to to get the the the scanner and the the associated the software or if you are using you know the auto scan whether you use the antenna system, Diaco or.

0:18:45.810 --> 0:18:49.480  
Harry Graham  
Like a bond, those are all pretty expensive equipment.

0:19:9.180 --> 0:19:9.460  
Angela Angle  
Mm-hmm.

0:18:50.350 --> 0:19:14.280  
Harry Graham  
Four companies, especially small to mid size companies, it may not be a good investment because if they are using this for a small warning testing the you know they don't, they just don't have the volume high enough to to justify for all the all the costs for the equipment.

0:19:15.350 --> 0:19:24.680  
Harry Graham  
Yeah, and same e-mail for the flow cytometry. You know, whether you use the temples or for Tessa Fessas also quite expensive and now they are Symphony, right?

0:19:25.800 --> 0:19:56.930  
Harry Graham  
And if it doesn't justify for, you know, by spend the more than half million to buy a instrument and then you only have, you know, limited number on the other side, if you go to Seattle because they get the samples from different sponsors, they they can run the NSA in high throughput you know 96 well played for formats or even 384 by doing that they each per sample cost is much lower.

0:19:57.10 --> 0:20:1.410  
Harry Graham  
And the the biotech or bar not do it themselves.

0:20:1.850 --> 0:20:2.160  
Angela Angle  
Mm-hmm.

0:20:2.660 --> 0:20:13.370  
Harry Graham  
Well, the farmaceutica companies because they have a big portfolio and they do have that they can have the volume if they coordinate among different trials, you know different programs.

0:20:14.380 --> 0:20:26.410  
Harry Graham  
But for startup biotech or Bafana like us, it's not a oftentimes, it's not cost effective to buy all the instruments and doing things in house.

0:20:27.840 --> 0:20:43.570  
Angela Angle  
For the flow cytometry is I I caught a few of the instrument names. Are these conventional postiton meters or do you have any use for the spectral flow cytometers or sikov? Do you need to get up to that level of number of markers per test?

0:20:45.90 --> 0:21:2.790  
Harry Graham  
Yeah, I I think you know for for test that you can go to this, that's the BD platform you can do like a 16 color Symphony. You know you can test I think up to 50 color, yeah, side top you can get high high.

0:21:4.120 --> 0:21:7.800  
Harry Graham  
You know, Multiplex high number of analysis.

0:21:7.990 --> 0:21:16.160  
Harry Graham  
A Ann and ice at a time and then in the was a tune system and also.

0:21:16.240 --> 0:21:39.870  
Harry Graham  
On the the side tech right, so there are multiple platforms. So it's really, you know it depends on what kind of testing do you need and sometimes it boils down to what the lab scientist feel, what they are experiencing. You know some of my team, you know they prefer to use for example.

0:21:41.160 --> 0:22:11.490  
Harry Graham  
The the temples or or contessa some maybe say tell me they are more comfortable with the cell tack and I have you know my my previous team like to use the attune so it it it it that is really you know the number of analytes right now for flow is not really the bottleneck because the other way you can address multiple analyze is you can break into multiple tubes right can.

0:22:11.340 --> 0:22:11.630  
Angela Angle  
Mm-hmm.

0:22:11.690 --> 0:22:14.780  
Harry Graham  
One sample you can run you know if if one.

0:22:16.300 --> 0:22:27.430  
Harry Graham  
True, but you can run 8 color IF8 color is not enough. Then you run two tubes that can give you up to 16 color or or even more. It just by adding the tube numbers.

0:22:28.910 --> 0:22:57.980  
Harry Graham  
So it is really depends and and then depending on what kind of you know phenotyping, are you going to look at oftentime? You know, up to, I think 16 color, oftentimes 8 color. You know it is sufficient unless you know we do a discovery work. We don't know exactly what marker we wanted to use in our essay. So we cast a wide net to do a screening.

0:22:58.140 --> 0:23:2.580  
Harry Graham  
And then narrow down to, umm smaller number of panel.

0:23:3.910 --> 0:23:5.320  
Angela Angle  
OK. That makes sense.

0:23:6.250 --> 0:23:8.200  
Angela Angle  
And for the.

