ANC-80: LATEST UPDATES ON THE NOVEL ANC-AAV GENE THERAPY VECTOR

SPOTLIGHT

INTERVIEW

Flexible, Modular Manufacturing to Address Viral Vector Capacity Bottlenecks

XIN SWANSON serves as the Commercial Development Lead for Lonza's Viral Vector Gene Therapy Business. She has over 20 years of experience in the Pharma/Biotech industry, developing viral gene therapies and monoclonal antibody therapeutics. Over the course of her career, Xin has held various positions in R&D, Process Development and Commercial Development functions. She has been with Lonza for more than 10 years and has played an instrumental role in the growth of Cell and Gene Therapy business. Xin holds a PhD in Biochemistry from Texas A&M University and an MBA degree.

Q The sector has been experiencing tremendous growth and investment – what have been the standout moments for you thus far?

XS: I think the excitement around developments in the cell and gene therapy space has been building for the last 20 years, but last year's approval of the two CAR T- programs – and also Spark's AAV programme – was definitely a turning point for the industry. We finally got a positive verdict on therapies that are curative and can now take that forward to the commercial setting.

The ongoing excitement among investors and the whole community is fully warranted: more and more trials are demonstrating the curative nature of these therapies, and moving forward we should see many more cell and gene therapies reaching the market – last year's approvals are just the tip of the iceberg.

I think the regulatory framework development – the passing of the 21st Century Cures Act, for example – and the general trend of regulatory

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agencies working very proactively with drug developers in this sector, are also giving the industry a lot of momentum.

I expect to see the excitement continue as more therapies follow current pathways towards niche markets – viral gene therapies achieving Proof of Concept in the monogenic disease space, for instance – and then continuing on towards larger disease indications in the coming years.

Q There's been reported bottlenecks in the manufacture of these innovative therapies – what's your perspective on the critical challenges across the manufacturing pathway for cell and gene therapies?

XS: I think supportive manufacturing technologies represent THE critical challenge for this space. They need to be matured. We are effectively mirroring the development path of monoclonal antibodies (mAbs) over the past 20 years or so, and current technology has to be more mature for the industry to be able to support that degree of growth. Some of the shortages stem directly from the immature processes used for current therapies – a lot of viral vector production is still based on adherent cell culture platforms, which means poor scalability and robustness.

But the increasing weight of evidence that these therapies are curative will lead to maturation of the whole industry, including the manufacturing piece. We'll see increasing investment in the reinvention and optimisation of vector production platforms to improve scalability, robustness and productivity. This will result in the sort of acute shortages we are currently observing becoming less of an issue.

Q Do you think as a sector there's been an overreliance on trying to retrofit technologies traditionally used in biologics into cell and gene therapy, when in reality they often require a novel approach?

XS: Definitely. Over the past two decades, the cell and gene therapy sector focused on pursuing technologies solely on the basis of what was demonstrating clinical relevance at any given time, and only now that Proof of Concept has finally been achieved is it turning attention towards questions of

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manufacturing productivity. Again, we can borrow the example of the mAbs field: when the first few mAbs were approved, productivity was very low and the industry then moved ahead quite rapidly in seeking to address that issue. However, that change takes time and investment. Returning to cell & gene therapy and the present day, with the lessons we've learned through mAbs and other biologics and also the new technology available in our toolkit, I think the revolution will take far less time for us to realise within this sector. The technology will still require some time and there are a number of immature processes still in use, but it will get there. The key challenge in the viral gene therapy arena will be catering for larger indications as these open up.

Q How will the recently opened cell and gene therapy facility in Pearland Texas, help to address some of these challenges and shortages?

XS: At Lonza, we have always put a lot of emphasis on development of scalable, robust processes to support these kinds of products. With the opening of the new facility, we will establish a world class centre of excellence for cell & gene therapy process development, showing our ongoing commitment to the space. And not just focused on developing processes, but also providing the capacity at both clinical and commercial scales to really serve the needs of a maturing industry.

Lonza has a lot of experience in supporting biologics from clinical all the way through to commercial – we're also leveraging a lot of that experience and applying it to the cell and gene therapy space.

Q How do the flexible modular facilities that are a key part of Lonza's facility in Pearland help support clients' requirements?

XS: The modular setup again shows that we have an eye on the future because right now, a lot of cell & gene therapy platforms in the

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clinic – on both the viral gene therapy and autologous cell therapy sides – are not yet established with mature, validated, commercially viable bioprocesses. Our emphasis is on developing robust, automated processes, designed with flexibility in mind, so we can quickly put together clean room space in a very short timeframe and in a very cost-effective manner.

The flexible modular setup means that once we know what kind of process to use in order to meet a specific product's needs, we can quickly add as much capacity as is required to meet demand. So it's the whole concept of flexibility being built in not just on the bioprocess side, but also in the overall facility design. You won't have to wait 18-24 months for your required capacity to come online – the modular clean room approach means capacity can be added very quickly using existing shelf space.

That is obviously going to be a crucial factor for many companies where there really is a race to the market. So if you're removing some of that lag, it could make a real difference in what are potentially make-or-break situations for some companies.

And we already have a lot of engineering concepts worked out to make the new facility very capital-efficient as well as time-efficient – we feel both are critical to meet our clients' needs. As you say, it's increasingly about a race to market in cell & gene therapy, and we're working with developers to reduce factors that can create bottlenecks in the product development lifecycle. We're definitely working closely with industry to get these products to the market sooner.

Q What factors do you consider to be critical in ensuring the sector continues to build on this positive momentum over the next 5-10 years?

XS: Firstly, the science – continuing to demonstrate the curative nature of cell & gene therapies is crucial to the ongoing growth of the sector.

From the manufacturing side: coming up with innovative production platforms to support robust, scalable production – Lonza has also invested considerably in internal R&D resources to support this effort.

And from the facilities perspective: providing sufficient (and sufficiently) flexible capacity to quickly meet demand.

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It is also vital that the industry continues to work very proactively with regulators to pave the way for these kinds of products to reach patients as quickly as possible – especially given the fact that many of these novel therapies, often personalised therapies, have very different mechanisms of action to traditional biologics. That is an important step if cell & gene therapy is to join the mainstream – these therapies have to be available to patients as part of the day-to-day management of disease.

I think the most exciting thing of all is that we get to talk about cures – it keeps everyone working in this sector excited!

Q How important are Lonza's partnerships with researchers and potential treatment providers?

XS: Yes, I think that providing a solution to go from gene to therapeutic product as quickly as we can is a key strategic focus for us.

When we look at the drug development piece, a lot of researchers definitely know their genes – they know what gene to use or correct – but then other pieces of the overall gene therapy puzzle may be missing, such as the delivery method, for example. And then how to make this delivery vehicle in a very cost-effective and efficient manner is a further missing piece. So when we are working together with academic collaborators like Luk Vandenberghe, we try to basically provide a toolkit for the researchers, providing the blueprint for the delivery vehicle – and then we have the method to actually produce it, too, through our manufacturing platform. This helps to shorten the development timeline from gene to product: once you have a gene, you can just plug it into the toolkit we have – the 'master piece', if you will.

And on the cell therapy side, we are also working with automation platforms like Cocoon, which is like a 'GMP-in-a-box' solution. This allows us to make that kind of therapy much more efficiently, whilst also opening up the possibility of actually producing it at the patient's bedside.

At the end of the day, all stake holders are working together to find solutions to develop and deliver these life-changing, curative therapies to patients more quickly and cost-effectively and we at Lonza are strived to contribute significantly to these efforts.

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