Case Study

Automating Cell Therapy Manufacturing and Enabling Rapid Multi-Site Tech Transfer.

CTMC and Ori Biotech partnered to improve biological performance and accelerate product development through flexible, automated manufacturing with the IRO® platform.

August 2025

CTMC, a joint venture between Resilience and MD Anderson Cancer Center, partnered with Oribiotech to automate critical steps in the CAR-T-cell therapy manufacturing process and demonstrate multi-site comparability of their clinical-stage CAR-T asset.

Ori Biotech's IRO® platform enabled CTMC to:

- Significantly increase CAR-T cell yield and transduction efficiency compared to a process run on an existing static platform.
- Demonstrate process reproducibility across two manufacturing sites.
- Complete technology transfer into process development in under two weeks.

Overcoming Manufacturing Bottlenecks in CAR-T Therapy

Cell and gene therapies (CGTs) have captured the attention of medicine for their ability to offer unprecedented outcomes — including cures — for patients with life-threatening diseases. Nowhere is this more evident than with CAR-T cell therapy, where a single, personalized infusion can drive durable remission in patients with otherwise untreatable cancers.

Nevertheless, hundreds of thousands of patients are unable to access these life-saving therapies. The manual manufacturing process which are difficult to optimize and scale with legacy systems represent a significant bottleneck contributing to the high costs and limited availability of these therapies. Additionally, it can take months to transfer a process between manufacturing sites, further delaying process development and scale up of manufacturing.

CTMC and Oribiotech share a common goal: to help accelerate the development and delivery of cell therapies to patients. Ori developed the IRO® platform to support both early development and GMP production by automating some of the longest and most biologically consequential steps in the process — including T-cell activation, transduction, and expansion. Together, Oribiotech and CTMC set out to evaluate whether the IRO® platform could replicate — or even improve upon — the performance of an existing optimized clinical CAR-T-cell manufacturing process while supporting faster scale-out and regulatory confidence.

Designing a Scalable, Reproducible CAR-T Manufacturing Process

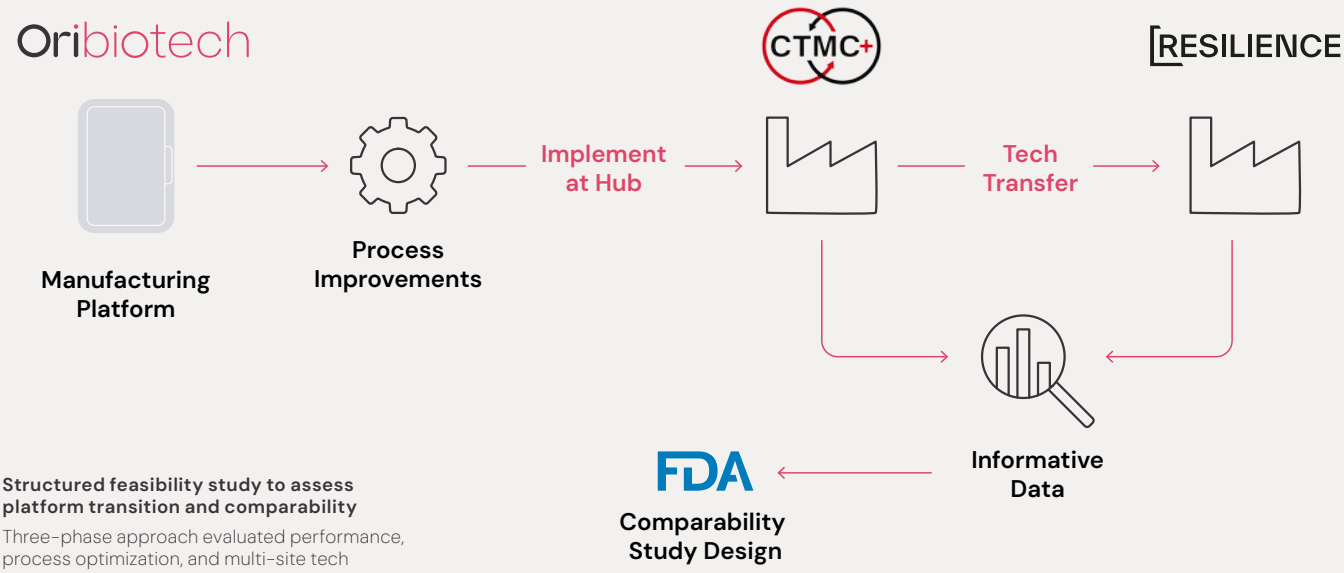
To explore whether a platform transition could improve biological performance while supporting regulatory comparability and multi-site scalability, Oribiotech and CTMC launched a feasibility study using a CAR-T cell product invented at MD Anderson with a process developed at CTMC.