0:23:8.890 --> 0:23:27.400  
Angela Angle  
For the test that you're using in the clinical stage that you mentioned that need to be often run at a clear CAP certified lab, are the biopharma biotech companies developing these assays or is the Sierra of who's gonna eventually run the assay, the one developing the tests?

0:23:28.480 --> 0:23:59.550  
Harry Graham  
Yeah, we actually try to avoid essay transfer to the S transfer can be a very lengthy process and also you know can can be problematic. You know, very costly and time consuming. So what we will do is we would check all the different vendors and to see if any vendor has already have the NSA developed and validated on their menu because that will save us time and the cost.

0:24:0.660 --> 0:24:0.970  
Angela Angle  
Mm-hmm.

0:24:0.530 --> 0:24:16.270  
Harry Graham  
I don't, but if it's a essay that, you know, no one is offering it, then we have to develop it ourselves and then work with the vendor to transfer to them and have them validated in their lab to make sure that as a is performing.

0:24:17.390 --> 0:24:20.370  
Harry Graham  
You know as what? Clear cab required.

0:24:21.140 --> 0:24:34.380  
Angela Angle  
Umm, maybe starting with some of the immunology tests? Is it common that a vendor has the right off the shelf test available, or do you typically have to customize or panel of six or however many markers that you need?

0:24:35.470 --> 0:24:50.80  
Harry Graham  
Yeah, in a for some of the thunders, they actually you know they develop a very big panel in there. They they do their homework, they look at all that, you know, pharma, all the the popular markers.

0:24:50.190 --> 0:25:21.350  
Harry Graham  
And in the in in the farmers pipeline and they develop a big panel and then sometimes it can happen that they have the big panel developer that and the validated you may only need a subset of that and that's you, you can still leverage the existing panel even though it's not identical to what you want. You may get you know some actual bond market information which you know you just don't need use that for decision making.

0:25:21.820 --> 0:25:22.100  
Angela Angle  
Mm-hmm.

0:25:21.650 --> 0:25:26.990  
Harry Graham  
But have you seen her already have your Obama care of interest to cover the in the existing panel?

0:25:28.60 --> 0:25:36.220  
Harry Graham  
Sometimes you may have a special bond market that the UH testing labs to the COVID existing panel.

0:25:37.120 --> 0:26:4.170  
Harry Graham  
You should don't cover and then in that case you need ask them to add your additional Obama coffee interest as them to do another validation afterwards. And this can happen and and sometimes if you have a very special essay the the file has to develop from the scratch and do the validation, all those happens.

0:26:5.610 --> 0:26:24.450  
Angela Angle  
When you get to the clinical stage and you're for example doing a flow cytometry test, can you use one of the off the shelf test that have a really large number of analytes even though you don't need half of them for example? Or does it need to be very specific so that you only collect the data that you need at the clinical stage?

0:26:26.110 --> 0:26:34.900  
Harry Graham  
You you can get more data than what you need as long as the SA has been appropriately validated for the regulation.

0:26:36.130 --> 0:26:44.750  
Harry Graham  
Yeah, and this is the, you know, you probably know the, you know, for example the F1C DX as it has 324 genes in the in the panel.

0:26:45.770 --> 0:27:17.120  
Harry Graham  
And the meaning farmers and and the above farmer, you know biotech use that as a because it covers almost all the known actionable uncle gene. So tumor suppressor genes. So it's fine you get extra data as long as you don't take a platform that requires a large amount of tissues because for all the clinical testing you won't need to gather the ethical committees approval for the testing. And if the testing involves.

0:27:17.240 --> 0:27:19.170  
Harry Graham  
I know invasive.

0:27:20.160 --> 0:27:51.280  
Harry Graham  
A method to obtain the tissue and if you need to use a large amount of tissue then you need to justify that the why you need the the the the big amount of tissue and the the has the committee may have questions that's actually is a beauty of using the NGS panel because you know for NGS I think the foundation medicine you can use anywhere from 20 nanogram to 50 nanogram. You can get a readout.

