AUTOMATION

SPOTLIGHT

INTERVIEW

TIM MOORE has more than three decades of leadership experience in biopharmaceutical manufacturing and operations. Most recently, he served as Senior Vice President, Head of Global Technical Operations – Biologics of Genentech, Inc. and as a member of the Genentech Executive Committee since 2010. In this role, Mr Moore oversaw global leadership for more than 7,500 professionals across 10 internal sites and over 37 contract manufacturing organizations, as well as global manufacturing and end-to-end quality supply performance of more than 20 biological product families. Prior to that, Mr Moore was Genentech's Senior Vice President, Global Supply Chain and Global Engineering from 2007 to 2010. Previously, Mr. Moore served as Vice President, Operations at ZLB Behring (formerly Aventis Behring). He is currently a member of ISPE, PDA and has been a part of the Executive Committee of BioPhorum and the Manufacturing Leadership Council. Mr Moore received a BS in Chemical Engineering from Tulsa University and a MS in Engineering Management from Northwestern University.

Q Exciting times ahead for Kite, a Gilead Company, with the ongoing roll out of Yescarta – how are you approaching the challenge of scale out on a global basis, and how/where will manufacturing automation play a critical role in this?

TM: Yes, it is certainly an exciting time. We are busy with the global expansion of Yescarta and are currently taking the existing process and transferring it to additional manufacturing sites in appropriate regions. For example, we just recently announced plans to establish a new manufacturing facility in Europe at Schiphol Airport just outside Amsterdam. We are also continuing to expand our manufacturing operations outside the US

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and have partnered with companies in other regions – for example, the formation of our joint venture with Fosun Pharma, named FosunKite, in China and our collaboration with Daichii Sankyo in Japan. We are focused on expanding this type of treatment to reach more patients.

Automation is clearly going to play a very important role in the future. This is an area where we are devoting significant effort. I'm confident that in the next few years, automation will make a significant difference enabling us to get treatments to patients more quickly – and reduce costs and improve logistics.

What we're therefore doing with each one of our manufacturing facilities is designing them with an automated future in mind, so that we can quickly and efficiently convert to automated solutions and processes when the technology becomes available.

Q How does an established major biopharma company such as Gilead Sciences approach manufacturing model development – including automation – in what is still a fledgling technology area, relatively speaking? What lessons can the cell & gene therapy space as a whole take from their philosophy in this regard?

TM: Cell and gene therapy is a new space in the biotech industry and a lot of our manufacturing development work is still evolving, so we remain focused on internal operational excellence. Gilead is a company that typically seeks to outsource manufacturing, so there isn't necessarily a direct model, or an 'insource versus outsource' debate because of the differences between cell therapy and small molecules.

To that end, we do have a philosophy and a model that has been developed, which takes into account not just autologous products such as Yescarta, but also future allogeneic products. It also accommodates

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future indications that we're moving toward, such as those in the solid tumour space.

The key to all this is making sure our model is built with flexibility in mind – in particular, so we can expand production rapidly when required. Utilizing fungible technologies enables very fast expansion, for instance. That is the sort of consideration we keep well in mind when we look at how to set up our new manufacturing sites. For the autologous world, that's a bit complicated, but once we get into allogeneic products, it will open up a different approach.

Q Where specifically does more work need to be done on unit operation connectivity?

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TM: Obviously, there's lots of work being done on automating the manufacturing process – fluid dynamics and that type of thing – but the biggest area that still needs a lot of development and focus is in-line quality control analytics. The question is, how much can we embed in the manufacturing process through automation?

Today, we have to pull samples and take them offline to conduct in-process testing for cell count, cell viability and transduction. When I look to a future, continuously monitoring the cells – counting them, assessing their viability, as well as check the transduction – would be very powerful. I think this is a vital area in terms of automation.

Q Do you see the future of manufacturing automation in this space favouring all-in-one solutions or unit operations, ultimately – or will it be a blend of the two?

"there are obviously automated unit operations out there, but all-in-one has a way to go yet."

TM: I think we will see a blend: it all depends on the complexity of the given process as to which automation model will work best. The more complex processes the more unit operations

are likely to be the right solution. with a simpler process, you might be able to have an all-in-one solution.

I will say that today there are obviously automated unit operations out there, but all-in-one has a way to go yet. Prodigy gets tagged as an all-in-one solution and it does incorporate a lot, but there are still things you have to do outside of its capabilities. So that's a particular field that's going to evolve over the next 5 years, but again, I do believe unit ops or all-in-one will remain a choice for manufacturers.

Q You've already touched on the importance of bringing bioanalytics in-line, but are you comfortable that we as a sector know exactly what we should be bringing in-line yet? What are the next steps we need to take along this road?

TM: We certainly talk a lot about it at conferences, aside from any question of automation, I do think we need to continue to advance some of the bioanalytics for autologous therapies – to help us better understand incoming patient's cells, for instance. We clearly already have visibility as to the phenotypes, CD4/CD8 ratios, etc., but there are other things we still need to study because it's clear for all of us that the starting material creates the greatest amount of variability that an autologous therapy manufacturing process will have to deal with. Novel bioanalytical methods will continue to emerge and evolve.

Q Are you happy with the pace of that evolution in bioanalytics?

TM: Going back to our earlier conversion about in-line QC analytics, I'd like to see that advance a bit faster, However, bioanalytics that I would say are outside of the manufacturing process itself are generally advancing well.

Kite recently announced a partnership with Sangamo Biosciences to access the ZFN platform, an example of the ongoing trend of convergence between cellular immunotherapy and gene editing. What are your aspirations for this partnership, and for the continuing evolution of technologies such as gene editing that could transform manufacturing processes for cell and gene therapy?

For me, what's really exciting about working with Sangamo is the potential we see in the Zinc Finger Nuclease genome editing platform to create allogeneic treatments in a really standardized process – that's obviously a

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> " we see [the potential] in the Zinc Finger Nuclease genome editing platform to create allogeneic treatments in a really standardized process – that's obviously a huge opportunity."

huge opportunity. You will increase patient access to these therapies due to the fact you will be able to carry a little bit of inventory: if a patient is very sick, you would be able to treat that individual immediately, versus maybe taking a couple of weeks to begin treatment – and of course, that extra two weeks can prove to be significant. This would also potentially lower costs.

This technology will simplify the process and as I mentioned earlier, the ability to simplify a process will help in the development of automated solutions that potentially cover the entirety of manufacturing operations.

Q If you could wave a magic wand and conjure up three automated bioprocess and supply chain-related solutions that don't currently exist, what would they be?

TM: My first one would be the QC analytics we discussed previously – I'd love to see those! Another one I've been thinking about, which I might describe as data management, would involve an analysis of incoming patients' cells – for instance, to follow different process steps according to the relative health of a cell sample. It kind of gets to what a lot of clinical centres would love, which is point-of-care manufacturing. If you can only imagine an automated solution which would adjust automatically to a given patient's health status and disease status data... that would be amazing.

I think that one's a dream right now. It will start becoming more of a reality when we better understand the variable aspects of incoming patients' cells, and how gene editing or cell engineering processes may need to change or adjust to accommodate that variability. But today, there is still so much to learn, and you can't automate something when you are missing that sort of fundamental understanding.

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Q And if you had a third wish?

TM: My third would be to be able to cure cancer for 100% of patients. I'm excited by what we've achieved so far, but how do we up the game further?

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