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How to de-risk cell & gene therapy manufacturing

Cell and gene therapies (CGTs) hold incredible promise, offering potential cures for diseases once thought to be untreatable. Over the past 20 years, the regulatory approval of 32 CGTs and the clinical investigation of more than 2,000 new products highlight their growing impact in healthcare. However, despite these advancements, manufacturing CGTs remains a challenge.

The complexity and high costs involved in producing these therapies have limited their production and so limited their accessibility, leaving many patients without access to potentially life-saving treatments.

Let's talk risks

- Current manufacturing practices can't be scaled to meet demand
- High production cost (labour & facilities)
- Requirement for manufacturing space
- Risk of human variability, error and contamination
- Regulatory risk of introducing new technologies while commercialising products
- Single, disconnected technologies and processes, and lack of unified control, data handling, traceability and chain of identity
- Cost/space inefficient all-in-one solutions

As your scale of production multiplies, so do the risks. To address these barriers, industry leaders are increasingly focusing on strategies to scale CGT manufacturing, and to de-risk doing so. By harnessing full automation of existing semi-automated processes, companies can reduce labour and facilities costs, improve efficiency, and enhance product quality, which is increasingly important as production requirements increase steeply. What strategies could be employed to achieve this?

Full automation

One of the most promising solutions to de-risk CGT manufacturing is the use of robotics to integrate and fully automate existing bioprocessing tools. Traditional manufacturing processes for CGTs consist of isolated, semi-automated unit operation requiring manual intervention at several stages, manual transportation of product and materials, and manual connections between them. This increases the risk of contamination, human error, process-to-process variability and inefficiencies, all of which contribute to higher costs, increased risks, lower reproducibility and assurance. Cellular Origins® fully automates those existing processes in its industrial-scale mobile robotic ecosystem, Constellation®.

Cellular Origins is partnering with leading technology providers to unite existing, individual bioprocessing tools into a fully automated platform, **Constellation,** controlled by one unified software layer.

> “Our fully automated robotic platforms can reduce labour by 16-fold and production costs by 51%, by allowing 24/7 operation and a much more efficient utilisation of manufacturing space. This not only streamlines production but also vastly improves scalability, ensuring CGTs can reach more patients in a cost-effective manner.”
>
> Jason Jones, Global Business Development Lead

Flexibility with reproducibility

In CGT manufacturing, balancing flexibility and reproducibility is essential for success, even though these goals may seem at odds. Therapy developers require a unified platform with the flexibility to bring together various pipeline products, and different modular unit operations, as well as being able to incorporate new technologies as they arise. Constellation provides this flexibility in one manufacturing platform, allowing manufacturers to adapt to increasing scales of production with the most efficient unit operation densities, fitting to current or new facilities as required.

Adaptability must not compromise reproducibility which is fundamental for fixed and standardised GMP-compliant manufacturing and robotic handling.

Through precise robotic handling, and full digital control and traceability, Constellation automates complex processes and distinct unit operations, and the connection between them, with full reproducibility. It does this physically with accurate handling, precise fluid transfer and automated sterile connections.

Digitally, it unifies all operational control, traceability, and data handling within one unified software layer. Every step is executed identically every time, with every second of the products' journey digitally recorded. This strict adherence to proven processes is essential for ensuring the safety, efficacy, and the regulatory compliance of the therapies being produced.

As production scales, so do the risks of variability and error, underscoring the need for robotics and strict standardisation to maintain high-quality, reliable outcomes at every stage. To mitigate this, incorporating the same technologies used for clinical trials for commercial manufacturing reduces regulatory risk.

Constellation integrates the same process technologies used at clinical stage manufacturing in to a commercial production platform, without changing them. This reduces the regulatory risk of changing processes while commercialising and potentially avoids timely and costly redevelopment and comparability studies.