0:27:51.370 --> 0:28:11.340  
Harry Graham  
Now for over 300 things and that's actually end up saving the the tissue. So getting that additional data is not a problematic is actually good as I as the team of you get a very you know valid and high quality data for the gene of your interest.

0:28:13.460 --> 0:28:35.990  
Angela Angle  
Yeah, that makes sense. You've mentioned, UM, solitude more versus liquid biopsy before. And I'm curious how frequently you anticipate liquid biopsies being used for clinical trials? And is this a key capability that you see that zeros have or are many of those zeros out there able to perform liquid biopsy tests and develop liquid biopsy tests?

0:28:52.870 --> 0:28:53.100  
Angela Angle  
Umm.

0:28:37.110 --> 0:29:8.910  
Harry Graham  
Yeah. And that's about it has, you know, now, you know, the technology evolves advanced so quickly, right? If you ask me this question a few years back, I will say, well, you know the the technology is still in development, but now the technology is becoming very mature and they are leader players that I'm showing, you know like, you know, gotten health and you know some other companies, they have the approved the CDX essays and those essays for CDX as is.

0:29:9.0 --> 0:29:39.250  
Harry Graham  
We have developed in a way it's very user-friendly. Uh, because by design, right? They they need to be very easy to to operate and the in terms of the knowledge and experience in running such assays is become pretty. I wouldn't say you know standard but it's become and the more and more adopted in clinical trials. The only caveats there which is you know.

0:29:39.330 --> 0:29:48.40  
Harry Graham  
The will recognize in the field is because the liquid biopsy we are looking for very rare events.

0:29:48.960 --> 0:30:16.690  
Harry Graham  
So you need to use a platform using the sequencing power allow you to detect those real events and those type of testing tend to give you false negative results. So you do need to for example, I work on actually a CDX approval for both liquid biopsy and the tumor biopsy for the same gene at the same time and.

0:30:17.360 --> 0:30:47.920  
Harry Graham  
It's in that case, you know, we have to we first we can use one the tissue is not available. It's OK for the clinicians, oncologist to use the plasma samples to look for certain mutation. And if the result is negative, if it's positive, that's sufficient to make a treatment decision. But if it's an active, the test has been reflected to tishu because you know the negative results.

0:30:47.980 --> 0:30:59.790  
Harry Graham  
Can be false negative, so that's the the big drawback of the liquid about. See testing so we can get the negative results. You may still have to reflect 2 tissue testing.

0:31:1.40 --> 0:31:8.0  
Angela Angle  
So the sensitivity of the liquid biopsy is not quite there with the that's the tissue level I suppose.

0:31:8.930 --> 0:31:39.690  
Harry Graham  
Yeah. So the the, that's just because of the nature of the liquid biopsy, right, because we are looking for circulating tumor DNA or RNA, that's shaded from the tumor cell. So the content in situation in you know plasma or in blood is is very, very low. So you need a for example for some tissue testing you know with 250X coverage you if the mutation is there or.

0:31:39.850 --> 0:31:42.720  
Harry Graham  
The infusion is there. You should be able to detect it.

0:31:44.400 --> 0:31:44.700  
Angela Angle  
Umm.

0:31:43.920 --> 0:31:58.460  
Harry Graham  
But for a little bit about see because it's such a rare event, you may need to increase your sequencing coverage to much high level in order to catch those real events. This is just a nature of the specimen.

0:32:0.610 --> 0:32:29.420  
Angela Angle  
OK, I want to get back to one other test type or platform type. I guess you mentioned the single cell and spatial omics analysis that are you're using occasionally and I'm trying to understand what the timeline of these technologies is for when they're gonna see a lot more frequent use and development. And at the clinical stage and what what I guess what purposes are you currently using these types of tests today?

0:32:30.380 --> 0:32:40.330  
Harry Graham  
Umm yeah, the the value of such testing is is a very, very high, but in reality you know is still.

0:32:41.100 --> 0:33:12.460  
Harry Graham  
Very expensive. You single cell as example in order to get the. So first of all you know the advantage of use this type of sequencing testing because the traditional bulk sequencing we mix everything together right? You know I used to it, there's an analogy is you know very well very good analogy about this. It's almost like you know it's a smoothie. You have all kinds of food that you know.

