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INTIENT SUMMIT INNOVATION IN CLINICAL TRIALS LUMINARY SPEAKER VIDEO

VIDEO TRANSCRIPT

Our next, our next guest speaker probably won't need an introduction to many of you. Craig Lipset is the co-chair of the decentralized trials and Research Alliance and actually launched the first remote clinical trial. He was formerly head of clinical innovation at Pfizer and now advises biopharma tech companies and the venture industry. Is also an assistant professor at Rutgers University. And he has a whole of Fame hold of fighting recognition from Pfam voice. Also found that pretty interesting. The Craig study music at university and I wonder how much that contributed to his creative mindset, but he brought to the industry. But I'm very happy that he's here with us today as well, so it's a pleasure to welcome you, Craig, and I'll ask you to kick off this discussion for us.

So thanks very much. It's great to be here. And how much did that music degree influence? Well, what I will say is when, when we had built out a Clinical Innovation Team at Pfizer. Originally, some time ago. It wasn't until after we had much of that team in place that we were doing a few icebreakers and came to appreciate how many people actually had a creative arts background. So I went to a small liberal arts school in New England. I studied music there. There were only about eight music majors in my graduating class. Two of us wound up working in clinical development at Pfizer. So we used to joke that we would go back on Career Day back to that school, let them know that 25 percent of you will wind up working in clinical research. Maybe the rest of you will wind up in careers in music will say, Well, it's, It's great to get to spend some time with you and share some opening perspective around the state of decentralized trials, which I know it's come up a few times so far today it was great hearing Dr. Topol share some reflections on his work in that area as well. I see the the man holding up the fist that it looks like we're about there.

Yeah. Good to go. Good to go. Great.

I thought I would start with, with a definition, because it's very easy for different stakeholders to have different ideas in their mind when they hear a term like decentralized clinical trials. And so this is a definition that I use that's largely based off of definitions created by the Clinical Trials Transformation Initiative, a public-private partnership here in the US with the FDA and used by the IMA and Europe with their trials at home program. And so the definition that you'll see here, the use of technology and or processes that enable visits to take place outside of a traditional research site.

So this is a story of technology. Electronic consent, video for visits, remote patient monitoring, modernizing and digitizing our endpoints. But it's equally a story about process innovation, home health and our use of visiting nurses. Our ability to acquire specimens locally, whether whether blood or imaging or otherwise, often supported with central review. Our ability to extend the drug supply chain so that investigational product can reach people from home. It's a story of using these in a way that can enable visits outside of a traditional research site. It's not forcing all visits. And so you'll hear trends and themes at all. I'll bring into this conversation around optionality and choice and flexibility for how patients can engage in research going forward. Just like we're all getting more and more used to how we engage in our everyday lives, whether with health care or restaurants or everything else that we're touching today. And it's a story about research outside of a traditional clinical trial site.

Now, during the pandemic, this was a story about home, because during the pandemic, everything was his story about home. But now we're starting to see much more expansive location starting to emerge. Then we'll spend some time talking about pharmacy, community health centers, local physicians offices, pop-up sites, mobile sites, and beyond.

Now the intent, the purpose for decentralizing this is a graphic taken from the Clinical Trials Transformation Initiative and a set of recommendations in 2018. So pre-pandemic. And you'll see most of the value proposition anchors around patient facing attributes. Whether it's around recruitment and retention, or experience access, diversity and inclusion. But added another purpose, another intent, which I think really only came to light over the last 2.52 years. And that's around business continuity and resilience, which has always been a cornerstone for us in pharma and zeros and management consulting and tech. But we haven't really applied it in the same way as we have in the last two years for our clinical trials. And decentralization as quickly emerged as another countermeasure for an unpredictable environment. I don't know if that and predictable environment means COVID 24 or war in Eastern Europe, or fires in the West Coast or murder hornets or whatever that may be. But what I do know is there will be environmental effects that conspire to get in the way of a participant being able to get to a site.

