Just
EVOTEC BIOLOGICS

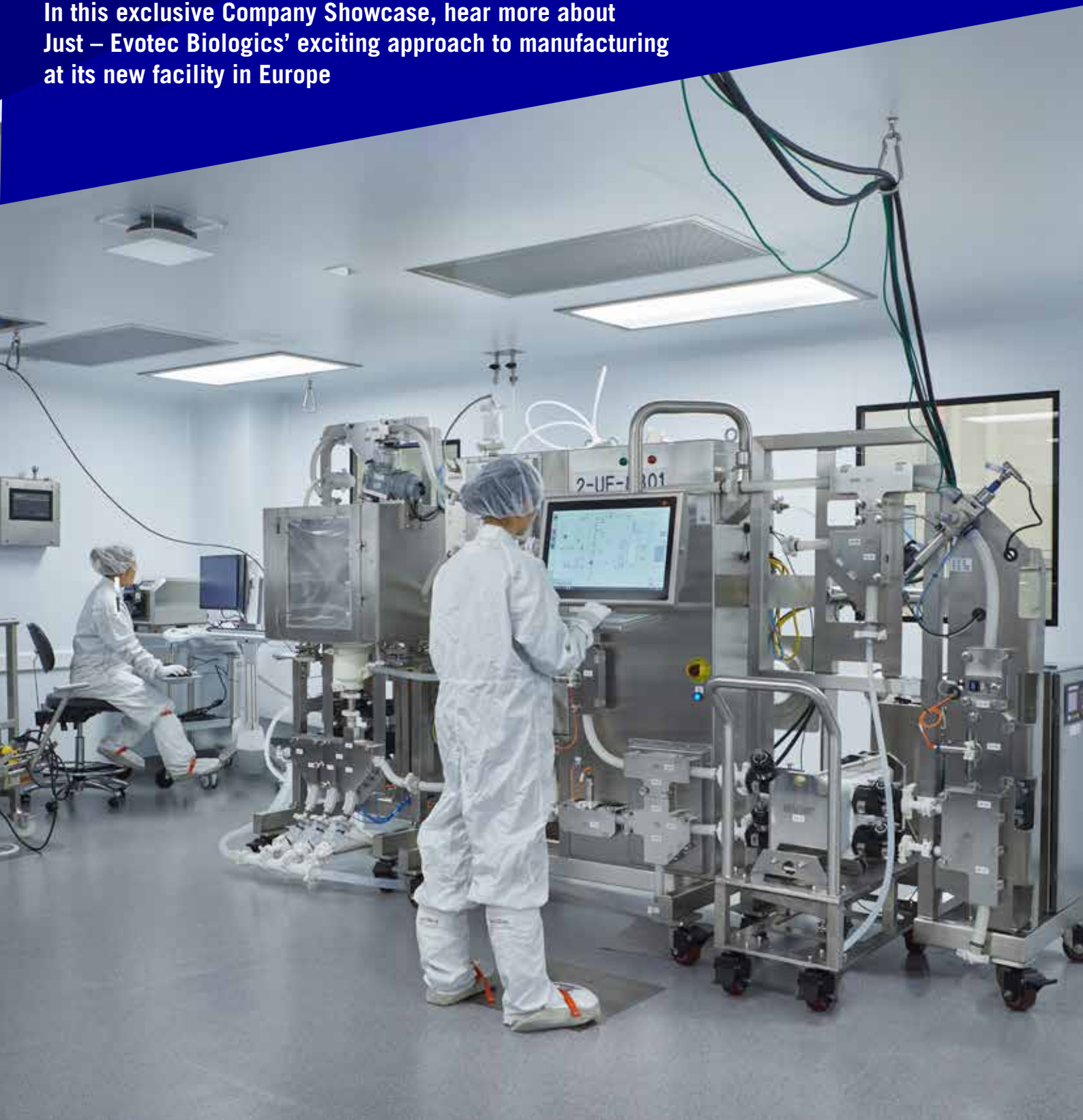
in association with

EBR
European Biopharmaceutical Review

SHOWCASE

Just – Evotec Biologics

In this exclusive Company Showcase, hear more about Just – Evotec Biologics' exciting approach to manufacturing at its new facility in Europe



