# Customer Implementation: Cell & Gene Therapy Orchestration in a Point-of-Care Manufacturing Model

November 2021

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Published in the USA 11/21.

## BACKGROUND

Personalized cell and gene therapies, based on a single patient's needs, holds great promise for humankind. As an emerging capability that is transforming patient care, the manufacturing and logistics processes in personalized therapies are ripe with opportunities to reduce costs and improve productivity. Optimization will help accelerate and expand the possibilities and use cases for personalized treatments. CellPoint, together with Hypertrust Patient Data Care**, and using Dell Technologies solutions, has built a new approach that is revolutionizing personalized cell and gene therapies.

Personalized treatments, like autologous cell therapies, are based on a single patient's input, either in the form of physical material (e.g., blood or tissue cells) or patient-specific data analysis. From this input, a medicine is produced specifically for each patient. Inherently, this process uses very small batch sizes (often a batch size of 1) for production, which limits the potential for productivity improvements via volume or scale as in traditional manufacturing approaches.

The manufacturing process for personalized medicine starts with input generation and ends with the final product/medicine. The entire supply chain is both closed loop and highly distributed across many touch points, providing multiple opportunities for productivity-enhancing measures.

A significant root cause of higher cost and effort in a closed loop supply chain is the heavy reliance on logistics. Specialized service providers deal with fast transports that must fit into tight time frames and may also require rigid temperature conditions, including -150° C (cryogenic state).

A novel point-of-care production model is a promising approach that reduces costs and production times for personalized cell and gene therapies. The point-of-care model eliminates the need to freeze and thaw physical materials and eliminates the need to transport materials altogether. By installing the production facility at the hospital where the patient is treated, the manufacturing process can take place at the point-of-care, centrally managed by specialized biotech companies. This is what CellPoint is doing to transform autologous cell therapies, such as chimeric antigen receptor T cell therapies (CAR-T).

## ABOUT CELLPOINT

CellPoint is a Dutch (EU) company founded to provide affordable and readily available CAR-T therapies for all patients in need. The CellPoint CAR-T treatment workflow is designed for quality and patient safety, while driving down time-to-treatment and costs by leveraging automation at the point-of-care. Find out more at www.CellPoint.bio.

** Hypertrust Patient Data Care is a spin-off of Camelot

## CELLPOINT APPROACH: POINT-OF-CARE MANUFACTURING MODEL

### CONVENTIONAL CAR-T

To establish proof-of-concept of the point-of-care manufacturing model, CellPoint is developing CAR-T products targeting validated targets, such as CD19. Other companies have several approved CD19 CAR-T products on the market, like Kite-Gilead Yescarta, Novartis Kymriah, and BMS Breyanzi, using a conventional manufacturing model in large central factories where the patient cells are shipped in liquid nitrogen conditions.

These current CAR-T therapies are used for treatment of patients diagnosed with blood cancers, characterized by diffuse large B-cell lymphoma and certain types of acute leukemia,. Due to the complex manufacturing and logistics, the cost of these products are high, in the range of 300-500 thousand U.S. dollars. The entire treatment process, shown in the figure below, takes 1-2 months. During this time, the cancer is progressing and many patients drop out and are not able to receive their treatment, unfortunately. Furthermore, the conventional treatment process involves freezing the patient cells. The lengthy processing time outside of the body negatively impacts the quality of the patient's cells and thus the product.

The closed loop supply chain for this type of treatment displays some of the most common attributes of a personalized medicine production process:

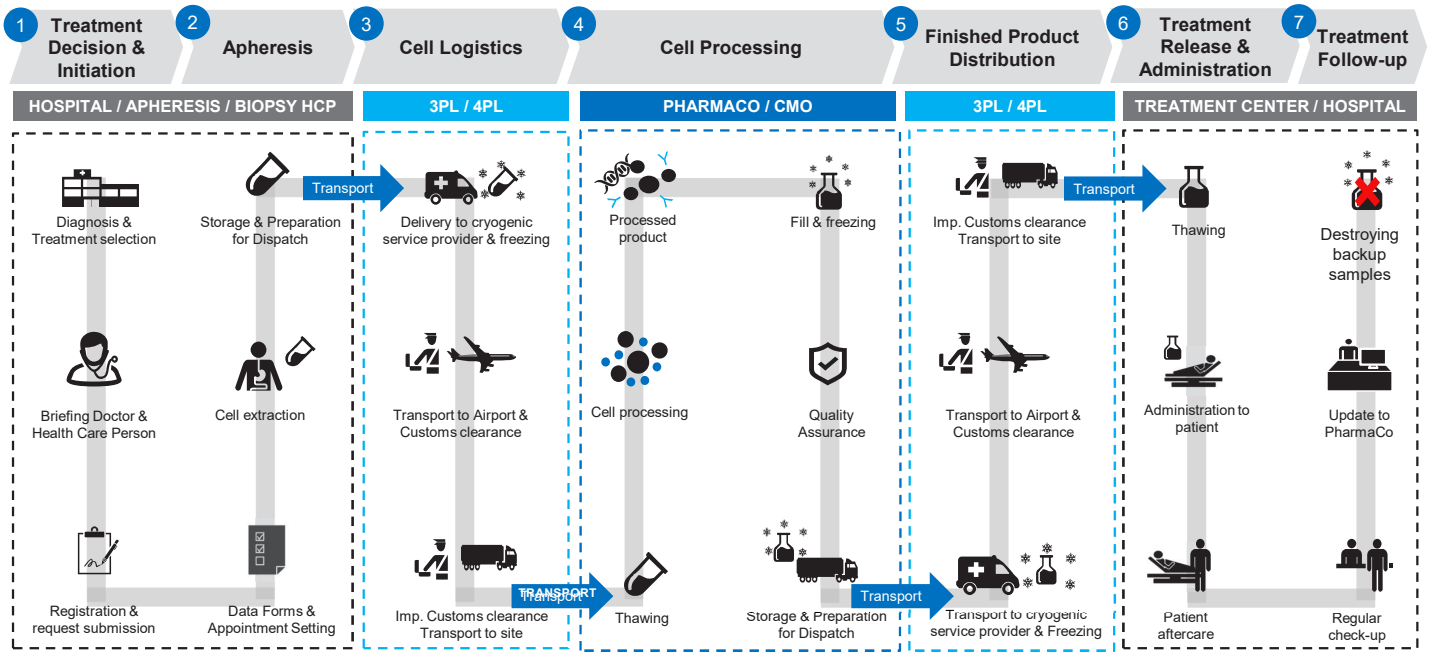



**Figure 1.** Centralized manufacturing process of cell therapy cancer treatments (mainly seen today)

### INNOVATIVE, POINT-OF-CARE CAR-T

To address these challenges, CellPoint designed an unconventional point-of-care CAR-T manufacturing and supply model using innovative technologies. Clinical centers of excellence have been selected based on the presence of experienced hematology teams and local cell processing facilities. These centers are equipped with a closed and automated manufacturing platform and required QC (quality control) equipment. Staff at the centers receive full training and support to manufacture CAR-T therapies and treat patients.

Clinicians are able to schedule and perform CAR-T treatments within one week, without complex logistics. CellPoint's secure and online xCellit platform, developed with Hypertrust Patient Data Care based on their X-Chain solution, is used to facilitate scheduling and monitoring of the CAR-T treatment workflow for the various stakeholders as shown here:

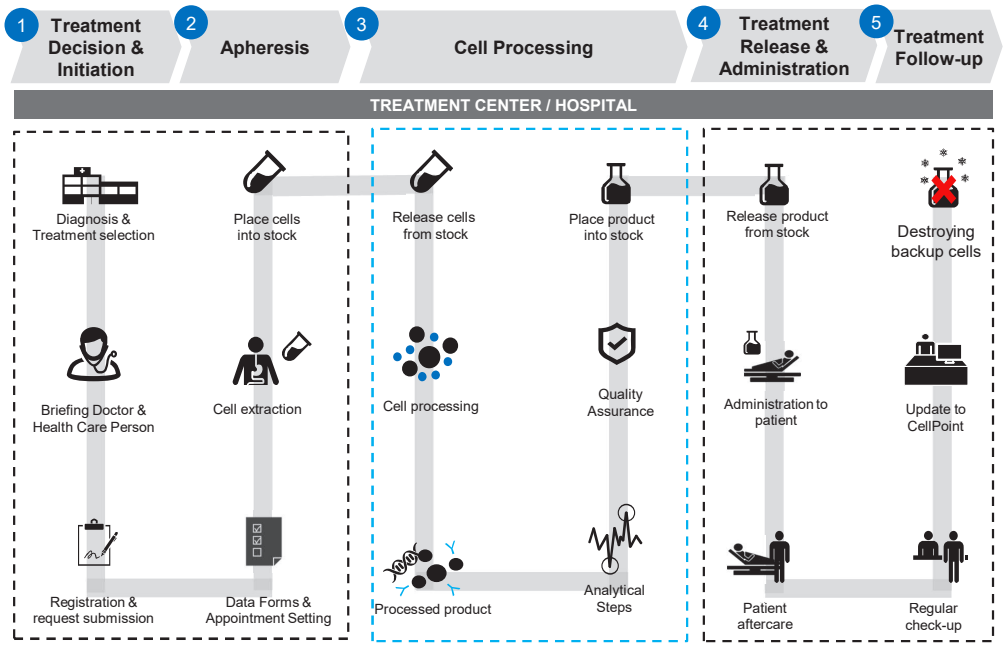



**Figure 2.** Decentralized manufacturing process of autologous cell therapies (CellPoint target process)

Results include:

- A short vein to vein time with a turnaround of 1 week
- Flexible scheduling controlled by the healthcare professional
- Point-of-care manufacturing without complex logistics
- Real time monitoring of the entire process
- Lower costs due to
  - A simple supply chain
  - The use of automation via innovative technologies

Point-of-care production eliminates certain – and significant -- deficits from the distributed manufacturing of personalized therapies. In fact, it makes personalized medicine both feasible and effective. Simultaneously, new challenges are emerging that require solutions in order for the point-of-care production model to scale further and more broadly succeed.

CellPoint, the coordinating point-of-care product development company, supports and monitors the manufacturing processes at many different sites in clinics around the globe. The latest digital technology is used to enable global implementation and control.

## DATA PROTECTION

Since its early days, personalized medicine has been challenged by data protection regulations such as GDPR (General Data Protection Regulation) and HIPAA (Health Insurance Portability and Accountability Act). Further, personalized medicine must navigate sharing confidential patient information among health care providers, insurers, policyholders,

and patients while complying with legal regulations. Different regulatory rules in different countries further complicate the situation. A secure and defensive solution is needed to ensure personal and patient data protection and processing requirements across very different jurisdictions.

### CHAIN OF IDENTITY AND CHAIN OF CUSTODY

An integral part of a closed loop supply chain is to ensure that the final product is returned to the correct patient from whom the starting cell material was extracted. This chain of identity and its precision and accuracy is of utmost importance for the manufacturing process of personalized medicines. Any deviation in the chain of identity could result in serious consequences, such as physical injury, or even death.

The chain of custody refers to the chronological documentation that records the sequence of custody, control, transfer, analysis, and disposition of physical or electronic evidence. The chain of custody is of particular importance in the supply chain of personalized treatments as it assures the traceability and quality of the final medicine. In many legislations, an immutable chain of custody is required to allow for release of medicinal products.

### ORCHESTRATION AND AUTOMATION WITH CONDITIONAL CHECKS AND DEPENDENCIES

The manufacturing process of personalized therapies starts with input generation and ends with application of the final product, regardless of point-of-care or centralized production. Even when produced at the hospitals, the process entails a distributed manufacturing approach, involving many different clinical wards and some external parties. From a process owners' point of view, this approach is difficult to manage, especially when manufacturing is running at many clinics concurrently.