In these decentralized research methods will continue to be an important countermeasure for that unpredictable environment. Decentralizing isn't anything new. In fact, this was a slide I had first prepared for conference in January of 2020, where the theme at the time was we have an oversupply in the market. The theme at the time was decentralized approaches had been around for 17 years prior to the pandemic, dating back not only to work we did at Pfizer with the remote trial, but to hybrid study, worked on it, Lily and some even earlier work done out of Boston University. In the five years prior to the pandemic.

We saw investments from venture as well as from pharma. We saw capabilities announced from incumbents like big CROs and tech companies, as well as capabilities from new companies that had raised capital. And at the time it seemed like a lot of capital. It was probably around a $100 million in aggregate venture investment at that time. Which of course today sounds like a Series, a round. Maybe last month it sounded like a series it around. You would think with all of that activity that these approaches were being adopted at some radical pace. But in truth, in most organizations at best there was an experiment or cluster of experiments. At best. So what felt like an oversupply of capability prior to the pandemic actually turned into a tremendous resource of know-how of knowledge of technology capability for the research community to quickly draw upon when it was absolutely needed in that spring, that March timeframe of 2020.

Decentralized adoption today has been meaningful in terms of setting expectations with both sponsors, sites and patients themselves. Most sponsors are pointing to accelerating and increasing their commitments related to decentralization within their portfolio. Importantly, investigator sights have also indicated commitment to using these tools and approaches. Prior to the pandemic. Only around a quarter of research sites had made use of telemedicine within their clinical trials during the pandemic. And the earliest day is that shop up to close to two-thirds.

But even in 2020, we were seeing three quarters of investigator side saying they plan to continue to use telehealth in their trials beyond the pandemic. Importantly, patients themselves have long voiced a preference for some flexibility in how to engage. And pharma sponsors for years, well recent years have had some very significant commitments to listening to patients when they're planning and designing their studies. And so this voice isn't anything new. 79% indicating they would find home visits and draw somewhat or very appealing. 58% saying they were more likely to participate in studies incorporating telehealth.

So let's think for a minute about what implementation and scale and adoption is actually looking like. Because it sounds like a lot of companies are accelerating some level of commitment here. And I would, I would describe most of those commitments and implementations today inside a farmer or something of a, of a toolkit that then needs to be paired on a study by steady basis.

So going beyond the last two years where things were implemented with protocol deviations and SOP waivers. Then we start to see organization said pause, look at the needs within there go forward portfolio. What are the decentralized tools and methods we need to have available inside of our organization. And we talked about some of those at the outset. Whether they're a technological like electronic consent and video and remote patient monitoring and other ways for patients to self-report herself, track or whether they were process innovations like home health and other capabilities. After knowing what tools and methods and processes those organizations need, is then to look at your existing landscape of partners, vendors, and see if that's already available or if these represent gaps that need to be filled through procurement process.

For many, there is a step of looking within and SOPs and processes to make sure. Not only that it's speaking appropriately about expanding roles such as home health, but in particular that we don't have prohibitive language in our legacy SOPs. Not by design or intent, but just because that's the way we used to do things that we don't have ourselves locked in in any of our SOPs or even our protocol template language. That's actually limiting our ability to use these approaches.

Today. Many of the number of pharma of even updated those protocol templates to consistently include aspects like mobile health and, and other decentralized approaches. The next step for most organizations. So it gets a little trickier. Because for most pharma, identifying a new category and updating training and, and, and processes is it's kind of a no known. The challenge today is how do I know which of these decentralized methods I should be pairing to which study in the portfolio. Not every trial needs all of those decentralized tools.

So what are the inputs and insights that I need to be considering, whether it's the profile of the study drug or how it's being administered, or the countries in which we're operating. In truth, in most organizations today, it's tends to be limited more by culture, then it tends to be limited by lots of thoughtful insight. What can I get through my organization? What do I have support for within my organization tends to be the rate limiter. I'd say though, that it's not the organizations fault. We don't have data and evidence. We don't have decision support based on data. To say for this protocol, this is the tool or method that you need.