0:33:22.20 --> 0:33:22.420  
Angela Angle  
Umm.

0:33:12.530 --> 0:33:33.990  
Harry Graham  
Put it together and you know you grounded it. Get a smoothie. You really don't know what's exactly what's in there. If you are not told. So it. Fox sequencing is like that. You have DNA from, you know, the two-month sales JSON normal immune sales. It could be all kinds of immune cells. TCL, BC, Li, NK.

0:33:35.90 --> 0:33:44.30  
Harry Graham  
You know 10 rated the sales myeloid suppressor cells, regulatory T cells and then you also have you know fibroblast there they are.

0:33:44.790 --> 0:33:59.150  
Harry Graham  
Basically, it's a mixture of everything. So when you get a signal, you really don't know where the signal come from, what kind of cells, single cell on the other side will tell you. OK, you actually have, you know.

0:33:59.950 --> 0:34:8.90  
Harry Graham  
UH-1 banana. You know, some two oranges or or you know exactly what's in there, right? That made it.

0:34:9.360 --> 0:34:38.750  
Harry Graham  
So have you see, you know what? What? What? What they are. And then you you can say. Ohh. OK, my this signal I'm looking at is actually not coming from the tumor cell actually come from immune cell. Not from all the immune cell. It's probably come from let's say regulatory T cells. That's exactly what you wanted to know. If you have a flag that's typically the regulatory T cells, right that you know you have the confidence that your drug is is targeting that the sales.

0:34:42.180 --> 0:34:42.420  
Angela Angle  
Umm.

0:34:38.880 --> 0:35:9.930  
Harry Graham  
And as you, you know, hypothesized, that's very important. And then Special Genomics is almost like a, you know, not only you know, you have one banana, 2 orange, you know, three apples in your smooth, but also how they are in context of each other. Right. And and that's very important from the understanding the biology of your target. So you you know OK you know you have the signal in individual cells and what cells.

0:35:10.60 --> 0:35:15.770  
Harry Graham  
In in in close proximity with the other cells because that will tell you.

0:35:39.700 --> 0:35:40.30  
Angela Angle  
Umm.

0:35:16.560 --> 0:35:46.430  
Harry Graham  
Sales selling trash interaction is immuno oncology as example just to know there are a lot of immune sales in a given tissue sample to my tissue sample is not enough. You also wanted to make sure you wanted to know how many immune cells are in contact with the tumor cells. So once those are activated it can kill the tumor cells not the immune cells inside the vasculature. That's not gonna help because they are not in contact with you myself.

0:35:46.910 --> 0:35:56.790  
Harry Graham  
So those are the examples and that, you know, explain why single cell spatial genomics is catching a lot of attention now.

0:35:57.690 --> 0:36:7.560  
Harry Graham  
And when you go to big conference like you know, uh SCR will start this weekend, right? You know there are over promising two 20,000.

0:36:7.640 --> 0:36:25.240  
Harry Graham  
Yeah, I researchers promo over the world will be there. And if you go to the poster session, I bet you you will see a big session. You know, talk about how people using single, they are using special genomics to help understand the mechanism of targets.

0:36:41.420 --> 0:36:41.620  
Harry Graham  
Yeah.

0:36:26.440 --> 0:36:42.210  
Angela Angle  
Do you see this more as a these technologies more as a biomarker discovery use or do you see them being used as routine biomarker assays for say like beat optimization or even in preclinical or clinical settings and the next three to five years?

0:36:43.160 --> 0:37:14.330  
Harry Graham  
Yeah. In the next three to five years, I'm, I'm very optimistic. But at the current time, I think you know they are mainly used for exploratory research purpose because for any technology to be ready for prime time in clinical practice is requires a lot of you know from a regulatory perspective, quality perspective. There are high bars for them to meet. So you know in it takes more time for the technology to mature.

0:37:14.770 --> 0:37:25.60  
Harry Graham  
To be clinical ready, you know, ready to be used by, you know, conical practice. With that said, I I'm optimistic and I I believe in.

0:37:26.90 --> 0:37:43.150  
Harry Graham  
Three to five years, you know, given how fast the technologies uh developing is evolving, I I'm you know I wouldn't be surprised that this will become you know pretty common clinical practice just like look at the biopsy.

