

Preparing CGT manufacturing for the next decade

Cell and gene therapies have demonstrated transformative clinical potential for patients, yet their broader adoption will depend on how effectively the field addresses persistent manufacturing, operational and economic challenges. Over the next decade, success will require not only technological innovation, but also new models of collaboration that integrate automation, decentralisation and hospital realities into scalable, sustainable systems of care

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Cell and gene therapies (CGTs) have moved from scientific ambition to clinical reality. In oncology, and increasingly in other indications, personalised cellular medicines have delivered response rates that would have seemed unattainable only a decade ago. Yet, despite this progress, access remains limited to only a tiny fraction of patients.

If the next decade is to fulfil the promise of CGTs for patients living with cancer and other diseases, the industry must look beyond incremental optimisation and confront structural challenges in manufacturing, hospital integration and affordability. Reducing complexity, cost and time is not simply a matter of efficiency and sustainable healthcare delivery; it is a prerequisite for equitable access for patients across geographies.

The increasing burden of cancer

Giving even greater urgency to increasing access to CGTs are projections that global cancer incidence and mortality will increase substantially over the coming decades, driven primarily by population growth and ageing. In 2023, cancer had already reached an estimated 18 million new cases and over 10 million deaths worldwide, underscoring its position as a leading cause of mortality, second only to cardiovascular disease.¹ As populations continue to age and exposure to modifiable risk factors persists, the number of cancer diagnoses are projected to rise from 2024 to 2050 by 60.7% and deaths by 74.5%.²

Behind these numbers are real people – patients and their families. As the incidence of cancer grows, more people are living more years of life with disease.³ Many will have a variety of different treatments in an effort to be cured of cancer, treatments which may or may not work and which affect their quality of life as they undergo them.

In addition to this enormous human cost, the rising burden of cancer will also bring significant economic pressures on

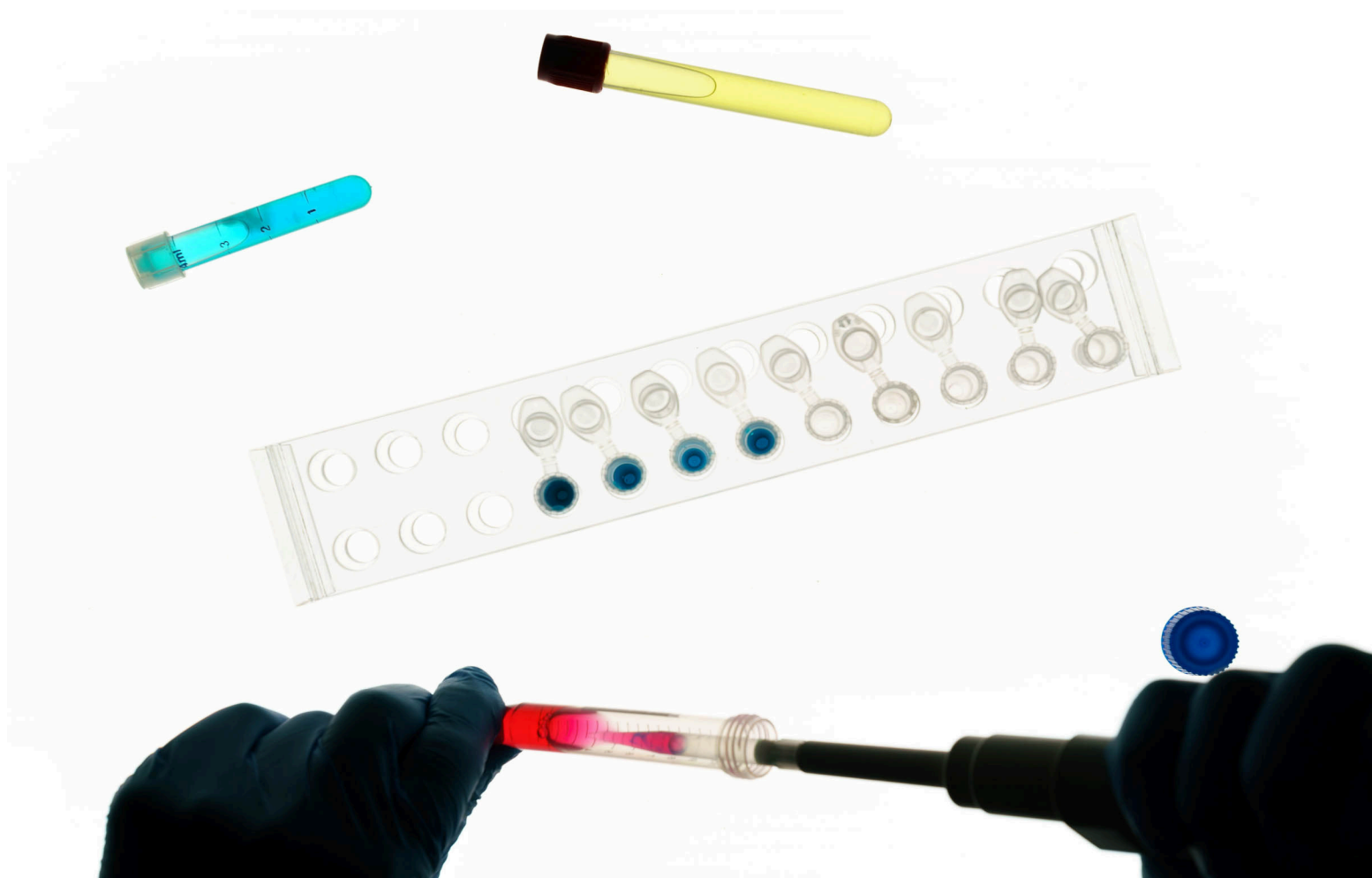
healthcare systems and economies. The macroeconomic cost of cancer is substantial, reflecting both direct medical expenditures and broader societal impacts. High-income countries spend more on treatment per person, while low- and middle-income countries experience the largest increases in cancer deaths.⁴ This growing financial strain underscores the urgency of redesigning care models to ensure sustainability.