I think through collaborations will start to be able to get some of that data. And certainly as some of the organizations had been leading in implementations, hopefully some of that evidence is starting to come to light. Most implementations we're seeing today our hybrid three quarters of sponsors had indicated that most of what they were implementing were some decentralized approaches and their trials. That is not a compromise. This is not a midway half step on the way to a future that everything is fully decentralized. When we stop and listen to patients. That's not what they're asking for. This survey in Europe, 57 percent of patients indicating they want only some visits to happen at a site. 19 percent are saying they prefer a fully decentralized. Only 11 percent saying they like everything to still be at an investigator site. And so this continuing to validate this theme of needing to have choice and flexibility to be able to meet all of our

patients where they are. Now drop this term hybrid is if you know what I'm talking about. I've said it a few times in these first few minutes. When I said hybrid, did I mean, it was a study that's hybrid by site that maybe there's brick and mortar sites that are running alongside of a centralized or Meta site. Where did I mean, it was a protocol that was hybrid by visit where? Visit 1, 3, and 5 and the schedule in the protocol are taking place at a site and visits to 46 are taking place at home or did I mean something in-between? And truth are jargon is one of a number of barriers that stand in the way of meaningful scaled adoption. But perhaps one of our most significant barriers is around regulatory ambiguity.

During the pandemic, we saw a guidance for most every regulatory authority around the world. Guidance that helped us to have clarity of our roadmap for developing the rest of the medicines portfolio across therapeutic areas. And in most cases, those guidance documents pointed to the adoption of these, these decentralized methods we've been talking about. Now, question on many people's minds is what happens as we get beyond this pandemic? Will the regulators continue to be as friendly and as receptive in truth, when you look at most of those guidance documents, they are not changing the rules of the game. No guidance document from a regulatory authority indicated that our threshold for safety or a threshold for data integrity, we're now reduced or lowered in some way. We still had to live up to the same standards.

But today we only have a handful of regulatory authorities that had been progressive and forthright, open and transparent in making clear their continued support for these approaches. We see it from the FDA with resources like their pandemic Readiness Plan, which was published last year and other really positive and affirmative messages. We see it from Danish and Swedish and Israeli and other regulatory authorities. We don't see it from every regulatory authority. Now what we don't see is the opposite. We don't see regulators coming out and saying they will not continue to support these approaches. So what we're left with is ambiguity. We don't know from some agencies. And that will be a cause for some conservative drug development organizations to pump the breaks of it. But want to slow things down during that ambiguity. And we'll talk about some strategies to fill some of those gaps. I'm going to jump ahead, but there are other barriers that exist will call out. Our endpoint constraints tend to be a significant barrier if we're still relying on legacy endpoints like a six minute walk test, where you need to go in the hallway of my office. And I'll put two cones down or tape on the floor and I'm going to watch you walk for six minutes. When you just walk 20 minutes to get to my office from the parking garage or the bus stop. We know we have better ways to measure or endpoints. And we know that digital is going to be an important way for that to happen. But we also know that modernizing and updating an endpoint takes time and investment and planning. And without that, we kind of get stuck for a lot of those challenges that we were able to bring to life, the decentralized trials and Research Alliance D TRA. And I did not put Accenture's name at the front of that list just because I'm standing in their offices today. That is purely alphabetical, but they are joined by about 125 other organizations on that list.

Hopefully you see your organization up there among others, these are from pharma and biotech from site organization zeros tech companies, regulators like the FDA and, and other stakeholders working together to ease the global adoption of decentralized research. And so through that collaboration, we have a dozen initiatives that involve a couple of 100 subject matter experts from those organizations working together in areas such as how do we expose and daylight on regulatory messaging and signaling.

How do we proactively engage with regulators where there is ambiguity to fill in those gaps for the community. I'm going to end with two quick thoughts here and then I'm going to look forward to some conversation. One is I hinted at this a moment ago, thinking about what adoption is going to look like over the next few years. Now, Prior to the pandemic, adoption was pretty flat. This was all about experiments. And obviously during the pandemic there was a spike in the adoption of these approaches.