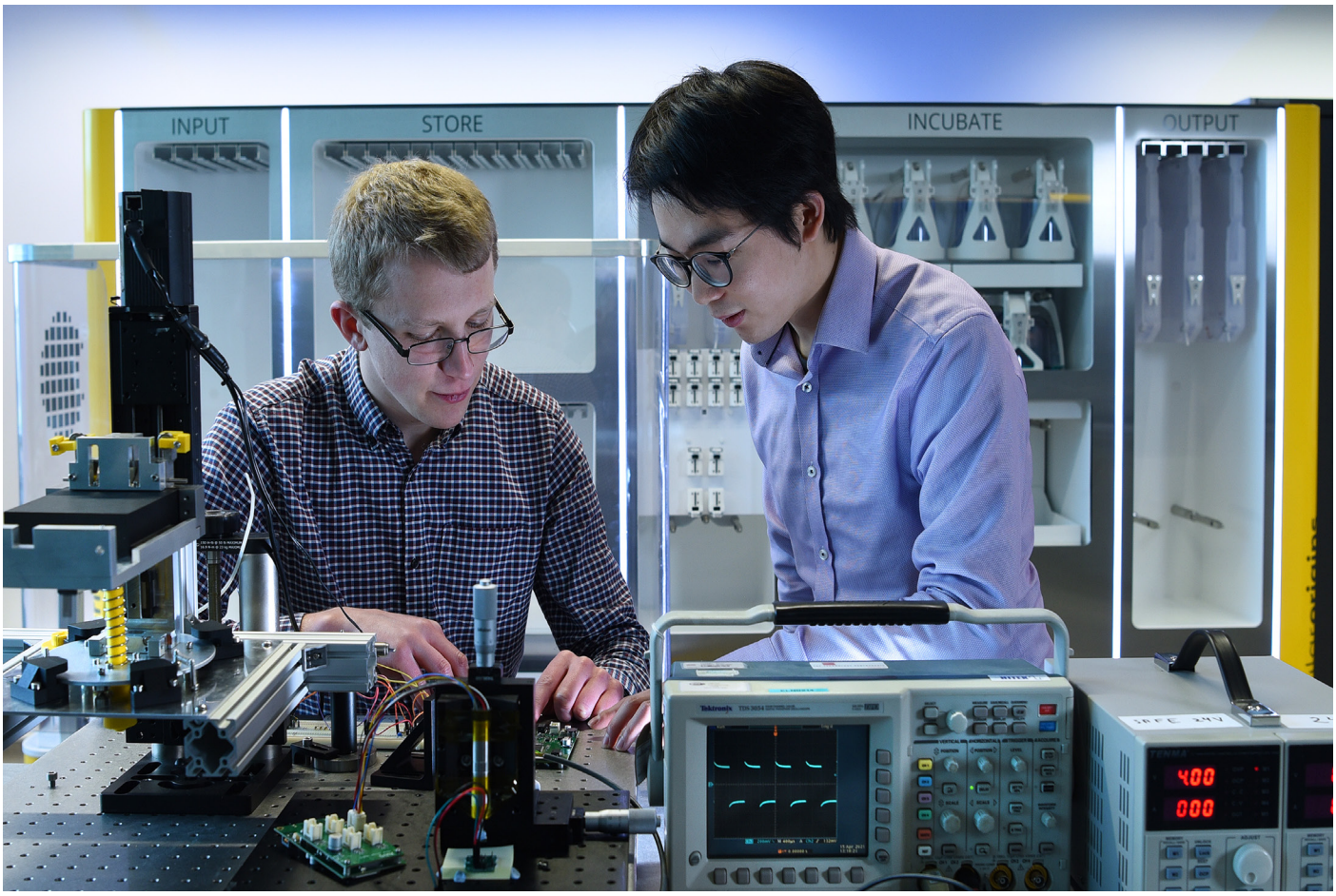
Constellation allows flexibility and adaptability for current and future process integration, whilst preserving complete reproducibility for manufacturing.