Continuous biomanufacturing arrives in Europe

Nick Hutchinson at Just – Evotec Biologics explains the benefits of this new approach, why Evotec's new J.POD Toulouse facility is the first of its kind in Europe and what this means for the industry

***EBR*: Can you give us a brief overview of who you are and what you do?**

Nick Hutchinson (NH): Our mission at Just-Evotec Biologics is to expand access to biological medicines through the use of innovative technologies. This includes artificial intelligence (AI) technologies to support our customers through antibody discovery, development, selection and optimisation.

Importantly, we have a unique continuous manufacturing platform for antibody therapeutics.

We install this platform within agile, small-footprint Good Manufacturing Practice (GMP) facilities which we call J.POD facilities – with the newest being our soon-to-open J.POD facility in Toulouse, France.

Our clients can bring us the gene for their antibody and we'll create a cell line, fit a production process to our platform, and then manufacture GMP materials for both clinical trials and commercial supply. Continuous manufacturing allows for significantly better process economics compared to fed-batch processing.

I come from an engineering background and have worked with biologics all my career. I developed a particular interest in continuous manufacturing (CM) as a better way of manufacturing therapeutic antibodies. This prompted me to join Evotec – we are leading the industry at implementing CM and have the opportunity to effect radical change in the biomanufacturing sector. There are very few companies with CM capabilities, and it's exciting to have a technology that is so impactful in expanding patient access to biotherapeutics.

***EBR*: Where do you see the main challenges for biomanufacturing going forward?**

NH: Manufacturing costs are a significant challenge for the industry. Biopharmaceuticals are extremely expensive and that limits the number of patients that can gain access to them, especially at a global level. The average industry manufacturing cost component of therapeutic antibodies is around $200 per gram but our analysis shows that, because our CM process is so efficient, we can drive the cost down to below $50 per gram. Such a reduction can make biopharmaceuticals much more affordable and help overcome the cost barrier to access.

Another challenge is the risk associated with biologics development. Companies that are completing their phase 1 and 2 trials start looking for commercial manufacturing solutions. There are a number of large-scale manufacturing assets in the world and that number is increasing, but there is huge risk with transferring processes from a small-scale manufacturing facility and scaling-up to these stainless steel facilities. This can often involve massive upfront investments and come with no sense of assurance that processes will necessarily work in the large-scale production environment.

However, with our J.POD facilities, that can be avoided because there isn't this enormous leap in scale. Companies stay in the same facility and with the same equipment, we just run the process for longer to achieve the throughput they require. The agility we can provide is key. It can take several years to build a large-scale stainless-steel facility, so companies are left at the mercy of trying to predict future demand. It can take only 18 months to build a new J.POD facility and less time to add

additional PODs to an existing facility. Such short timelines for expansion allow companies to respond to fluctuations in demand more rapidly. They don't have to build enormous facilities or commit to investments based on best-case scenarios. Instead, they can predict the most likely scenario and then build out as and when the market data provides justification.

***EBR*: Is it possible for a partner to switch from an existing fed-batch manufacturing process to continuous manufacturing?**

NH: Yes it is possible and there are a number of companies that are currently doing just that. For example, one major pharma organisation recently reported on how they took a commercial life cycle protein therapeutic and converted it to a CM process.

This is a really exciting development. I think there is a lot of opportunity for companies that have commercial products to re-evaluate their manufacturing strategy as products progress through the different stages of their lifecyle and encounter greater competition. The publication I describe has shown that just because a company went through the launch phase with a fed-batch process they need not stick with it until the end of the product lifecycle. Nevertheless, we recommend that our partners make the switch to CM at an early stage if possible. If a switch from a fed-batch process is going to occur, the ideal time is after first-in-human trials and before late-stage clinical development. This allows for more experience with the process and extra clinical manufacturing data to support regulatory filings.