0:37:44.40 --> 0:38:6.760  
Harry Graham  
When it first came up, people you know wouldn't believe it can be used in coming call practice very soon, but now you know it's become a quite commonly used they are FDA approved the CDX test that had been used in clinical as well. So I think that you know it will be there with the technology become more mature.

0:38:33.880 --> 0:38:34.440  
Harry Graham  
Mm-hmm.

0:38:7.690 --> 0:38:37.960  
Angela Angle  
Yeah, makes sense for the the last part of the call, I wanted to ask a little bit about your experience with a few of the different zeros that you mentioned in the screeners and we're familiar with a lot of the, the larger ceros and maybe they can ask a little bit more of a general question on the larger version, the more specialized zeros. But I do wanna go into some of the smaller ones that you mentioned. I think the first one on the list was cell Carta. And then just curious on your experience with that company and.

0:38:38.240 --> 0:38:46.330  
Angela Angle  
Your what you saw as kind of differentiating factors that would lead you to pick them over another smaller one or a larger 0?

0:38:47.350 --> 0:39:16.620  
Harry Graham  
Umm yeah, so Carta in? Uh, you probably know them, right? I actually first know Histogenics Histogenics is a company formed by, I think the CEO. His name is Chris something. It's a pathologist in Spain. And they actually did a pretty good job. And not only you know they they they they were specializing in you know histochemistry and some digital pathologists.

0:39:17.310 --> 0:39:25.730  
Harry Graham  
Assays because the founder you know himself was a pathologist and.

0:39:26.580 --> 0:39:56.730  
Harry Graham  
I I had experience at work with them closely when I was in a big pharma and they they overall they deliver pretty good quality and and the other smart thing they did was they actually they were originated you know started in in Europe but they expanded to North America and Asia. So basically the e-mail they established the global footprints to enable them to support the global trials.

0:39:57.410 --> 0:40:6.960  
Harry Graham  
And the by, you know, doing the the good work that they, they did get a good reputation on especially in the IC area proteomics area.

0:40:8.70 --> 0:40:39.130  
Harry Graham  
And then I believe other acquired them, right, so that you know, gives them cell Carta itself. They have a more than just, I should see they can do molecular testing. And a recently they bought another company combo SEC by acquiring you know those companies expanded their capabilities. And I think overall you know from for ICC as I do think they they are.

0:40:39.320 --> 0:40:42.470  
Harry Graham  
Doing pretty good high quality work.

0:40:50.380 --> 0:40:50.700  
Angela Angle  
Mm-hmm.

0:40:43.250 --> 0:40:52.270  
Harry Graham  
And compared with other companies, I will give you an example. You know the the Q2, the lab is is quite right.

0:40:53.370 --> 0:40:55.740  
Harry Graham  
I think almost just like.

0:40:56.680 --> 0:41:26.130  
Harry Graham  
You know a big pharma and biotech we always you know, compare them with the pros and cons. I think that that's similar observation also apply to the testing labs for smaller labs, they are more nimble and they are relatively fast in, in, in turn around time turn around time not only you know turn around time or testing the sample but also turn around time in developer validated assay big.

0:41:26.600 --> 0:41:51.20  
Harry Graham  
I was like, you know, Q2 or rose and they have a lot of experience. They have the, you know pretty well established the infrastructure you know the quality system, the regulatory, you know, oversight. But they tend to be slow in decision making and slow and and less adaptive than the small companies.

0:41:51.600 --> 0:42:18.10  
Harry Graham  
So that's uh, you know, basically the the the pros and cons or pros small companies they you know they they they are small they may have limited capability and some small companies they don't have the global footprint and that prevent them from participating in global trials. So yeah that's general you know the the comparison between small and the big testing labs.

0:42:19.430 --> 0:42:33.640  
Angela Angle  
With so Carta, you mentioned the expansion from histopathology to also including proteomics and molecular testing, and I'm curious how much of a of a differentiating point that is, is this? Are these tests the different types of tests that?