The study was designed around a phased approach that mirrored real-world clinical manufacturing conditions. It aimed to test the IRO® platform's ability to replicate or enhance a clinical CAR-T process run using an in-house static platform . The feasibility study also evaluated how easily that process could be transferred to a second site, and whether the resulting data would support FDA engagement on process comparability via a Type-D Meeting.

Study Structure and Objectives

The collaboration followed three structured steps:

- **Process Replication:** Execute a head-to-head comparison of CTMC's existing CAR-T process being run on a static platform and the IRO® system using the same donor material, reagents, and workflow.
- **Process Optimization:** Apply targeted adjustments to the IRO® process (e.g., mixing parameters) to evaluate flexibility and performance gains.
- **Tech Transfer and Reproducibility:** Transfer the optimized IRO® process to Resilience's Philadelphia site and run the same protocol to assess reproducibility across manufacturing environments.



Structured feasibility study to assess platform transition and comparability

Three-phase approach evaluated performance, process optimization, and multi-site tech transfer to inform regulatory strategy.

Each phase was designed to answer a set of key questions:

- Could the IRO® platform match or exceed performance in cell yield, viability, transduction efficiency, and phenotype?
- Could the process be transferred rapidly and reliably to a new site with minimal burden?
- Would the results generate the kind of data that could inform a regulatory comparability strategy?

With these objectives defined, CTMC began by deploying the IRO® platform into their Houston PD laboratory. Once the protocol was established, the exact same protocol was deployed at Resilience's Philadelphia manufacturing facility.

Improved Biological Results Through Flexible Automation

Using cryopreserved, positively selected T-cells from three unique healthy donors, CTMC evaluated the performance of the IRO® platform compared to their established process on an existing static platform. The control was run at 1/10 scale. The first IRO® run — out of the box with minimal setup — delivered a complete, successful process with the resulting growth data scaled X10 for comparison.

Process Overview:

1. Cryopreserved positively isolated CD4/CD8+ T-Cells from healthy donors
2. Starting Viable Cells: 200M in 75mL
3. Activation on D0: GMP TransAct
4. Transduction on D1: CAR-LVV

Qualitative Goal	CQAs
High Total CAR+ Yield	Greater than 700M CAR+ cells
High Viability	Greater than 70%
Vector Copy Number (VCN)	Less than 5 copies/transduced cell

Initial establishment of the CAR-T manufacturing process on the Ori IRO® platform was completed in under five weeks from kickoff. The first production run (**Run 1**), conducted with a healthy donor sample, resulted in a lower total cell yield compared to CTMC's established process.

To address this, the team conducted **Run 2**, incorporating targeted adjustments to the process. Specifically, mixing speed and base height were modified during the compression phase of culture to improve cell resuspension. These changes led to a substantial increase in fold expansion, demonstrating that the IRO platform could be effectively adjusted for improved biological performance.

Run 3 tested the updated protocol with a second, slower-growing donor. The run produced a similar improvement in cell expansion, confirming the reproducibility of the optimization across donors. (Figure 1).

The IRO® platform's programmable mixing modes — static, rock, and compression — enabled optimization at each stage: activation, transduction, and expansion. This flexibility supported rapid process tuning while maintaining control and reproducibility.

> **"What initially attracted us to this partnership was the flexibility of the IRO platform in terms of the design of the novel bioreactor system which returns control of process optimization to our process scientists, enabling comprehensive optimization."**
>
> Jason Bock, CTMC Co-Founder and CEO