When we work with partners, we offer a low-risk feasibility study that allows for them to test the technology and demonstrate the CM platform will deliver the quality attributes required. It also demonstrates the likely improvement in productivity and helps them evaluate whether it worth proceeding with converting their existing fed-batch process to the CM platform. Our cost modeling experts are able to calculate the manufacturing costs for the new CM process based on the data from the feasibility study, so that the partners can be sure that the investment in additional process development is worthwhile.

Showcase: Just – Evotec Biologics

***EBR*: What would be involved in such a conversion process?**

NH: Firstly, we assess the client cell line in our CM process as the preference would be to use the existing cell line. If the existing cell line is not suitable then we can generate a new cell line with our own proprietary expression system. Once we've made that evaluation, we demonstrate that the existing cell line grows in a 'mock perfusion culture'.

This is not a true perfusion culture but can help us assess likely productivity and product quality outcomes. The perfusion process is then scaled up to 3L bioreactor runs in the lab, which gives us a stronger indication of the true performance within the manufacturing platform. There is great scalability from 3L to 1,000L and we're always confident in these results. We use some of the material generated from the cell culture experiments to demonstrate performance in the downstream process.

This can be an important part of the conversion as it gives useful information around impurity clearance and how this compares with previous data from the fed-batch process.

***EBR*: Can you tell us a bit about J.POD Toulouse, your new GMP manufacturing facility in Toulouse, France?**

NH: This is the first facility of its kind in Europe (and only the second in the world). Its grand opening is in September of this year and it will be ready for manufacturing projects shortly afterwards. We took a 'copy, paste, improve' approach based on our J.POD Redmond facility in the US.

Our engineers and operations teams built on all the knowledge and learning gained since the opening of the Redmond site in 2021 and put that towards this new facility. It is great to be able to bring continuous manufacturing to our European partners and shorten supply chains to European patients.

We have the same CM platform at both sites and so it is very easy to transfer processes between continents. The automation can be transferred from one site to an identical platform at the same scale but on another continent. This allows companies to move process between facilities to take advantage of capacity as and when needed. The J.POD Toulouse site also offers more than just manufacturing – there is also a highly experienced process development (PD) team and laboratories.

Producing large quantities of antibodies within a small cleanroom footprint with a highly intensified process leads to sustainability benefits

They perform cell line development, process development and characterisation through to formulation development. This is critical for our partners as manufacturing sites in the industry can often be very operationally focused at the cost of not having PD expertise onsite. Both J.POD Toulouse and J.POD Redmond offer manufacturing and PD expertise under one roof. Our development experts can provide advice or troubleshooting if it is needed.

They can explain how the process performed previously in the laboratory, all in a face-to-face environment.

***EBR*: How has the new site's development been influenced by sustainable practices?**

NH: We often place a focus on cost reduction and trying to expand access to medicines but there's no doubt that sustainability is incredibly important for us and our partners.

Producing large quantities of antibodies within a small cleanroom footprint with a highly intensified process leads to sustainability benefits. Our research with a third party is showing that the use of single-use bioprocessing plastics will be reduced by around 65% due to the highly intensified nature of our CM platform. Similarly, given the cleanrooms are so small compared to the amount of product that they produce, we estimate that CO_2 emissions from the production process can be reduced by approximately 75%.

We're also expecting a reduction in water usage of around 50% compared to a manufacturing facility of equivalent output as we don't need to clean, flush and sterilise large stainless steel tanks.

Showcase: Just – Evotec Biologics

***EBR*: Can you describe how your partnering model differs from most other CDMOs?**

NH: First and foremost, we're extremely flexible. The common model for a CDMO is to do all the manufacturing on behalf of their clients, and they don't want their clients to move that process in-house as that would lose them revenue. A typical CDMO doesn't want its customers to build their own production facilities and take their processes back in-house.

