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ALEX MAIERSPERGER: Welcome to season three of the audio and video podcast, The Health Pulse. I'm your new host, Alex Maersperger. And in this season, we are celebrating the health heroes making a difference in life sciences and health care around the world. We have some terrific guests lined up, and I can't wait for the conversations to come, and for the optimistic view that together, we can create a healthier future. Today, we get to celebrate and welcome Dr. Sean Khozin, chief executive officer of ASCO's CancerLinQ, a board-certified oncologist, physician, scientist, and data science expert. Welcome, Dr. Khozin.

SEAN KHOZIN: Thank you, Alex. It's great to be here.

ALEX MAIERSPERGER: So there's a quote that is used to refer to someone a lot of times that they've done a little bit of a lot. And I think in your case, we can amend the quote to someone who's done a lot a bit of a lot. You've founded companies, including Hello Health.

You've held executive roles across government agencies like the FDA, where you were the founding executive director of their first data science and technology incubator. You've worked for the largest private companies, focused on cancer care as previous global head of data strategy and data science innovation at Janssen R&D. So why CancerLinQ? Sort of what throughout this journey has led you to the CancerLinQ now, and is there something unique to this opportunity that drew you in?

SEAN KHOZIN: Sure, that's a great question. I think CancerLinQ occupies a very special place at the convergence point of technology, biomedical research on health care delivery, areas that we've historically viewed as being distinct entities as opposed to, say, a single vector of opportunity focus on improving human health and reducing the burden of diseases on society. In the past century, the biomedical enterprise and the practice of medicine have been largely focused on super specialization. And lately, we've been, in fact, lamenting about the symptoms of this fragmentation as working in silos and the lack of adequate cross-functional collaboration. Cancelling to me represents an opportunity to break the silos, bringing medicine, engineering, and biomedical research together in a bottom up manner and starting with the two most critical players in the ecosystem-- patients and providers.

So that was one of the most attractive features of CancerLinQ, and my vision for the organization is essentially centered on harnessing the latest innovations in technology and data science to empower patients and oncologists with the right tools to advance cancer care quality and research, including therapeutic development and an integrated, multidisciplinary fashion.

ALEX MAIERSPERGER: You talked about the lamenting portion, and I think there's a large portion of society which you touched on that is recognizing some of those silos and some of that difficulty or barriers to access or whatever it may be that we all are well-versed, I think, in the challenges of health care. And I think from a societal perspective, we see a lot of that curing cancer versus treating cancer.

And so serious question, because I think we've seen the conspiracy side throughout the pandemic and we've certainly also seen some bad actors maybe profiting off of the human suffering side. So there's a lot

of that societal perception, money is made off of sick people and not healthy ones. Can you speak to that, the convergence of your mission at CancerLinQ on the curing and treating of cancer.

SEAN KHOZIN: Sure, I think, Alex, conspiratorial thinking has always been at the fringes of the fabric of society. I guess the only difference today is that these conspiratorial voices have been amplified, primarily with the use of social media. I don't think it's worth paying too much attention to these conspiratorial tendencies about profiting off sick patients. In a free market economy, like we have in the US and much of the West, if someone found a cure for cancer or any other diseases for that matter, you can bet private investments will flow as they have in the past in support of any disruptive innovation.

Now it is true that the prelude for all progress, be it scientific or socioeconomic, is directly challenging status quo thinking. Einstein turned Newtonian physics on his head with his theory of relativity, which we forget at the time was highly controversial in the early days as he was formulating his hypothesis. And Arnold Schoenberg rewrote the language of music theory with a lot of criticism and backlash, with his 12-tone system of composition.

So I think it's perfectly legitimate to question the incentives today we have in our health care system. And that's different, I believe, than having a conspiratorial frame of mind. And I think if we think about our health care system today, it's really inherently designed to treat illness as opposed to prevent disease and keeping individuals healthy. And that's just a function of the incentive structures we have in place.

And the fact that in order to do prevention and early detection, we have to have broad access to very expensive tools and technologies. And I think all players in the ecosystem, from providers to insurers to therapeutic development organizations, are following this incentive structure that's firmly in place today. And in using oncology as an example, it's much easier to treat patients in advanced stage disease because that's when the majority of patients with cancer present and develop therapies to treat advanced stage disease. Now the good news is that we're starting to see this paradigm being challenged by technologies like liquid biopsies that I believe are poised to play a critical role, namely in cancer prevention and early detection, but also in disease monitoring in the advanced stage.