Furthermore, due to the high interdependence of some production steps, additional repetitions or quality checks may be required before the final product can be released. To achieve this repetition, flexible, rule-based, conditional checks need to be evaluated between process steps based on certain parameters.

## CELLPOINT XCELLIT

The CellPoint xCellit model, based on Hypertrust Patient Data Care X-Chain for Decentralized Manufacturing, is shown below.


**Figure 3.** CellPoint xCellit model

## SOLUTION DESCRIPTION

The Cell and Gene Therapy Orchestration Platform X-Chain has been used as a base to develop CellPoint xCellit – which offers dedicated features required for the point-of-care manufacturing model.

The system provides an end-to-end solution to automate, streamline and secure supply chains for personalized treatments. The solution also includes an event system to inform affected parties about upcoming actions.

Due to the highly modularized implementation, the system can easily be expanded:

- External APIs can be connected
- Additional services can be added
- New members or stakeholders can be added with a simple, one-click confirmation process
- Simple validation is achieved via an optimized system for good manufacturing practice

The system is designed to cover and manage the end-to-end supply chain steps of personalized medicine, including:

- Patient enrollment
- Scheduling and tracking of apheresis and treatment appointments
- Scheduling and tracking of hospital pick-up appointments
- Tracking the position and temperature of raw materials and final products throughout the entire process
- Production planning optimization for personalized medicines
- Workflow orchestration for decentralized production processes
- Monitoring of treatment outcomes after administration
- Raw material stock management
- Fully fledged MES (manufacturing execution system) capabilities and production device integration

## SOLUTION BENEFITS

By decentralizing the aforementioned processes, it is now possible to provide the required level of trust between multiple parties to securely handle personalized treatment data. The system provides transparent, immutable and trustworthy patient data security.

One of the greatest benefits of this solution is the secure and highly customizable workflow process engine for personalized medicine supply chains, which supports the patient's treatment and recovery. During proof-of-concept implementations together with leading global pharma companies, a production cycle roundtrip time improvement of up to 25%, relative to traditional processes and tools, was observed.

### CENTRAL CONTROL OF A POINT-OF-CARE MANUFACTURING MODEL

The point-of-care system guarantees a smooth and automated orchestration of all preparation, manufacturing and QA/QC steps for cell and gene therapies produced at many different hospitals. Because of the distributed system architecture, all participating clinics are onboarded to a standard protocol, but could retain their own process variations if required. Overall control and transparency are acquired by CellPoint through their main system node operated in the cloud. Since xCellit features a fully distributed audit trail, immutably stored on a blockchain network, the solution is highly secure against tampering, attacks, and outages.

### DATA PROTECTION

xCellit offers a trendsetting system architecture (patent pending), combining the advantages of decentralized system networks and privacy-based computing capabilities. The underlying technology is Camelot Trusted Computing Appliances, powered by Intel SGX technology. Depending on the regulatory requirements for captured person-related data, it can either be stored securely in the cloud, or remain on the local clinic node. Even in the case of locally stored data, it is possible to confidentially process that private data (e.g., for automated patient eligibility checks) within a secure SGX enclave based on evaluation logic.

A more detailed explanation of the concept of Camelot Trusted Computing Appliances can be found in a joint case study of Dell EMC, Intel, Camelot ITLab and SAP HERE.

### CHAIN OF IDENTITY AND CHAIN OF CUSTODY

The xCellit platform creates and preserves a trustworthy and immutable chain of identity and chain of custody for personalized treatments. Even if certain data is only available within a local clinic instance, it is still securely interconnected with the overarching therapy record to fully retain these important data chains.

### ORCHESTRATION AND AUTOMATION WITH CONDITIONAL CHECKS AND DEPENDENCIES

The cloud based xCellit platform implements a novel workflow engine fully optimized for highly integrated and GMP validated computerized systems. The Workchain Engine, paired with a Microsoft Excel based design time tool, reduces validation efforts while realizing full flexibility – a characteristic desperately needed by the many process variations in the emerging personalized therapies domain.