That's not true for Just – Evotec Biologics, which may at first seem counterintuitive. The reason is that, in order to expand CM technology globally at the fastest rate possible, we're actually encouraging some customers to take the technology in-house under a licensing agreement, and build their own J.POD facility.

We see ourselves as playing a leading role in enabling the spread of CM technology and facilitating the adoption of this impactful technology in addition to developing processes and manufacturing antibodies on behalf of clients.

A good example of this is our recent partnership with Sandoz AG, wherein they licensed our technology to develop their own continuous manufacturing capability.[1] We're absolutely delighted that they've chosen the J.POD design to be a key part of that facility. It makes perfect sense for a biosimilar company to begin manufacturing in a low-cost continuous way. There can be benefits to partners in conducting manufacturing in-house.

It can allow more control, extra responsiveness and adaptability. It also increases ownership of the technology and accelerates the development of CM competencies as this is incorporated into the technology transfer.

***EBR*: How do you see the CM technology landscape evolving?**

NH: The productivity gains we are seeing are really just the start in my opinion. It has taken fed-batch processing two decades to reach its current level of maturity while CM is really new technology. The immediate gain I see is even higher bioreactor titers. Our proprietary cell line technology that we call our

> *Importantly, we have a unique continuous manufacturing platform for antibody therapeutics. We install this platform within agile, small-footprint Good Manufacturing Practice (GMP) facilities which we call J.POD facilities – with the newest being our soon-to-open J.POD facility in Toulouse, France*

J.CHO High Expression System is generating titers of over 4g/L/d, that is equivalent to over 30g/L in a fed-batch bioreactor. That's more than three times what most people experience in fed-batch systems. This number is likely to increase in my view. Already at smaller scales we are seeing titers as high as 6g/L/d. It's only a matter of time before we see these titers at the production scale. Once this happens the COGs will drop again still further because the process output will have increased, but the facility operating costs will not.

It's important to note that these higher productivities are not coming at the cost of lower product quality.

We have a toolbox of options within the expression system that allows expression of afucosylated antibodies, cytotoxic proteins and biosimilar molecules. J.CHO combined with our J.POD platform is proving very useful for the production of bispecific antibodies, which can be somewhat more fragile if they have undergone significant protein engineering.

Our POD facilities are adaptable, and we can take advantage of new technologies as they become available. Our scientists are always investigating new technologies as the field continues to develop.

We have built this evolution into the design of our facilities to allow for future developments to be incorporated as part of our CM technology roadmap. This future-proofing ensures that our processes will be able to remain adaptable as time goes on, allowing us to always offer the best partnering options for clients.

References:

1. *Visit: evotec.com/en/news/just-evotec-biologicslaunches-tech-partnership-for-biosimilarsdevelopment-and-commercial-manufacturing*

Nick Hutchinson is head of Market Development at **Just – Evotec Biologics**. He holds an Engineering Doctorate from University College London and an MBA from Durham University, both UK. His passion is working with people in the biopharmaceutical industry and challenging the existing paradigm of batch production methods in favour of smarter, more continuous manufacturing in agile small-footprint facilities will lower their costs of goods and environment footprint.

Just
EVOTEC BIOLOGICS

Just – Evotec Biologics

Just – Evotec Biologics, wholly owned by Evotec SE, is a first-to-industry biologics platform company that leverages AI/ML technologies and world-leading molecular design, cell line development, process intensification and continuous manufacturing strategies to advance biotherapeutics from discovery through clinical stages to commercial launch. The Just – Evotec Biologics team combines deep industry experience in the fields of data, protein, process, and manufacturing sciences including automation with highly integrated and flexible capabilities to break through the scientific and economic barriers associated with the development of protein therapeutics. Our focus is to accelerate and expand access to biotherapeutics through scientific and technological innovation for our proprietary projects and on behalf of our partners. Learn more at:

www.just-evotecbiologics.com
info@evotec.com