0:42:34.390 --> 0:42:48.790  
Angela Angle  
You would want to go to A10 for all these different types of biomarker testing. Or do you see one CRO as being really good and histopathology and then another CRO is very good in proteomics. So you'll split your work between the two.

0:43:13.890 --> 0:43:14.210  
Angela Angle  
Umm.

0:42:50.190 --> 0:43:21.820  
Harry Graham  
Yeah, the this is also depends right. In general you wanted to use a test of each testing lab to leverage their, you know, expertise in specific and you know acid technology platform. But in reality, given the complexity of reagent you know manage the specimen logistics, there are advantages by one stop shop because you can have you know sample send it to 1 lab, have them to do all the testing.

0:43:21.900 --> 0:43:41.540  
Harry Graham  
You want instead of. You know coordinate with different companies and sometimes I give you example right because you know tissue is always limited. We we used to say tissue is the issue especially in clinical study that ethical community is very careful to make sure the.

0:43:42.740 --> 0:44:8.400  
Harry Graham  
Sponsors. Don't, you know, waste any patient samples. If you send the samples to different lab, one lab for proteomics testing, the other lab for testing you, then you may end up with some samples like HEHE. If you do it in one lab, you only need 1HE for all the testing. But if you do it in different lab, each lab needs to have their own HE standing.

0:44:9.540 --> 0:44:25.190  
Harry Graham  
And yeah, you can ask. You know, one lab to send the HE after they are done, but that may be cause a delaying for you to get the results. So there are tradeoffs when you use the best of each testing the app.

0:44:26.300 --> 0:44:35.600  
Harry Graham  
And if you do have confidence that a lot you selecting can provide you the good one, stop shop services, that that's.

0:44:35.900 --> 0:44:38.590  
Harry Graham  
Umm, you know, there are some advantages there.

0:44:40.360 --> 0:44:50.680  
Angela Angle  
So if you were to compare between or, I guess evaluate Q2 and cell Carta, would you? There's specific types of testing I'm I'm just gonna give an example like.

0:44:51.960 --> 0:45:6.430  
Angela Angle  
Some IG histopathology test that that's the differentiating test that I need to go, right? So I'm gonna select my vendor based on their ability to perform that test or is it more of a holistic evaluation of the quality of all the tests that they perform?

0:45:9.20 --> 0:45:32.890  
Harry Graham  
So, you know, depends. Let's say if we, you know we have a bond market plan, right, you know bond market plan you know for some testing like I said we have we have to use clean CAP lab but because you know it's used for treatment decision and if that's the case then we know we have to use the lab qualify the lab and then you look at the.

0:45:34.70 --> 0:45:47.920  
Harry Graham  
They are overall they are capability to provide high quality testing for the specific marker or markers of your interest as well as their overall quality system.

0:45:49.160 --> 0:46:18.270  
Harry Graham  
And they are staff training and then the other decision factor is, you know, oftentimes you ask for what is the study project team that you will be interacting with and you you make a comprehensive holistic evaluation and then make a selection oftentime ideally you want it to at least the review a couple of candidates candidate labs.

0:46:18.350 --> 0:46:20.0  
Harry Graham  
And then you pick the best one.

0:46:21.190 --> 0:46:27.560  
Harry Graham  
And using some of the criteria, right, you know the reputation, you know they are specialty in, in the.

0:46:28.680 --> 0:46:54.380  
Harry Graham  
A particular essay platform you're looking for? The cost. They are study teams, experience and responsiveness, the quality system. They are knowledge of regulation that's required for your particular testing. So you have a list of criterias you use to determine which lab is you know best suited for your particular project.

0:46:55.220 --> 0:47:9.880  
Angela Angle  
Umm. And how important is geographic presence? I guess if you have a development program or a trial running in Europe, do you need to have those samples tested in Europe or can you have it sent to a site in Asia or the US?

0:47:10.940 --> 0:47:40.830  
Harry Graham  
Yeah. So that's actually can be very important when you have a a global trial, you have, you know, samples from the the different geographical region because from the two two important consideration, one is the turn around time. You know if you ship all the samples to one lab the but you have all the sizes all over the world and for you know some labs.

0:47:40.910 --> 0:47:47.880  
Harry Graham  
It's gonna take quite long time before the samples to reach the testing lab, so that that itself is.

