Cost-Benefit Analysis

of Using the Cellares™ Cell Shuttle™ Platform for Autologous CAR-T Cell Therapies

Authors

Victoria Hodgson, Michael Lemenze, Eric Edwards, John Tomtishen

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Abstract

Total manufacturing costs continue to be one of the biggest challenges currently faced by Cell Therapy (CT) developers and manufacturers. This has resulted in higher per patient costs, which negatively affects the scalability and accessibility of these highly innovative and effective therapies. To help address this challenge, Cellares has pioneered the Cell Shuttle™ - a fully closed and automated, high throughput platform for CT manufacturing. To demonstrate the advantages of this solution, Cellares has developed a cost analysis model based on multiple cell therapy processes. This analysis was used to evaluate per patient costs for the manufacturing of autologous chimeric antigen receptor (CAR)-T cell therapies at commercial scale. The analysis includes costs associated with goods, labor, operating expenses (OpEx), and capital expenses (CapEx). For a typical autologous CAR-T product, the model estimates that the Cellares Cell Shuttle will decrease the total manufacturing costs by up to 65%. This reduction in total manufacturing costs can make life-saving cell therapies manufactured using the Cell Shuttle more accessible to patients in need.

Introduction

Cell therapies have proven to be one of the most efficacious and durable treatments for certain types of hematological malignancies. With multiple U.S. Food and Drug Administration (FDA) approvals and over 1,000 clinical trials in progress across multiple therapeutic indications, it is clear that these treatments hold the potential to revolutionize the treatment paradigm for cancer and other diseases[1]. Despite these successes, high manufacturing costs and challenges with scaling production limit the industry's ability to meet patient demand. Addressing these challenges is therefore imperative to increasing patient access to lifesaving cell therapies.

Figure 1 shows the average cost breakdown for the cell therapies analyzed herein. The categories include:

1. Per patient costs - This includes the goods and labor.
2. Facility costs - This includes capital expenses (CapEx) and operating expenses (OpEx).

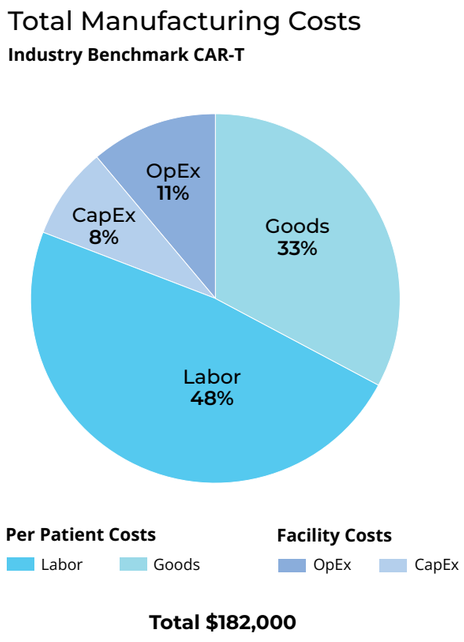

Figure 1. Costing breakdown for autologous cell therapies.

Introduction continued...

Labor, CapEx, and OpEx represent significant opportunities for reducing CT manufacturing costs. Current CT manufacturing processes require a large number of manual steps, resulting in a significant amount of operator touch time[2,3]. In compliance with cGMP requirements, two operators are required for every critical manual step, one to execute and one to verify, thus doubling the required headcount and associated labor costs. A shortage of skilled workers and high rates of operator turnover across the industry drives the need for extensive new-hire training, which further contributes to labor as a primary driver for CT manufacturing costs.

While labor is the largest cost driver, CapEx and OpEx also contribute to total CT manufacturing costs. These include significant upfront construction and equipment expenditures in addition to ongoing facility operating costs. For example, a typical facility targets the capacity to manufacture production volumes ranging from 500 to 5,000 batches per year[2]. Such a facility would require a footprint of approximately 100,000 sq. ft. or more, costing $200 million to build and qualify, with several million dollars to operate and maintain on an annual basis[4]. With market forecasts estimating the addressable CT patient population to be 2 million patients per year globally between 2025-2030[5], it's clear that current manufacturing paradigms are unable to meet patient demand, and that reducing the cost and size of facilities holds massive potential for decreasing per patient manufacturing costs and meeting increasing patient demand. To address the labor, OpEx, and CapEx challenges, Cellares has developed the Cell Shuttle for CT Manufacturing. The Cell Shuttle integrates all the technologies required for the entire manufacturing process in a flexible and high-throughput platform that delivers true walk-away, end-to-end automation. The Cell Shuttle is a closed system that maintains an internal ISO 8 controlled environment, enabling deployment in a controlled, not classified (CNC) environment. The Cell Shuttle dramatically reduces labor costs through automation by reducing hands-on manufacturing time. Additionally, the Cell Shuttle enables the manufacturing of 16 CT batches in parallel, thereby increasing manufacturing capacity by more than an order of magnitude when compared to a manual facility with a similar footprint and labor force. Since Cellares manufacturing facilities have been designed and optimized to use Cell Shuttles, the manufacturing efficiencies of these facilities are likely higher than retrofitted locations.