## ARCHITECTURE

The Camelot Hypertrust Platform is a decentralized cloud application platform. It enables developers to securely develop applications, whether centrally operated in the cloud, with added satellites on-premise, or fully decentralized through one of the many supported blockchain protocols. The platform even supports privacy-based data processing scenarios based on Camelot Trusted Computing Appliances powered by Intel SGX technology.

xCellit (based on Hypertrust Patient Data Care X-Chain), operates on top of the Camelot Hypertrust Platform, enabling decentralized networks to support distributed manufacturing models. Features such as a therapy control tower, dashboards, and reporting can be used to fully control end-to-end therapy process, even if manufacturing is happening remotely.

xCellit's Workchain Engine is the glue between different clinics, facilities, users, and many other entities and builds the foundation for a full digital twin of a closed loop supply chain.

The following diagram is an abstracted high-level architecture of xCellit in the CellPoint point-of-care production model.

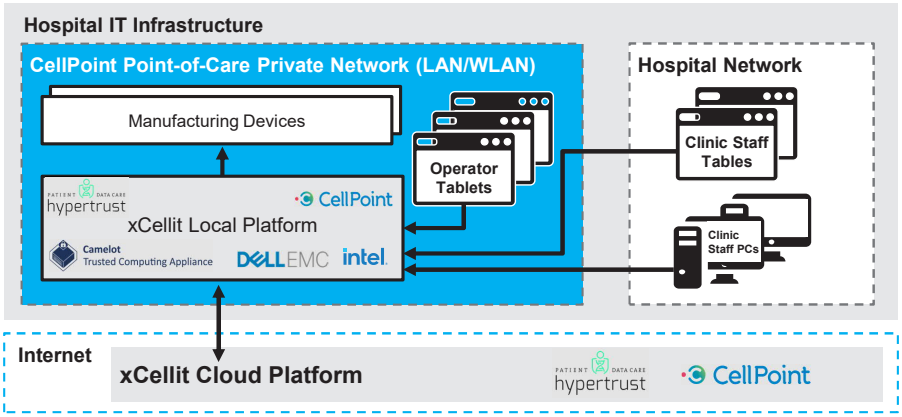



**Figure 4.** Confidential Computing at the Point of Care

## REQUIRED COMPONENTS

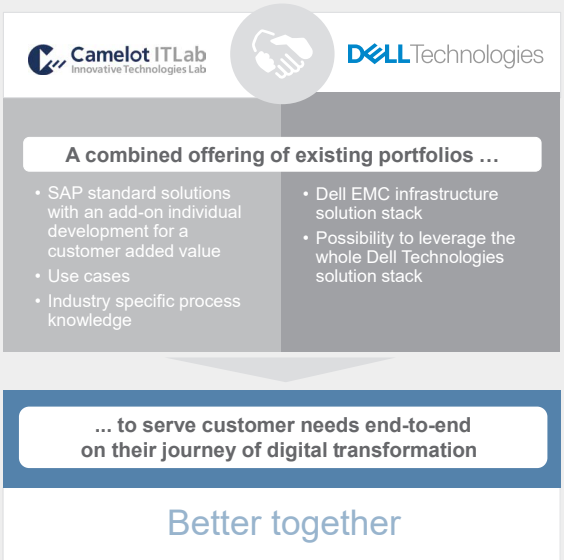
To implement the point-of-care architecture, the following components are needed:

- Cloud:
  - Camelot Hypertrust Platform Central Instance
  - xCellit Solution (Cloud)
  - ERP system, like SAP S/4HANA, SAP Business ByDesign or equivalent (for a commercialized environment)
- On-Premise:
  - Camelot Hypertrust Platform Local Instance
  - xCellit Solution (On-Premise)
  - Camelot Trusted Computing Appliance
- Dell PowerEdge MX Servers with Camelot Hypertrust Platform and Hypertrust X-Chain application

Dell's role in supporting the CellPoint use case started with consulting to set-up devices in a production environment while complying with clean room requirements. Today, in addition to the Cocoon® Platform itself, supplementary infrastructure components are needed, based on whether within the clean room or not. These components include server components, Wi-Fi switching, label printers, uninterruptible power supply (UPS) and tablets which Dell provides as a single supplier, comprised of Dell's portfolio and/or via a 3rd party.