The promise of CGTs

CGTs have the potential to transform diseases like cancer. These treatments typically involve extracting cells from a patient, modifying or manipulating them outside the body, and then returning them to the body to restore or alter specific cell populations. Often used as a later-line or last-resort treatment, CGTs give hope to patients fighting cancer, neurological disorders, autoimmune diseases and other serious conditions.

A primary example is chimeric antigen receptor T-cell (CAR T-cell) therapy, a personalised immunotherapy that harnesses a patient's own immune system to target and eliminate cancer cells. The process begins with the collection of a patient's T-cells via leukapheresis. These cells are then genetically modified ex vivo to express a synthetic receptor – the CAR – designed to recognise a specific antigen on the surface of tumour cells. After modification and expansion to achieve sufficient cell numbers, the engineered CAR T-cells are reinfused into the patient, where they bind to target cancer cells, become activated, proliferate and induce cytotoxic destruction of the malignant cells. Unlike conventional chemotherapy, which acts broadly on rapidly dividing cells, CAR T-cell therapy provides targeted immune-mediated killing and can persist in the body, offering ongoing surveillance against relapse.⁵

CAR T-cell therapies have demonstrated high overall response rates and durable remissions in a substantial proportion of cases.⁶ For these individuals, CAR T-cell therapy represents not merely an incremental advance,



but a potentially life-extending or even life-saving option when other treatments have failed. Across Europe, uptake of CAR T-cell therapies varies widely despite their potential, and treatment rates for eligible patients remain on average below around 18% in several countries (UK, France, Germany, Italy and Spain).⁷ This disparity highlights the need for manufacturing models that can scale equitably and sustainably.

Manufacturing capacity as the primary bottleneck within a multifactorial challenge

Autologous CAR T-cell manufacturing today typically follows a centralised, multi-step process. Patient cells are collected via apheresis, cryopreserved, transported to a specialised manufacturing facility, enriched and activated, genetically modified – approved products as of today using viral vectors – expanded over several days, tested, cryopreserved again and shipped back to the treating centre. Vein-to-vein times commonly extend to four to six weeks.⁸

While this approach has enabled the first wave of patient access to CAR T-cell therapy, it introduces multiple constraints:

- **Logistical complexity and administrative burden:** coordinating patient eligibility windows, manufacturing slots, shipping timelines and chain-of-identity safeguards requires significant administrative effort

- **Capacity limitations:** centralised facilities can become bottlenecks as demand increases
- **Economic burden:** multi-site logistics, cleanroom-intensive processes, specialised labour and viral vector production contribute substantially to the cost of goods
- **Clinical risk during delay:** most important of all, for heavily pretreated oncology patients, weeks of waiting can be clinically critical.

Complex manufacturing, logistics and scheduling as well as reimbursement challenges are barriers to scale. Clinicians point to staffing requirements, training demands and the strain on hospital infrastructure.⁷ It is patients who experience the cumulative impact of delays: uncertainty, additional bridging therapies and, in some cases, disease progression before infusion.

As cancer incidence rises, so will the need and demand to make this therapy available across geographies to an ever-growing number of patients, making the current model increasingly difficult to sustain.