Robustness and redundancy

Some full automation approaches seal their robotics and manufacturing processes within enclosed pods and with their own managed environments. Whilst this can offer advantages for maintaining sterility, we recognise that it can also present challenges with flexibility and process redevelopment, as well as space constraints and redundancy.

Cellular Origins has taken a distinct approach to this problem. Constellation consists of autonomous mobile robotics that can range within a larger manufacturing space of a lower grade background (i.e. Grade C/D), performing closed-system unit operations and transporting product and materials between carefully scheduled actions and movements. Their built-in safety systems allow human operators to move within the same space as needed. Some human access to fully automated systems is essential for quick decision-making around minor problem-solving, error recovery, and possibly even product recovery, as well as servicing and repairing hardware when required.

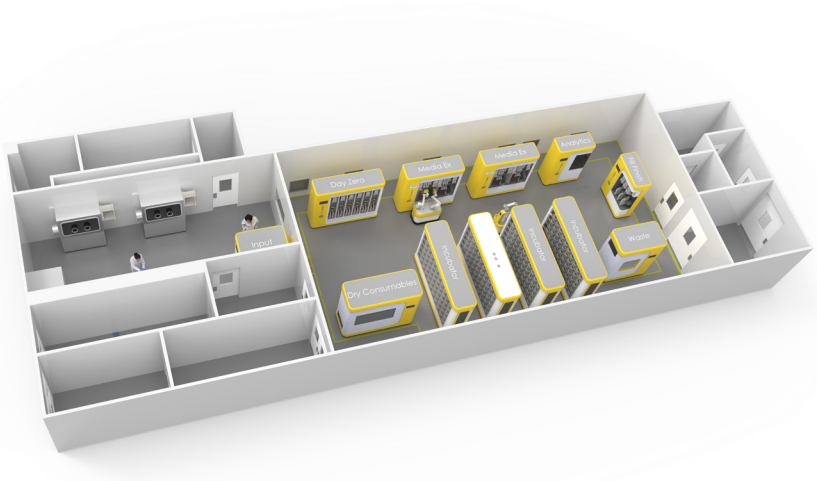
With long term, 24/7 manufacturing enabled, occasional faults and routine maintenance are inevitable, but Constellation's mobile, modular design allows for easy replacement of process devices, workstations, or the robotics themselves without disrupting any production. In contrast, robotics tethered to pods would require shutting down the entire pod for human access, a dangerous disruption of all products being manufactured within it at that time. As manufacturing scales up, ensuring production continuity with inherent robustness and redundancy will become increasingly critical.



Partnership

As cell and gene therapies advance to address more prevalent diseases, the demand for scalable, standardised manufacturing processes becomes increasingly urgent. Fully automated and space-saving technologies will play a vital role in scaling up production to meet growing demand.

With a shared vision and purpose, Cellular Origins is partnering with all the major technology providers in the field to unite diverse devices and technologies into a single, integrated platform. This ecosystem is robotically connected and operated, and digitally controlled and managed. Cellular Origins is creating a seamlessly coordinated solution powered by collaboration.



In the longer term, there may be the need in the industry to utilise decentralised manufacturing models, bringing CGT production closer to patients and facilitating the potential use of fresh products. Fully automated networks of robotic near-care facilities, capable of reproducibly delivering therapies nearer to hospitals offer the potential to reduce quality, regulatory and logistical barriers, and bring therapies to patients faster.

Conclusion

As the reach and the promise of cell and gene therapies continues to evolve, the industry needs to meet the growing demand for them, ensuring access for patients worldwide.

At Cellular Origins, we feel the responsibility that manufacturing bears in making this a reality. The risks are considerable but we believe our approach to industrialise the production of these therapies, to fully automate currently used processes and technologies, and to do so through close collaboration and partnership is the only route through these challenges. The next 2-3 years are pivotal for our industry, and together, we must succeed for the sake of all the patients that can benefit.

Want to find out more?

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