Deloitte TECHTalks | EPISODE 15 | NextGen Gene and Cell Therapies
*With **Hussain Mooraj**, Principal, Leader of the Next Gen Therapy Practice, Deloitte Consulting LLP*

Buscaino, Raquel: Welcome to Deloitte **TECHTalks**. I'm your host, Raquel Buscaino and I lead the Deloitte US Novel and Exponential Technologies team where we sense and make sense of emerging tech.

In the rapidly evolving world of healthcare, NextGen Cell and Gene Therapies or CGTs are revolutionizing the way we approach and treat diseases. These cutting-edge therapies hold the promise of not just treating symptoms, but potentially curing previously intractable conditions, such as certain cancers and rare genetic disorders. On this episode, I'm delighted to be joined by Hussain Mooraj, who leads the NextGen Cell and Gene therapies practice at Deloitte Consulting LLP. We're going to dive into the fascinating journey of CGTs, from the early days of clinical trials to the current state of the industry. We'll explore what sets CGTs apart from traditional pharmaceuticals, discuss the challenges facing the industry, and look ahead to the exciting future of the biotech sector in general. I'm very excited, we have a lot to cover. So Hussain, welcome to the podcast, it's so great to have you.

Mooraj, Hussain: Fantastic to be here Raquel.

Buscaino, Raquel: I know that you've been working in the space for quite some time. Before we dive into NextGen Cell and Gene Therapies in particular, can you just give us a lay of the land for what we're seeing in the biotech space generally?

Mooraj, Hussain: I've been in the biotech space, over two and a half decades. And how rapidly the sector is evolving is just mind blowing right? It's driven by the technology advancements. It's driven by the massive increase in investments and a growing demand for innovation. And so you've got these big, broad themes, at least in my mind, that are really driving just such excitement in the sector, right? You've got everything that's going on with CRISPR, and gene editing, and the advancements in precision medicine, and therapeutic applications which we're going to be talking about later today. And you've got the synthetic biology side with bio-manufacturing and cell programming, and how synthetic biology is enabling cells to perform specific functions which are applied in drug development and agriculture, and in the environment. You've got a whole regenerative medicine side of the house, which is stem cell research, tissue engineering, the advances of which, including 3D bioprinting for tissues and organs are just amazing stuff. And then, of course, with the advent of AI and machine learning and drug discovery, you've just got some incredible predictive modeling capabilities to speed up drug discovery processes, to speed up research, and, you know, speed up all those hardcore labor-intensive processes and have the scientists focus on more strategic tasks. And then, there's the whole digital health integration which is creating a pull on the biotech side which is also just incredible with all the wearable technologies and the telemedicine which got a huge surge because of COVID. And it's, by and large it's stayed. So lots of great stuff happening in biotech and very exciting, still.

Buscaino, Raquel: I love hearing you paint that picture because it's almost like we're able to harness biology and harness the natural world itself that AI is super charging those advancements. And then to your last point about health, we now have unprecedented access and visibility into the data that we

generate from our own bodies, and what that means for us, so it does feel like a very exciting time, where so many different innovations are coalescing into one.

Mooraj, Hussain: Totally.

Buscaino, Raquel: Let's now take that double-click into NextGen cell and gene therapies in particular. So CGTs, what are they? And how have they developed over time?

Mooraj, Hussain: This whole space is evolving pretty rapidly and all the time, and huge amounts of learning for everybody involved. Cell and gene therapy essentially leverages the power of the human body's immune system. It sort of reinvigorates the body's ability to fight diseases via genetic manipulation. That's how I kind of look at it, right? The two broad types of cell and gene therapies. The first one is the gene therapy, which is in vivo, which means that the genetic manipulation is done within our own body, and there are many ways to do this. One of the most common is using viral vectors like AAV [Adeno-Associated Virus] which carry genetic payload that is deposited into a target tissue in the body and delivered. The other type of cell and gene therapy, the broad category is cell therapies, and these are most commonly represented by ex-vivo, which means that that genetic manipulation is done outside of the body of the patient.