ALEX MAIERSPERGER: I love your optimistic view of cancer prevention and early detection because we can all agree, right now, getting cancer is the worst. All of us will be affected by it in some way, shape, or form over the course of our lives. Right now, it really matters where you get cancer care. Certain physicians may have more information or better technology. How is CancerLinQ helping get information to the clinician that's treating you so that maybe in the future, where you go doesn't matter as much.

SEAN KHOZIN: Sure, that's a great question. We always talk about democratizing access to best available care, and there are variations in oncology practice patterns. And I think some of that, there are technical solutions where we can bring, for example, decision support tools to the point of care in order to optimize decision making in near real-time. And that's an important consideration because when we think about what oncologists have available to them to treat patients, to rely on first and foremost their own clinical judgment and intuitions-- still to this day, clinical judgment and intuition is a primary driver of the majority of clinical decisions.

Why? Because clinical trials don't tell the whole story, and there are a variety of different reasons for that. In oncology, only about 5% of cancer patients have access to clinical trial participation. So the results of clinical trials sometimes tend to be very much confined to the experience of highly-selected patient population that may be very different than patients that are being treated in the real world. So a lot of oncologists cannot get the information they need by examining the results of traditional clinical trials.

There's a mathematical definition of that, which is that a lot of cancer clinical trials lack external validity, and external validity is what we need to be able to extrapolate the results of a study to treating real-world patient populations. And then the other option that an oncologist has would be to follow guideline recommendations, which are mostly consensus-based and quite helpful as a foundation for treating patients.

However, our treatments are becoming more personalized, and it takes a long time nowadays to even update treatment guidelines. So our approach at CancerLinQ is to collect real-world data that reflects the nuances and the diversity of patients that may not be represented in traditional clinical trials to analyze that data and deliver those insights to oncologists as algorithmic decision support tools. Decision support tools that helps them use the data that we have on our entire patient population that is connected to CancerLinQ in order to help oncologists individualize treatment decisions for the n-of-1 in a near real-time fashion.

So I firmly believe the guidelines of the future are going to be algorithms that collect data, analyze data, and then provide near real-time insights to clinicians at the point of care. And I believe that is something that a lot of other technology companies are also in a great position to do in other settings, but also in oncology because there's a lot of data out there, and the data currently is mostly supporting the biomedical research enterprise.

And using the same data assets to bring insights to the point of care I believe can really improve health outcomes, especially in oncology, where things are quite complex, multimodal, and in the past 10 years, we've had a lot of new therapies, and it's becoming very challenging for oncologists to appropriately, in some cases, connect all the dots in individuals their treatment decisions.

ALEX MAIERSPERGER: That incredible amount of complexity, like you said, and then there's the intuition versus the guidelines versus the sort of current data that you're getting thrown at you now. And so as an individual physician, putting that much time and energy and resources into just the training that goes into being a specialist in some of the highly specialized areas which you talked about, the data sharing-- there was a story when I was working as a hospital administrator that was told about two competing hospitals that shared a parking garage.

A physician at one of the hospitals invented a new method of doing a certain heart surgery that led to better outcomes. And it was nothing intellectual property-based. It was kind of at this stitch you go under instead of over, and going under is saving this time and improving outcomes.

So she went across the street and wanted to share that with the competing hospital of saying, hey, if you just go under instead of over-- and I'm obviously way oversimplifying-- but if you just go under instead of over, you'll improve the outcomes, and your patients will go home healthier and happier and faster. That competing hospital didn't want to hear it, as the story goes of just, hey, we've got our own way of doing things. We're going to keep going over because this is how we do it. This is our maybe intuition, and our guidelines are better than yours.

Is cancer care data sharing a similar place now? Is it going to be different in the future? Is it way different than that story? Are there holdouts, or when you're getting hit with this new data presented in the right way, are you saying, OK, we're all in on this?

SEAN KHOZIN: Sure. I think today we're in a much better position than your example may suggest, but there's still a lot more work to do. And again, this goes back to the incentive structures in place. For

example, in academia, one of the primary metrics for career advancement is a number of publications. The saying is publish or perish, as you know.

Naturally, this creates a lot of complexities and letting go of data, and usually people hold onto their data and to try to, say, squeeze as much as possible in terms of a number of publications from the data, and they're just responding to the incentive structures that are in place in academia. In industry, lack of data sharing, I think, is primarily due to perceived competitive advantages of holding the data very close to the chest. And in some cases, in many cases, those perceived ideas may not be real. That there are a lot of pretty competitive opportunities when it comes to data sharing that can benefit industry. But again, industry is also responding to the incentive structures that are in place.