Automation as a foundation for scalability

A central question for the field is how to compress the manufacturing timeline while maintaining quality, safety and reproducibility. Closed, automated cell processing systems have emerged as one promising approach. These systems reduce unit operation processing times



Encouragingly, evidence showing the correlation between treatment efficacy and the presence of specific subsets of T-cells, rather than only total T-cell number, has led to new processes where cells spend minimal time in culture (eg, one day)



compared to manual approaches, while also avoiding operator-to-operator variability. However, even with the implementation of automated systems, week-long culture expansion to generate billions of CAR T-cells has long been an obstruction to substantially reducing processing times. Encouragingly, evidence showing the correlation between treatment efficacy and the presence of specific subsets of T-cells, rather than only total T-cell number, has led to new processes where cells spend minimal time in culture (eg, one day).⁹

With expansion now a small portion of the full process, further reduction in processing time can come from shortening the enrichment, activation and modification steps. Coupled with the potential to eliminate the activation step and utilise non-viral transfection, a goal is that production time could conceivably be reduced to less than one day.

In parallel, non-viral gene modification strategies are being explored to address the cost and complexity associated with viral vector manufacturing. Viral vector production remains resource-intensive and capacity-constrained; alternative approaches may reduce both production timelines and input costs, provided they demonstrate equivalent safety and efficacy.

The convergence of these elements – rapid cell selection, integrated activation and non-viral modification – has the potential to transform the ‘long middle’ of the manufacturing process. Steps traditionally requiring multiple days, expansion phases and repeated cryopreservation may be reduced or eliminated in certain models.

Shortening manufacturing from weeks to days would have implications far beyond throughput. It would redefine how and where therapies can be produced, thereby introducing the possibility of dramatically scaling this technology for patients living with disease.

From centralised production to hospital-based models

Decentralisation is not a new idea in CGT. Several initiatives have attempted to move manufacturing closer to the point

of care, but the results have been mixed. Technological feasibility alone has proven insufficient. The hospital is not simply a smaller manufacturing site. It is a complex ecosystem governed by clinical priorities, workforce constraints, reimbursement frameworks and regulatory oversight. Introducing advanced manufacturing into this environment requires alignment with existing workflows, not disruption of them.

Efforts across Europe are now examining how modular, hospital-based platforms could enable CAR T-cell production within days rather than weeks. The ambition with the ultimate goal to increase patient access in this set up is twofold:

- **Technical compression:** shrinking manufacturing time through non-viral gene transfer, innovative T-cell selection methods, new gene editing protocols combined with automation and overall streamlined processing
- **Operational compatibility:** including hospital workflows, staffing models and reimbursement structures.

Operational compatibility is often underestimated. Hospital-based production requires careful consideration of space allocation, training, quality oversight, digital tracking systems, and coordination between clinical and laboratory teams. Without this systems-level design, even technically robust solutions may struggle to gain adoption.

Importantly, Europe’s diverse healthcare systems provide a natural laboratory for understanding variation in readiness and barriers. Treatment rates for CAR T-cell in diffuse large B-cell lymphoma, for example, differ significantly between countries.⁷ Understanding these disparities – logistical, financial or infrastructure-based – is critical if decentralised models are to expand access equitably.

Looking beyond oncology

While CAR T-cell in haematologic malignancies has led the way, cell therapies are expanding into solid tumours and autoimmune diseases.¹⁰ If manufacturing models can be simplified and compressed, the same platform principles may apply across indications. For autoimmune

diseases in particular, where patient numbers may far exceed current oncology populations, scalable and affordable manufacturing will be decisive. Without structural innovation, widespread application may remain financially prohibitive. Thus, the manufacturing question is inseparable from the therapeutic future of the field.

The role of collaboration in the coming decade

The next decade of CGTs will be shaped by whether the field can address the opportunities and barriers discussed above through collaboration. It's likely that no single organisation can resolve the manufacturing, operational and economic constraints facing CGTs to bring about its enormous promise to patients living with disease.

Cross-sector consortia offer one model for aligning resources. By bringing together device developers, biotechnology firms, academic immunotherapy centres and hospital systems, collaborative frameworks can map barriers comprehensively before implementing new manufacturing approaches.

The voice of clinicians and healthcare providers is vital to the success of this effort. Integrating advanced processing systems into hospitals demands sensitivity to staffing pressures, accreditation requirements and budget constraints. The promise of CGTs is no longer hypothetical. For patients with few alternatives, it represents a tangible chance at remission and improved quality of life. Ensuring that more patients can benefit – regardless of geography – requires coordinated action now.

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