INTERVIEW with Lindsey Clarke, Cell Therapy Product Manager at Bio-Techne

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Building Robustness and Scalability into the Immuno-Oncology Supply Chain

Lindsey joined Bio-Techne at the end of 2018 as EMEAs Cell and Gene Therapy Product Manager. Overseeing the portfolio of tools, technologies and instrumentation applicable to Cell and Gene Therapy her role to date has been focused on building the team to support Bio-Techne's customers Cell and Gene Therapy applications, planning the roll out of a host of new innovations into the European market and developing strategic partnerships within the industry. Prior to this she spent 8 years in Miltenyi Biotec's Cell and Gene Therapy team, working closely with numerous process development and manufacturing teams to assist them in translating their varied cell

therapies to the clinic. During this time she contributed significantly to the national strategy for the successful roll out and market positioning of the CliniMACS Prodigy and GMP products for Cell Therapy manufacturing within the UK. Lindsey holds a First class degree in Pharmacology (MPharmacol) from the University of Bath and a PhD in Immunology from UCL. Her PhD research focused on surrogate markers of endothelial inflammation and repair in paediatric vasculitis and led on to a postdoctoral position at Imperial College in the Department of Bioengineering investigating atherosclerosis.

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Q Can you tell us about your background leading up to your current role at Bio-Techne?

Lindsey: I started out as a typical academic scientist, following an initial degree in pharmacology with a PhD in immunology at UCL and then moving into a post-doc position. When that was coming to an end, as with many post-docs, I wasn't sure what I wanted to do next. I liked talking about science and I was good at trouble shooting, so I ended up taking a position in the UK Cell and Gene Therapy account management team at a biotechnology company

That was about 8 years ago now and I feel like I can claim I've been working in cell therapy since before it became popular! The last 5 years have just seen phenomenal changes and it's been a real privilege to be involved in the industry and working with a number of big groups within the UK, helping translate their processes into the clinic.

Q What are you working on specifically in your role at Bio-Techne?

Lindsey: I joined Bio-Techne 7 months ago and we've been making some substantial investments in technology in the cell and gene therapy space. My role is to be the person on the ground who oversees the strategy of how we support customers and how we launch these technologies in Europe.

I'm focused on building the right team. I think it's critical to have the right people working with cell and gene therapy manufacturers, who really understand what the pain points in manufacturing are, but also understand the science of the cell processes they're working with. That way it allows us to develop solutions that can address the needs of the industry.

Things in this space have changed very rapidly and we need to be agile to meet new requirements. If you asked me 5 years ago what the biggest challenge was, it was always about GMP. Now the question manufacturers are asking is very different; it is not just, "can I make this GMP?" its "can I make this GMP AND at scale?"

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Q Talking about scale, how can Bio-Techne help build robustness and scalability of the cell and gene therapy supply chain?

Lindsey: One thing I've learnt over the years is that very small changes to a process can make a significant difference to how it can be delivered at scale. Particularly with regard to autologous manufacturing, where you have a really complex supply chain and you have to be in complete control of the process because, ultimately, you have one chance of getting this product to a patient.

Everyone talks about automation and closing the system, and those are critical, but we're starting to see bottlenecks around raw materials that we weren't necessarily expecting. So one thing we're looking at closely is the preparation of medias or buffers that go into your manufacturing process. Even though you might have a completely automated process, this element still requires a manual and open step to supplement things like cytokines or HSA. Without finding a solution that simplifies and de-risks this, scaling up and out is going to be very, very difficult.

So as well as developing exciting and innovative new products we're also working on problems such as this and thinking about how you can de-risk the raw materials coming into the process from the supplier side to enhance scalability. Innovations will of course be part of the answer but a very simple solution that we already offer for example is filling vials with the exact quantity of a reagent that a manufacturer needs. This then takes away from the manufacturer the risk to the process associated with measuring out exact quantities or aliquoting themselves. A simple change but one which can positively impact on their ability to deliver at scale.

Our other key focus at the moment is on raw material supply. Security of supply is critical and we know we need to be flexible because of the scale of change between trials. For instance, the number of patients that people are treating can quickly escalate from one patient a month to

potentially thousands of patients a year. As a manufacturer of raw materials we have to anticipate that and be ready when our customers need us to be. How do we do it – it has to be by working closely with the manufacturers of cell and gene therapies so there's no surprises around their needs if their early trials are successful.

Q As clients move through to clinical trials and commercial scale, do you get the impression that they have a strong awareness of what the implications of that scale will be?