There will be organizations that one hesitate as things get more endemic, as they're uncertain about some regulatory agencies and their continuing support. But we're going to be seeing clarity. We gotta be seen clarity with every regulatory decision that's made based on the drugs and biologics that were in clinical trials over the last two years that use these approaches is the part of the basis of their efficacy and safety. With every one of those regulatory decisions across therapeutic areas around the world, we're going to get clarity. We're going to see which regulatory authorities accepted those medicines for approval without cause or concern based on including these decentralized methods in which regulatory authorities raise concern. And if they have a concern, we want it raise. We want to have sunlight and transparencies so the community can address it. I would say that as we get operating confidence like we've had over the last few years and will continue to get in the coming years. And as we get regulatory clarity, as I was just describing, the last spike in adoption that I would expect to see is going to come from ethics committees and IRBs. Because when we have that operating confidence and clarity with regulators, I believe that there will be a final ethical question of how do we deny access to patients? How do we deny access to, to certain patient populations that we know are being marginalized and unable to participate when we know how to implement those tools and we know how to engage with regulators to use them appropriately. I would say. Where the beginning of this journey, these tools and methods I'm talking about are kind of your version 1 of decentralized with home health and some of these digital approaches. We still have to get better at. But I'd called next-generation participant support.

As people who are doing more from home, a help desk has to be more than just a technical resource. People enjoy the high touch they get with steady coordinators and others at the site. And if they're doing more from home, we have to fill that need. Will see more of this expansive thinking beyond the home as we see more experiments and Operations Scaling, mobile units, pop-up sites and other abilities to take advantage of in community resources from community health centers and retail pharmacy to other locations. I can't even envision which yet. We mentioned a moment ago about choice and flexibility for participants and more and more sponsors who are looking to make that a reality for their studies. It is hard, it is complex. It is much harder to incorporate choice than it is to dictate one model or the other. It really requires the right investment and endpoints so that we have confidence in data integrity, agnostic to where that data is being acquired. What we know we can do it. I think we'll see more site BYOL of their technology. Many sites have electronic consent. Many sites have video that they're using for visits.

When we introduce unfamiliar technology, we think we're normalizing and controlling things for our studies, we're bringing chaos on the sites. Chaos can't be cast as like matter. It, it can't be destroyed or created. It just gets shifted around. And because we're trying to avoid the chaos in our studies among our sponsors and zeros, we shift that chaos on to the sites and they're breaking their thin margin businesses and they can't handle this anymore. But the good news is, for any of your sites that are academic, they have IQ and said half of them are using red cap right now for their own studies. And if your site is a clinical practice that's provided a minute of healthcare in the last two years. Then they have a platform for using video that they know how to use. And so how do we enable sites to start to use more of their own tools because that's quality by design. Then we're not training and retraining them on unfamiliar stuff, but letting them use things that they already know.

Look forward to patients bringing more of their own real-world data into trials, need patients to be that conduit for connecting to their trusted electronic health record and other sources of data. Investigators, we can't expect investigators going forward to be the patient's provider who has an EHR that knows anything about me. That investigator might be across the city, they might be across the state, they could be somewhere else in the country. And so if you want to get access to EHR, another real-world data about me as a participant. You're going to have to come to me to connect to it.

Now in this country we have ways to do it. And I see my friend viewer over here and so I'm filling we'll have some good conversation on those. And just as a last note, I'll park this one. And the interests of time master protocols have seen the right amount of daylight that they've deserved for some time during the pandemic for the impact that they can bring. To create a more rational way for multiple studies to get rationalized into one. And let us test multiple interventions concurrently. How that world starts to collide with decentralization.

We can talk more about maybe during the break, but I want to make sure we have time for some good conversation, so I'm going to stop there and turn things back over to you, my friend.

Yeah, Thanks. Thanks for that.