And, one of the 1st kinds of cell therapies and very successful kind of cell therapy was CAR-T [Chimeric Antigen Receptor T-cell], and the first two products were launched way back in 2017, and, and there was lots and lots of excitement. And now they are almost 10 approved products in the marketplace, and these are curative therapies. This is not just attacking the symptoms. It's curing it. It's a huge boon for patients and mankind to have these therapies in the marketplace, and when they first came out, the market felt that, you know, they were serving a niche, and these weren't mainstream. And even within Deloitte, we faced resistance when we started expanding and investing in NextGen therapy capabilities. However, this has been proved wrong, and now you've got multiple blockbusters. Two years ago, nobody would have predicted that there's a tsunami of therapies in development as well which holds promise. So the science is evolving all the time, the technology to deliver the science is evolving all the time. And it's been hugely fascinating to watch. I mean, we are at an age which I am certain, we will tell our children that we experienced this advent of just incredible science coming to patients and mankind.

Buscaino, Raquel: What's been the cause of that dramatic change from even just a couple of years ago to now? Is it clarity of regulation? Is it the ability to scale production? Is it the accessibility of supplies within the market? How did we hit such a revolutionary trend in just a short amount of time?

Mooraj, Hussain: That's a great question. And you will get a variety of opinions on that one. What the marketplace and what private enterprise and academic enterprise have been able to do is really come together and focus. Cell and gene therapies have been around for decades. Right? Even before 2000, there was a talk of gene therapies holding a superior promise, etc. But the ability to mobilize deep science with the right amount of funding and finance, with the focus and skill sets and the regulatory bodies really coming and encouraging this. All of that coming together has really catalyzed these therapies coming into the marketplace.

Buscaino, Raquel: You mentioned earlier the difference between cell therapies and gene therapies, and so cell therapies, that genetic manipulation takes place outside of the human body. Gene therapies takes place inside the human body. So there's the difference there. Are there any differences between cell and gene therapies, in particular, with maybe traditional therapies?

Mooraj, Hussain: Many people who are not in this space sort of consider cell and gene therapy as just another small molecule product from big pharma, or a monoclonal antibody from a product. That's not the case here. These are live biological cells or tissues where the patient is the bioreactor and the raw material provider. It's a very different path to where everything around these traditional therapies is designed around the product. Whether it's the regulations, whether it's the SOPs [Standard Operating Procedures] within a manufacturing concern. It's pushed all the way from raw materials into the marketplace, where it's pushed into clinicians, or in some cases direct to patients. In cell and gene therapies, these are pull based. It's got a pull-based value chain. It's built around the patient and it's made-do-order in most cases. You've got to really have a different mental model shift when you were taking these therapies to market. And in the cell and gene therapy space. It's also really hard to differentiate between process variability and raw material variability, unlike in the traditional products of biopharma.

Buscaino, Raquel: Process variability and raw material variability. Can you give me an example of what that looks like?

Mooraj, Hussain: So the raw materials for a cell therapy, for instance, really come from the patient where the patient is taken into a clinical setting, and RECESSed [Red-Cell Storage Duration] - so that means they take the blood into from the patient - and they put them into bags, and then these bags are shipped to the manufacturing facility, sometimes fresh, sometimes cryo-frozen. Now you're talking about very sick patients. And in some cases these are fourth-line patients. So almost hospice patients. So the quality of the raw material itself is dependent very much on how well the patient is or not -- and in many cases these patients have already had chemotherapy administered to them, so which degrades the quality of their cells to begin with. And so, the input into the manufacturing process of these therapies has a degree of variability that can't always be controlled unlike in traditional production of small molecules of monoclonal antibodies.

Buscaino, Raquel: Sounds like that's probably one of the challenges in addition to potentially high costs, if you're talking about it at the made to order level. Are there challenges that the industry right now is working to solve to increase accessibility across the board for these therapies?