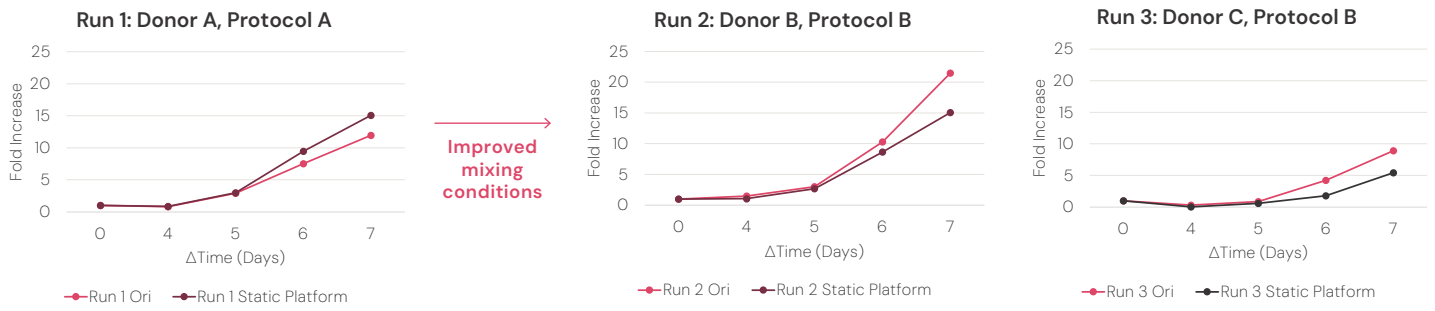


Figure 1. CAR-T cell expansion with Ori vs. In-house static platform. Ori Run 1 underperformed the control; protocol adjustments in Run 2 led to a significant yield increase. Run 3, using a slower-growing donor, confirmed the reproducibility of the optimized Ori process.

IRO® outperformed the in-house processing key biological metrics:

- Ori delivered a **21%**, **127%**, and **226% increase in CAR+ yield** vs in-house static control
- Transduction efficiency averaged at **~69%** in Ori vs **~45%** in the control, with VCN remaining below the FDA recommended < 5 copies per transduced cell (Figure 2)

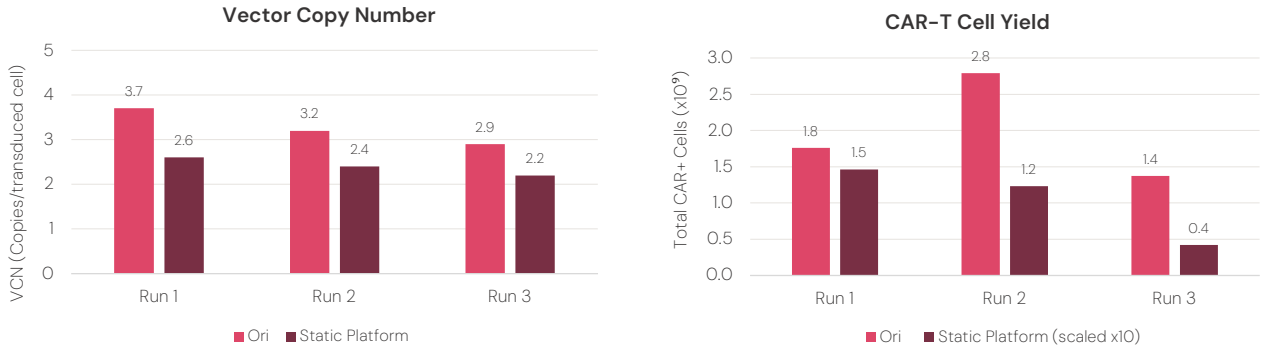


Figure 2. Using three independent donors, the manufacturing process for a CAR-T cell product was optimized to outperform the clinically proven protocol within two runs. The IRO® platform yielded superior fold expansion, total CAR+ cells, and transduction efficiency.

Across all runs, no trends were observed in CD4/CD8 composition or memory phenotype. (Figure 3).

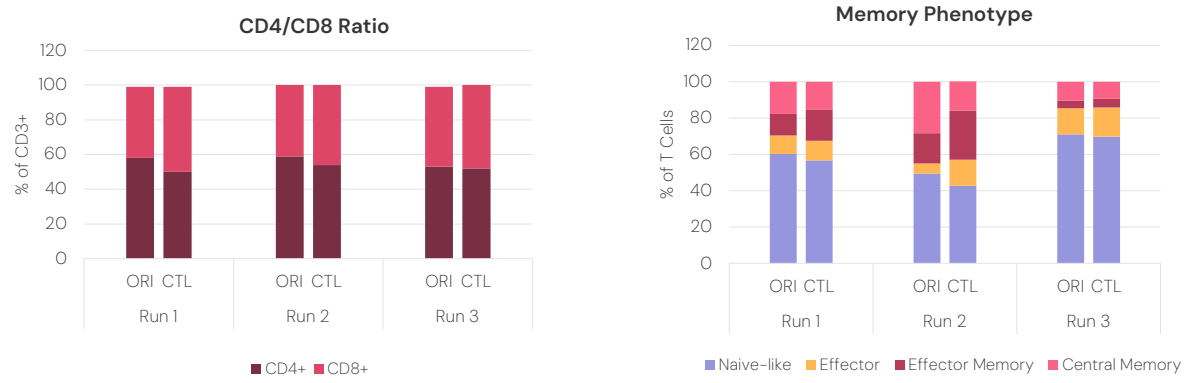


Figure 3. Consistent CD4/CD8 ratios and memory phenotype across all runs. No notable trends or variability were observed, supporting product consistency.