A key solution component is the Dell PowerEdge R340XL, which provides the SGX hardware needed for the Camelot Trusted Computing Appliance. Intel SGX is essential for the above application to ensure data protection in the xCellit platform. Intel Software Guard Extensions offers hardware-based memory encryption that isolates specific application code and data in memory. This enables the application to store data securely using hardware-based controls and allocate private regions of memory, called enclaves, which are designed to be protected from processes running at higher privilege levels.

For the future, Dell will aim to extend and expand the reach of the Camelot and CellPoint solutions to help more customers. Options for installations services, special support offerings or building specific OEM Solutions are all possibilities.




### Camelot IT Lab GmbH

Camelot IT Lab is the leading SAP consultancy for digital value chain management, with more than 20 years of experience. Camelot guides clients in their digital transformations from strategy to the implementation of innovative solutions. The company's blockchain journey started in 2015, and today Camelot offers a comprehensive portfolio of blockchain products and services leveraging Camelot Hypertrust Platform and SAP Cloud Platform Blockchain Services.

### Hypertrust Patient Data Care GmbH

Founded in 2018 as a spin-off of the broader Camelot Group, this is Camelot's dedicated brand for supply chain solutions in the area of Pharma and Biotech. Especially new and innovative treatment concepts that require mindset and paradigm shifts on many levels are the focus topics of this Munich based start-up company. The core of the Hypertrust X-Chain solution is Camelot ITLab's Hypertrust Platform.

### Dell EMC

Dell EMC, a part of Dell Technologies, services its customers — including 98 percent of the Fortune 500 — with a broad, innovative infrastructure portfolio from edge to core to cloud. A strategic SAP technology and software partner for more than 20 years, Dell EMC is a leader in server and storage performance benchmarks for SAP HANA® and SAP applications.

**Jeroen Voorham** Jeroen Voorham is Project Manager for Data & IT at CellPoint. He is responsible for the development and implementation of the xCellit Platform and joined the company upon launch, in July 2020. Prior to CellPoint Jeroen was involved in MedTech company, Novuqare Pelvic Health, which he founded in 2010. Jeroen has a Master of Science degree in Aerospace Engineering.

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**Dr. Marten Neubauer** is Dell Technologies Field Director Healthcare in Germany. A former CIO for a national German healthcare provider himself and a Ph.D. for system integration into OR theaters, Marten has a breadth of experience in the healthcare and life sciences segment. Marten is driving several thought leader initiatives to support solutions in the healthcare and life sciences space with Dell Technologies infrastructure.

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**Andreas Goebel** is Managing Director at Hypertrust Patient Data Care, a CAMELOT Consulting Group spin-off, and the technology mastermind behind the Hypertrust X-Chain product family. After spending more than 15 years in R&D at SAP in Walldorf and several years in blockchain technologies and cryptocurrencies, he decided to combine this expertise in his roles at CAMELOT Consulting Group to find real business applications of blockchain technology. Today, he is passionately evangelizing the blockchain topic throughout the SAP ecosystem and among customers with a strong focus on pharma and biotech.

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## TO LEARN MORE

For more information about the technologies discussed in this paper, visit the following sites:

Hypertrust Patient Data Care X-Chain:
www.hypertrust-patient.com

Camelot Hypertrust Platform:
camelot-itlab.com/en/digital-innovation/camelot-hypertrust-network

Camelot Trusted Computing Appliances:
camelot-itlab.com/trusted-computing

Dell Technologies Solutions for SAP:
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