Results

The analysis compares the total per patient manufacturing costs for a typical 7-day CAR-T process manufactured via the Cellares Cell Shuttle vs. currently used manual manufacturing technologies. A target capacity of 20,000 patients per year was assumed for both. Results shown in Figure 2 and Table 1 indicate an overall reduction in per patient costs of 65%, from $182,000 to $64,000. The cost analysis model demonstrates benefits at a smaller manufacturing scale as well, with a 63% reduction in manufacturing costs observed at 1,000 batches per year target throughput.

Breaking down the sources of these modeled cost reductions, manufacturing, and QC goods are estimated to remain equivalent between Cell Shuttle and manual manufacturing methods, while per patient labor, CapEx and OpEx costs are reduced by more than 90%.

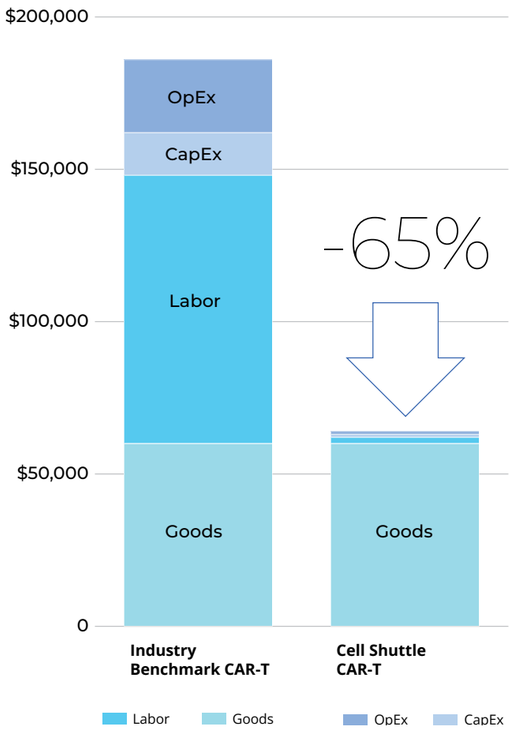

Figure 2. Total per patient manufacturing cost comparison at a 20,000 batch per year scale between a typical 7-day CAR-T process executed using the Cellares Cell Shuttle and currently used manual methods (industry benchmark CAR-T).

Table 1. Results from total per patient manufacturing cost comparison between a typical 7-day CAR-T process executed using the Cellares Cell Shuttle and currently used manual manufacturing processes (industry benchmark CAR-T) at a 20,000 batches per year target manufacturing scale.

[1] Assuming an equivalent commercial target of 20,000 patients per year.

[2] Assuming a representative CAR-T process is performed on currently available platforms.

CAR-T Manufacturing Cost Driver[1]	Industry Benchmark CAR-T[2]	Cell Shuttle CAR-T	Savings Provided by Cell Shuttle
Target Doses Per Year	20,000	20,000	n/a
Goods *(MFG, QC)*	$60,000	$60,000	n/a
Labor *(Fully Burdened MFG, QC, QA)*	$88,000	$2,000	$86,000
CapEx *(Facility and Equipment)*	$14,000	$1,000	$13,000
OpEx *(Utilities, maintenance, etc.)*	$20,000	$1,000	$19,000
Total Per Patient Cost	**$182,000**	**$64,000**	**$118,000 (-65%)**

Table 2. Key insights from total per patient manufacturing cost comparison between a typical 7-day CAR-T process executed using the Cellares Cell Shuttle and currently available methods (industry benchmark CAR-T).

[1] Assuming a representative CAR-T process is performed on currently available platforms.

Factor	Industry Benchmark CAR-T[1]	Cell Shuttle CAR-T	% Difference
Target Doses Per Year	20,000	20,000	n/a
Headcount	2,600	300	-88%
Facility Size *(sq ft)*	800,000	59,000	-93%
# of Cell Shuttles Needed	n/a	24	n/a
Annual Cell Shuttle Process Throughput	n/a	834	n/a
Total CapEx	$861 million	$174 million	-80%
Total annual OpEx	$118 million	$24 million	-80%

Table 2 summarizes additional key insights from the costing analysis at a target scale of 20,000 doses per year. Highlights include:

- 88% reduction in projected headcount
- 93% reduction in required facility size
- 80% reduction in projected CapEx
- 80% reduction in annual OpEx

These significant savings in labor, CapEx, and OpEx illustrate the achievable value attained by manufacturing on the Cell Shuttle.