Lindsey: Some people are starting to think about these things but often when you're a commercial organisation you've got to move as quickly as possible to derive your phase 1 data, to open the door to further funding. I think people can be focused on getting to the clinic as fast as they can and sometimes they're not planning for the five thousand patients a year that may be around the corner.

Some of the companies that are further ahead in commercial development are thinking about scale from the very beginning of their next trials. But they're learning from their first generation products which ultimately confers some advantages.

Q What excites you most about the immuno-oncology sector at the moment and where do you see on-going challenges that need to be addressed in order to catalyse more products into the clinic?

Lindsey: CAR-T has been a real game changer in this immuno-oncology space, with the results from some of the early trials really ushering in a new era of cancer care. However, these are very complex products to make and again, autologous manufacturing is difficult. There are just so many elements people are having to juggle around raw material supply and patient scheduling to meet the clinical need.

Nevertheless, it's a fantastic space to be in. There's a myriad of exciting new cell types coming through that may be less of a challenge to manufacture. What excites me about this space is we're just at the beginning; CAR-T has set the precedent, but there's such a wave of innovation and technology that is set to evolve the immuno-oncology field further.

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There have been recent reports about the efficacy of CAR-T therapies in solid tumours and whilst it is early days in that respect, it is incredible to think that cancer may not be such an insurmountable disease in ten years' time. Then we need to start looking beyond that, and thinking what's next? There is potential for new cell and gene therapy approaches to chronic illnesses and autoimmune disorders, and perhaps even cancer being eradicated.

Q How can collaboration help optimise and resolve current challenges in the raw materials area?

Lindsey: It's essential to collaborate both with people manufacturing the cell therapies but also with other suppliers as well. Nobody has expertise in everything and so to really drive the industry forwards, we need to harness individual knowledge and play to our strengths.

At the moment our focus is on raw materials and, as we don't have instrumentation platforms for manufacturing, it's been really beneficial for us to work with device manufacturers and map out the best ways to collaborate.

Standardisation around components coming into the process such as the weldable tubing on consumables and medias, and buffers is an area we as an industry need to work on. There are still issues regarding how we transfer cells between pieces of equipment and the only way we're going to overcome some of these is by working together, and defining what the standards are, to which manufacturers and suppliers can then adhere to.

Ultimately it's about getting the best therapy to the patients and that's going to be cell and process dependent as to which platforms and raw materials fit best which makes it the responsibility of the process development team to assess a variety of solutions in order to make the best cell product.

By working closely with providers of tools and technologies like ourselves, manufacturers are at an advantage too, we always have things in the pipeline that people may not know about. By working closely with us, we can provide early access to these new products, which we are keen to do as our collaborators can actually shape how we develop our products and ensure that what we deliver is what they actually need

Q You started in this sector before the glory years we're experiencing now. As more therapies get

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closer to commercialisation do you sense less openness and collaboration for fear of losing property benefits?

Lindsey: Because the intellectual property (IP) is in the flavour of the cell, the actual manufacturing challenges are common, regardless of where the IP sits, and so actually I think this is an industry where people are willing to talk about challenges. Obviously, they can't give away confidential information but people are willing to share information about how they solve a problem.

In meetings where you bring together technical experts, you see a lot of sharing of information. In the academic sector, collaboration is commonplace and because the early stage spinouts are still very closely tied to research, I think we're potentially a lot more open in this industry than others.

Particularly in the UK, we are seeing the work of advanced treatment centres and the collaborative environment around that, and it is clear that companies as well as academics are working together to further the field.