Mooraj, Hussain: First of all these therapies are not inexpensive. These are high-cost therapies with reimbursement models that really need to be invented from scratch in many cases. And so you've got to have the payers come together with the manufacturers, with the clinicians, with the national governments or regional governments depending on how you're negotiating. So, really figuring out how these therapies are paid for is one of the biggest challenges. Another big challenge is the lack of standardization in the industry. We are you know, at the bleeding edge, not even the cutting edge of taking the science to market, so the regulatory bodies are creating and inventing new standards. Manufacturing is basically inventing new ways, new technologies to manufacture these therapies right? So great, promising new levels of technology sort of coming into this space to scale this but that is a big

challenge, for now. You've got to learn, unlearn, and relearn how to launch these therapies right? So you've got a basically put aside 20 plus years of learning how to launch traditional therapies, really learn how to work together in a deeply cross-functional way, and using digital capabilities to the extent that have not been used connecting directly to the clinicians and the patients, relearn that space and then launch these therapies. So lots of challenges. But let me tell you the excitement and the vigor and the funding in this space has been incredible.

Buscaino, Raquel: And It's such a mission-driven industry, where you're talking about curing, previously unthinkable to cure diseases. I mean, talk about an industry that's as exciting and mission driven as that. What does the future hold for you here? Where do? Where do we go from here? Is it more accessibility? Is it more products hitting market? What is the future of CGTs?

Mooraj, Hussain: Yeah. Great question, Raquel, and I love your point about being mission driven. Even the mission of the NextGen therapy practice in Deloitte, which, as you know, is a dedicated practice all we do is cell and gene therapy. Our “raison d’être” - our reason for being, so to speak - is very much about helping our clients take these therapies to patients and mankind and we are very excited about what the future holds for the industry. So we have seen these therapies start off at the 3rd line and the 4th line, and moving to earlier lines of treatment where patients are healthier, their raw materials that we harvest from the patients are also, as a result, more stable and healthier. We are seeing manufacturing automation as you heard me talk about, just exponentially take leaps and bounds in developing new technologies. There's also, at the same time, cell therapy is undergoing a significant transformation and attracting massive interests from small biotechs, from major pharmaceutical companies, which are eager to tap into the burgeoning field of oncology, which was the first frontier, but now also shifting to autoimmune disorders and the autoimmune disorder arena is rapidly expanding, and the number of companies originally focused on oncologies have now shifted much of their portfolio towards cell therapy for autoimmune diseases. The shift is happening so fast because the oncology sector became saturated almost by an influx of huge amounts of funding over the last few years, and an emergence of cheaper alternatives like bispecific antibodies. But in contrast, the autoimmune sector remains relatively untapped. So we see a lot of energy going into really creating therapies for that whole sector, with a lot of potential for mergers and acquisitions a surge of new companies entering this space and major pharmaceutical companies are likely to intensify their focus in this area as well. And the pace of changes like I've never seen in my almost 30 years in this space.

Buscaino, Raquel: Just as you mentioned how innovations in cell and gene therapies can be applied across life science and healthcare. I think there's also a hunch that these innovations can be applied across industries as well. You mentioned earlier everything from biomanufacturing to energy, resources, and industrials. Can you talk about how genetic engineering might be finding its way in industries outside of life sciences and healthcare too?

Mooraj, Hussain: So you heard me talk about earlier around synthetic biology. In synthetic biology you basically reprogram the cells, and advances in synthetic biology are enabling the cells to perform specific functions which can be applied on the drug development side, on advancements in agriculture, in environmental management, in the creation of new textiles. So it has broad, broad repercussions in multiple industries, including, you know, renewable fuels, chemicals through fermentation processes,

and lots of promise in this space as well. Early days, and that space has a different level of challenges, we got to be realistic about it. But my, what amazing promise it holds.

Buscaino, Raquel: And like you said earlier, it's not just on the cutting edge, but on the bleeding, bleeding edge. And what an exciting place to be. Hussain, thank you so much for such an insightful conversation. I felt like I learned so much about Next Gene and Cell therapies. So thank you. To all our tech savvy listeners out there. If you enjoyed this episode, please share and subscribe, and if you'd like to learn more about the future of biotech and CGTs, you can follow myself and Hussein to stay up to date. Our socials are listed in the episode description. Thanks for tuning in, and I'll see you on our next episode. Until then, stay savvy.