0:47:49.80 --> 0:48:12.80  
Harry Graham  
Can be a limiting factor because you know it's especially for oncology. Many patients are very sick. You don't want make them wait for too long to get the testing result to the you know for the oncologists to determine how to treat them. The other is cost. If you ship the sample within the you know the the from the geographic.

0:48:12.720 --> 0:48:42.150  
Harry Graham  
The area, you know that the shipping cost that can be different and sometimes this type of request, local lab, local, regional testing can come from your investigators. I run into the situation before you know we were running global trials and there are certain investigators in Europe they were saying OK can can you guys send the sample you know can can I send the samples to a nearby lab.

0:48:42.230 --> 0:48:45.880  
Harry Graham  
Now to send it all the way to, you know US for example.

0:48:46.260 --> 0:48:46.520  
Angela Angle  
Umm.

0:48:47.330 --> 0:49:18.510  
Harry Graham  
Well, maybe of those reasons. You know, sometimes you do prefer a lab has a global presence, right? I use hisco jenica as an example. You know, I think that's a smart thing they did. They they originated in Europe, but that they have size in US and in Asia Pacific region and also you know, as you probably know in certain the country you cannot get the patient samples shipped it out. So the only way you can enroll patients.

0:49:18.590 --> 0:49:22.550  
Harry Graham  
Here testing patient there is make sure that you know your.

0:49:24.430 --> 0:49:27.10  
Harry Graham  
Ciao has a presence, has a lab there.

0:49:29.430 --> 0:49:43.660  
Angela Angle  
And for Histogenics or I guess not so Carta. It sounds like you were originally using them for the histopathology services. Are you now using some of the other capabilities that you mentioned, like the proteomics and the molecular testing services?

0:49:45.350 --> 0:50:11.420  
Harry Graham  
Yeah, proteomics, yes, but actually, yeah, we are yet to be evaluated because we we we do need to look into the you know what, what assays there have, what what platforms they have. Does that meet our requirement. But for the history, Histology and proteomics, yeah, we are already you know use them for for existing trials.

0:50:12.840 --> 0:50:15.810  
Angela Angle  
So I guess for existing trials, if you use.

0:50:16.570 --> 0:50:30.760  
Angela Angle  
So Carta for histopathology and proteomics. And you also need molecular testing. Are you? Do you? Do you actually need molecular testing for those trials or are you just using a different CRO to do those services?

0:50:34.470 --> 0:50:35.820  
Harry Graham  
But yeah.

0:50:53.520 --> 0:50:54.10  
Harry Graham  
Yeah.

0:50:54.60 --> 0:50:54.300  
Angela Angle  
Testing.

0:50:55.230 --> 0:51:26.80  
Harry Graham  
Yeah, for most of the drug development in the early stage, you know it's a seldomly you only need the wrong one or two by markers so you know oftentimes if you look at all the clinical protocols right, regarding to regardless of what company and the size of the company, you always see that there are quite a lot of you know by market testing. You know there is a biomarker testing session in the clinical protocol and there are multiple testing that's required because it's important for you to generate those data.

0:51:26.150 --> 0:51:27.980  
Harry Graham  
Do you understand how the drug works?

0:51:29.720 --> 0:51:59.290  
Harry Graham  
And from that perspective is almost a, you know, almost always the case you would need to do quite a lot of, you know, different testing in involved different platforms, but not all the platforms need that to be tested in the Clear tab lab, only in the once the testing results are used for treatment decision. So from that perspective you don't always have everything outsource to see how.

0:51:59.360 --> 0:52:20.520  
Harry Graham  
Because in general, if you have some internal capability, you know you, you and and also you have the existing instrument platforms. You can do some retrospective analysis in house. So because you're using Seattle in general is still quite expensive.

0:52:21.740 --> 0:52:51.580  
Harry Graham  
So to answer your question, you know yes. For many trials, there are multiple biomarkers and for some some studies we do look for Seattle can offer multiple platforms if it's called effective, but not always because for certain study like I said, retrospective exploratory study if we can do it in house, you know there's nothing wrong to to.