Now, I think a lot has happened in the past five years alone. And the good news is that I think we're moving in the right direction. Not long ago, we had folks that were using phrases like "data parasites" to describe data sharing and researchers that were interested in secondary uses of data, and we don't hear those phrases anymore. And I think the majority of incumbents today do believe in the merits of data sharing when it comes to advancing the needs of patients and the benefits that are associated with using sharing data broadly from a societal perspective.

So I think we're in a much better place, but there's a lot more that we need to do in terms of developing mechanisms and putting mechanisms into place that accommodate sharing of data broadly, but also in a responsible manner, in a way that it protects patient privacy. And there are tools and technologies like privacy-preserving protocols and federated learning models that are addressing the technical end of the equation, and we just have to start to demystify a lot of these tools and technologies so folks can start to trust them when it comes to sharing of data. Because trust, at the end of the day, is one of the most important components of allowing data to flow freely.

ALEX MAIERSPERGER: You touched on this a little bit earlier, and I think it plays into that trust of just what amount of people with cancer, diagnosed with cancer have access to clinical trials or are participants in clinical trials. And that 5% number is just a number that stands out loud and clear of 95% of people aren't represented in that. And so sometimes we don't know what we don't know.

Real-world data and clinical trials, how precise is precision medicine right now? How much do we know this certain drug affected this person because of the components of the drug versus this affected this person because they don't have a fan at home or air conditioning in their home and they're constantly breathing bad air and we didn't know that. How precise is precision medicine right now?

SEAN KHOZIN: Well, we're certainly a lot more precise just in the past 30 years in oncology. And in the past 100 years, we've become extremely precise. If you look at the history of medicine, not long ago, in the mid-1800s, we were still believing that miasma, bad air, was responsible for most diseases. And when you think about that from a historical perspective, it wasn't that long ago, so we've become much more precise.

But focusing on oncology and especially in the past, let's say, 20 years, if we've become incredibly precise with the advances in technologies, such as genomic sequencing, in developing targeted therapies. As an example, there was a study that several years ago we did at the FDA where we looked at all the approvals in non-small cell lung cancer. And starting with double chemotherapy, which was the only option we had before targeted therapies.

So in 2003, looking at the data, the number needed to benefit, which means how many patients do you need to treat with chemotherapy for one patient to benefit, the number needed to benefit in non-small cell

lung cancer for double chemotherapy was eight. So for every eight patients we treated, unfortunately, only one of them benefited.

And then we looked at targeted therapies and immune checkpoint inhibitors for patients that have the appropriate biomarkers-- in this case, PD-L1 positivity-- the number needed to benefit is about two, and that's remarkable progress. That's precision therapy and precision drug development.

But even in drug development, if you think about it now, the number needed to treat of two means that still half the patients are not driving optimal benefit. So that's a residual imprecision we have in therapeutic development, and we're making very rapid advances with next generation diagnostic assays, including liquid biopsies and deep genomic sequencing technologies. And also with the convergence of advanced analytical methods, like AI and machine learning, we're going to be able to extract a lot more insight from this massive amount of data we're generating in the context of therapeutic development. Now precision in health care delivery is a completely different story. Unfortunately, precision in health care delivery is lagging behind. The numbers that I told you with number needed to benefit were derived from a study we did at the FDA using registrational studies that are pristine data, very expensive studies that are highly controlled, and they are very different than treating patients in the real world. So when it comes to treating patients in the real world, and we already touched on some of that because of the complexities in making these treatment decisions at the point of care, precision in care delivery has been lagging behind. And there's evidence that, in fact supports that.

If we look at a number of studies that have been done in the past few years using real-world data, it's very clear that the patient outcomes in the real world are inferior to those observed in clinical trials. There are several reasons for that, but one of the primary reasons, I believe, is this lack of precision in care delivery and being able to tailor treatment decisions to the individual needs of patients in the real world.

ALEX MAIERSPERGER: I love the historical perspective that you brought in because I think looking at that sort of timeline view of the way that we've introduced medication or the way that we've introduced theories like bad air and disproved some and proved others, we're still in very early stages where you said it's just not that long ago truly. And so I love that perspective around precision medicine as sometimes as an industry, we can beat ourselves up a little bit in health care and life science that we're not as good as we want to be.