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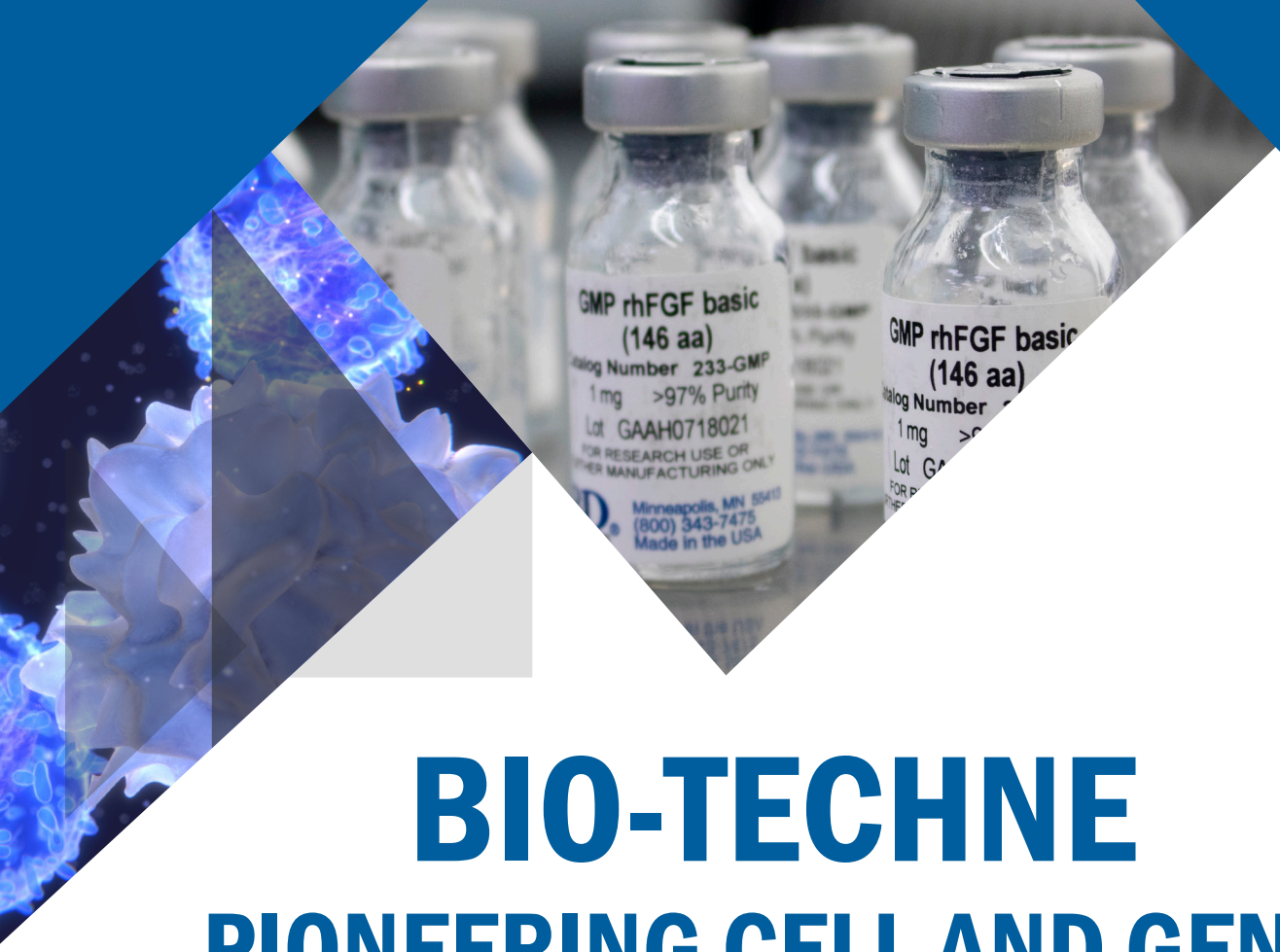
Q What's your vision for the future of the cellular immunotherapy space, and cell-based therapies in particular? Do you anticipate a more platform agnostic future as the sector matures?

Lindsey: I think as the sector matures, everyone is looking to the biologics sector and the way that they managed to bring the cost of goods down massively from where they started. I hope we will see this kind of progression in the immunotherapy space.

The challenges of meeting the scale of demand for these therapies is what is going to be keeping the industry busy for the foreseeable future. Are we going to move towards allogeneic products and off the shelf? Suddenly that's a whole new model of manufacturing. The autologous products are what we've seen efficacy with and are potentially safer because they're self-derived, but allogeneic is a more typical pharma model, and there is potentially more money to be made there. That is a factor which will drive the industry. Moving towards allogeneic is where I think the space is going, but whether we can achieve the same level of success as we have done to date with autologous therapies is unclear.

I've been talking with a few people lately about the vision of an "instant coffee pod style" kit for cell therapy, where the patient needs their specific CAR-T, presses a button, the kit arrives, you add cells put it into a machine and out pops the treatment. That would be amazing. We're not there yet but that's the vision I would love to see come to reality!

All I can say is we're just at the beginning. Everywhere I go people are working on the most amazing new technologies, new processes, smarter cells with clever targeting, switching on/off ability and improved efficacy. It really is an amazing environment to be working in and I feel privileged to be part of it. The fact that we are seeing cell therapies really making a difference to people's lives and we're even daring to talk about them being curative, suggests the beginning of a whole new era of medicine.



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