Conclusions

Based on the results of the analysis, Cellares' Cell Shuttle has the potential to reduce CT manufacturing costs by 65%, at a target commercial scale of 20,000 batches manufactured per year. Importantly, these cost savings can be attained at much lower scales - 63% cost reductions are achieved at scales as low as 1,000 patient batches per year. The three main drivers of cost reductions, labor, CapEx, and OpEx, are reduced by more than 90% when manufacturing in a Cell Shuttle facility when compared to a facility using industry standard manual manufacturing methods.

As more CTs become approved for earlier lines of treatment and indications with larger patient populations, the ability for manufacturers to scale and improve operating costs will become essential for commercial viability. The results of this analysis demonstrate how Cellares' Cell Shuttle can significantly decrease per patient total manufacturing costs, decrease facility sizes and costs, and lower required headcount while enabling commercial-scale manufacturing capacity. Reducing per patient manufacturing costs for CT companies is essential to make CTs scalable and ultimately more accessible to patients.

The large capital expenditures related to starting up an in-house manufacturing facility can be avoided by entering into a manufacturing agreement with Cellares through its IDMO services business.

Methods & Assumptions

This model captures the in-house per-patient commercial manufacturing costs, excluding costs assumed to remain unchanged between the Cell Shuttle and a manual process (i.e., Leukapheresis, QC, storage and inventory, stability, shipping, etc.). Multiple CAR-T products were included in the analysis, with an assumed annual throughput target of 20,000 patients per year. The actual throughput of manual versus Cell Shuttle manufacturing methods was determined by using the facility utilization from industry benchmarks. Compared to manual methods, it is estimated that the Cell Shuttle achieves a higher actual annual throughput. The process information and associated costs have been aggregated and used in the model built by Cellares to determine the total manufacturing costs. The percentage change was then calculated as per the following:

$$\% \text{ Change} = \frac{\text{Cell Shuttle - Manual Process}}{\text{Manual Process}}$$

The goods required to manufacture a single CT batch were categorized as general consumables, genetic modification, growth medium, buffers and reagents, and QC analysis. Estimates are based on the list prices of the materials and do not include any discounts. Genetic modification cost estimates were priced at $29,000 based on available references[6].

The per patient labor was estimated based on the total direct labor touch time to manufacture a single patient batch in a GMP setting. Labor costs include manufacturing, QC, and QA operators only. The total touch time was multiplied by the target number of patients/year to generate the target labor hours needed per year. The total headcount required was estimated by dividing the total labor hours required at 20,000 patients per year by the number of working hours per operator per year. The total annual labor cost is the annual headcount required multiplied by the fully burdened labor rate. The costs were then divided by the actual number of patient products made per year to identify the per patient labor costs.

Methods & Assumptions continued...

CapEx costs were determined by assessing both the equipment and the facility costs to meet the target throughput of 20,000 patients per year. These estimates consider both the number of instruments required, as well as facility size and facility cost per square foot. Total equipment costs were based on the publicly available instrument list price. Facility costs were modeled by estimating the facility size required multiplied by the estimated facility cost per square foot based on industry and internal data. CapEx costs were depreciated over a period of 10 years.

Operating expenses were determined by estimating the costs associated with operating controlled, not classified, and cleanroom space, as well as ancillary support areas. The standard utilities, annual property taxes, and rent were modeled on a per-square-foot basis using industry data, and the estimated facility size derived from the CapEx estimates. The annual HVAC costs were modeled using industry cleanroom data and adjusted for the estimated split between the proportion of facilities dedicated to ancillary support areas and cleanrooms. The values described above are scaled based on the facility space needed to satisfy the target manufacturing throughput of 20,000 patients per year.

To generate the comparison data, the same processes and throughputs were translated onto the Cell Shuttle, and the theoretical per patient and facility running costs were modeled. Costs towards reagents such as buffers, viral vectors, and other materials use the same values across the manual and automated models, and the price for Cellares consumables and CapEx contributions are included. Manufacturing hours and operator headcount are calculated using the methodology above. The estimates for equipment and number of Cell Shuttles are based on what would be needed for a 7-day process on a typical Cell Shuttle performing 16 processes in parallel. Facility running costs were evaluated using established benchmarks.

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345 Allerton Ave
South San Francisco, 94080