These gains were achieved without extensive trial-and-error. From the earliest runs, IRO® offered the flexibility and control needed to optimize key process parameters.

CTMC co-founder and CEO Jason Bock summed up the experience:

"I expected automation and more process insights, but I never expected better biological performance right out of the gate."

Proving Reproducibility Across Sites

To assess the Ori platform's suitability for clinical manufacturing and multi-site scalability, CTMC designed a set of parallel process runs aimed at demonstrating comparability between sites.

CTMC transferred the finalized protocol to Resilience's Philadelphia site. Process analytics for determining VCN, transduction efficiency, CD4/CD8 ratio, memory phenotype, and post-thaw viability were performed at CTMC to eliminate inter-site testing variability. These analytics showed minimal variation across both sites.

Together, these results demonstrate the potential of the IRO® platform to support streamlined tech transfer, reproducible clinical manufacturing, and regulatory alignment for platform-based production strategies. This study served as a proof of concept for IRO-enabled multi-site manufacturing — providing confidence that both product quality and operational performance can be maintained when moving from site to site.

Key Outcomes (Figure 4):

- The Ori platform **met all target release criteria by Day 7** across two independent sites, meeting the criteria a day early (Day 6) in 5 of 6 runs
- Protocol establishment time of **<2 weeks**
- Post-thaw product **viability exceeded 80%** across both sites
- Transduction efficiency averaged well **above target at ~64%**
- VCN **remained below FDA recommended <5 copies** per transduced cell

Figure 4. Transduction efficiency, vector copy number, and total CAR+ cell yields were comparable between CTMC and Resilience manufacturing sites by day six. We completed an RCA to review the discrepancies between the runs.

Supporting Regulatory Success

This case study formed the basis for a successful Type D meeting between CTMC and the FDA, during which the agency provided clear guidance on comparability study design, process optimization, and the regulatory implications of automation. Importantly, their guidance directly aligned with the IRO® platform's strengths and reinforced the role that IRO® can play in both improving outcomes and supporting regulatory success.

Conclusion: A Scalable, Flexible Platform for the Future of CGT

This collaboration demonstrates that automation and better biology are not mutually exclusive. By delivering on the study's core objectives — rapid process optimization, improved biological performance, and reproducibility across sites — the IRO® platform proved its value in accelerating development without compromising quality. The protocol was successfully executed at a different site after two weeks of training, reinforcing the system's potential for streamlined, scalable implementation. As the cell and gene therapy industry begins to explore the possibility of decentralized and distributed manufacturing, one of the key constraints is the transfer of manual processes between sites, which is expensive and time consuming. This study demonstrates the ability of the IRO® automated manufacturing technology to alleviate this constraint and facilitate seamless multi-site manufacturing.

With high transduction efficiency, consistent quality, and reproducibility across facilities, Ori's IRO® platform sets a new standard for CGT manufacturing. Together, CTMC and Ori Biotech demonstrated that manufacturing innovation is essential to improving the commercial viability of cell therapies — reducing time, cost, and complexity while maintaining product quality. These advancements ultimately help bring more therapies to market, and to patients who are still waiting.

a joint venture between Resilience + MD Anderson Cancer Center

About CTMC

CTMC is a co-development accelerator formed through a joint venture between Resilience and MD Anderson Cancer Center to fast-track the development and manufacturing of next-generation cell therapies for cancer. Located in the heart of the Texas Medical Center, CTMC combines deep expertise in TIL and CAR-T platforms with integrated manufacturing and regulatory capabilities to accelerate the path from discovery to IND. As a true partner, we work side-by-side with cell therapy innovators—advancing programs into the clinic faster and charting a clear course to commercial readiness.

Follow us on LinkedIn and visit www.ctmc.com to learn more.

Oribiotech

About Ori Biotech

Ori Biotech is a London and Philadelphia-based manufacturing technology company on a mission to enable widespread patient access to life-saving cell and gene therapies. IRO®, Ori's next-generation manufacturing platform automates better biology, accelerates product development and enables therapy developers to scale their products' clinical and commercial impact by seamlessly transitioning from R&D to GMP on one platform. The promise of the innovative Ori platform is to automate cell therapy manufacturing, increasing throughput, improving quality and decreasing costs by combining proprietary hardware, consumables, software, data and analytics.

For news and updates, visit oribiotech.com/news-insights

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