0:52:51.950 --> 0:52:53.970  
Harry Graham  
Perform some of the testing house.

0:52:55.260 --> 0:53:12.830  
Angela Angle  
OK. So I guess to ensure I'm understanding it that you when you're outsourcing, if you choose to outsource tests, you would like all those tests to be run by the same vendor, so you don't have to have sample shipped from vendor to vendor and that could create sample loss or loss of time.

0:53:13.470 --> 0:53:25.530  
Angela Angle  
Umm, but you for all the testing for a particular asset or trial, you could perform some of that internally and you would do that rather than sending your sample to two different zeros.

0:53:27.420 --> 0:53:54.30  
Harry Graham  
Yes, if you know this is under the assumption that that, that CEO has, you know, provide the good quality of testing cover different platforms, right on that assumption, the answer is yes. But if as CEO owning specialized or or good at you know one platform, they don't have other platform, then we still have to look for a multiple CRO, it's really depends.

0:53:54.810 --> 0:53:56.120  
Angela Angle  
OK. That makes sense.

0:53:57.150 --> 0:54:4.600  
Angela Angle  
And then see, we only have a couple minutes left. Just want to ask about one other company with the remaining time. You also mentioned precision for medicine.

0:54:5.560 --> 0:54:6.120  
Harry Graham  
Umm.

0:54:5.160 --> 0:54:12.730  
Angela Angle  
UM, curious on the types of testing that you outsource to them and what you see as their differentiating features?

0:54:14.250 --> 0:54:17.680  
Harry Graham  
Yeah, they are, you know, a mid size.

0:54:17.760 --> 0:54:23.310  
Harry Graham  
A A company. You know, that's just the, you know, not not, not.

0:54:24.250 --> 0:54:41.410  
Harry Graham  
A as well established as companies like you Know Roadshow or Q2, right, and we we happen to use them if it actually is not in my current company in my previous company we happened to use the.

0:54:42.610 --> 0:55:1.730  
Harry Graham  
So this canonical Seattle service and then we realized they have the testing capabilities. So we use them and for them, I think the advantage when you use the clinical CRO with testing capability which quite a few of the Congress have the.

0:55:3.10 --> 0:55:7.300  
Harry Graham  
You know, infrastructure, it does help you to.

0:55:8.460 --> 0:55:30.710  
Harry Graham  
Managers are simple logistics. Basically. You know you have Co which help you, you know, obtain the you know to to coordinate the drug treatment at the clinical sites and they also help with managing the sample logistics and testing from that perspective is it's a good.

0:55:30.790 --> 0:55:44.760  
Harry Graham  
Umm. Model to to use and as I said, you know that they are not the only clinical CRO have this type of service. I mean 22 is the example like the reason is called Q2 is a quest and.

0:55:47.510 --> 0:55:47.800  
Angela Angle  
Umm.

0:55:45.780 --> 0:55:51.680  
Harry Graham  
I Q via the you know there's a there's a used to be called.

0:55:52.800 --> 0:56:5.230  
Harry Graham  
With that call pong contact. Right. So that's why it's called Q2, because they have canonical operations provide clinical service as well as analytical service.

0:56:6.780 --> 0:56:7.740  
Angela Angle  
So for yeah.

0:56:6.400 --> 0:56:10.440  
Harry Graham  
So there are. Yeah, there are some advantages there. Yeah, go ahead please.

0:56:11.20 --> 0:56:16.390  
Angela Angle  
So. So for percentage for medicine, they had the logistics services and analysis services that.

0:56:17.710 --> 0:56:21.300  
Angela Angle  
Those additional services that as they're kind of differentiating point.

0:56:22.690 --> 0:56:50.440  
Harry Graham  
Yes. Yeah, it it. It's definitely, you know, compared with the other clinical seattles of their service without that capability, this does give them some differentiation when they provide them more like you know, comprehensive testing because they are I think they are probably better suited for smaller and mid sized CIO's and and also for the early development trials.

0:56:51.940 --> 0:56:58.700  
Harry Graham  
You know, because they offer the additional testing services, give them some some differentiation.

0:57:0.420 --> 0:57:0.700  
Angela Angle  
OK.