But to see how far we've come how quickly, and I love the optimist take of what will happen, that exponential growth from there that precision medicine has come a long, long way, and we're probably going to come a long, long way a little bit even faster than it took us to get to this point. I love that take. You said that about regulatory science. You said in a Stanford Precision Health Conference talk several years ago-- I think it was back in 2012-- you had said that you didn't know what regulatory science meant then, and that you may have known what it meant by 2017 in a follow-up talk. So you said at the time that it was about where we are now and where we should be. And so you defined regulatory science as translational research. Over the past 10 years or so, so you've given the same answer about regulatory science and not fully understanding having that grasp of what it is, how to translate what it is you do to the world, is that still how you view the needs and opportunities in regulatory science?

SEAN KHOZIN: So I'm still learning about the definition of regulatory science, Alex. And you know, I think translational science is still the best definition that I can come up with because you can regulate systems by making policy decisions and I think greater oversight in terms of enforcement of the law of the land is

one mechanism. But as we know, in drug development and what, for example, the FDA does, it's never black and white. We're always in the gray area.

And the best way to address these very complex challenges that we have in the regulatory space is by being able to translate the latest advances in technology to mechanisms where we can facilitate this safe and effective delivery of these tools and technologies into the point of care. And it's the translation of the technologies we have and the mechanisms by which we can bring these tools and technologies safely to the point of care that I believe is in the domain of regulatory science.

And that means that regulatory agencies have to take a very proactive posture in terms of advancing their mission, which is to promote and protect public health. And that requires a collaborative mindset where there's a little bit of skin in the game that as an agency that is really focused on not giving thumbs up or thumbs down to drugs, devices, or biologics, but really the mission is to advance public health, there are many opportunities, collaborative opportunities embedded within that directive and that mandate that may involve doing research on the ground and helping de-risk some of these tools and technologies with innovators in order to, again, accommodate the safe and effective delivery of these solutions to the point of care and to society.

So I think it's still translational science, and I believe as part of that, it's very important to have access to data to appropriate data sets and also have an outward-looking collaborative mindset that's focused on the delivery of innovations and accommodating the delivery of innovations to individuals and society in the most agile and efficient manner while protecting patient safety.

ALEX MAIERSPERGER: What's the best optimistic take you have for the future of cancer care? I think we see just a lot of negativity in the press and in the news, and I'm sure day-to-day, there's some frustrating moments of, hey, I wish we were able to do some of the basics better. I wish we were able to do some of the really exciting stuff. What's the thing that most excites you about the future of cancer care?

SEAN KHOZIN: You know, I think we are becoming a lot more precise in cancer drug development, and that precision is starting to have an impact on how we take care of patients. And I think the convergence of technology and data science with how we develop therapies and deliver drugs at the point of care is going to have a massive impact on both ends of the equation, cancer research and also cancer care delivery.

Now, there are fundamental structural problems that we need to address, but I think if we just look at the amount of investments that have moved into health technology in the past five years alone, it would no doubt have a major impact on how we treat patients, on how we develop new drugs. And I firmly believe what we do in the next 10 years is going to set the tone in cancer care delivery and research for the next 50 years, if not longer. So we're at an inflection point today, where we have an amazing array of tools that can empower us in how we not only develop drugs, but how we treat patients.

And if we're able to address some of the fundamental organizational barriers that are preventing us to best optimize the use of these new tools and technologies, I think we are going to be able to say that in 10 years, we have addressed some of the most critical needs of patients with cancer. And that doesn't mean that we're going to cure all cancers, but I think cancer is going to be a chronic disease. And, in some cases, it is today. But I think there's still a lot of patients that are left behind that in 10 years, if we do things right and if the current trends continue, we're going to be in a completely new domain.

ALEX MAIERSPERGER: I really appreciate that perspective. You had said we're at an inflection point of exponential growth of what comes next. And I love that throughout this conversation, you've been able to paint the historical aspects of where we were and how far we've come, and in a lot of ways, in how short of a time we've come so far.

But then provide that really beautiful roadmap for the future that we can really have data to the n-of-1 to your clinician who's treating you right in front of you that says, here's who you are, and here's the best drugs that are going to treat you. Here's the best sort of wrap around life services that will help you, and I really appreciate your perspective. I know that you have infinite demands on your time, so we thank you so much, Dr. Khozin, for spending a little bit of time with us here today.

SEAN KHOZIN: Thank you, Alex. This was a great conversation. Thank you for having me.

ALEX MAIERSPERGER: And to our listeners and viewers, there's also infinite demands on your time. We are so appreciative for listening and participating. We can't wait to continue creating a healthier future with you. There are so many real challenges in the world. We hope that wherever you are, there are ways to find and be the good around you. We welcome you to the conversation at our email address thehealthpulsepodcast@SAS.com and here in the comments on YouTube.

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