Implementation of ScaleReady Products to Streamline and Close Critical Stages of the AgonOx Cell Therapy Manufacturing Process

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Introduction

AgonOx and their collaborators the Providence Portland Cancer Institute have projects that focus on providing personalized T-Cell mediated therapies to patients of varying stages of cancer. Cell therapies are at the forefront of medical research and innovation and have the immense potential to transform the treatment landscape of various diseases and malignancies. As research in this field advances, optimizing and closing cell therapy manufacturing processes play a pivotal role in ensuring these life-changing treatments are safe and effective.

To better optimize their manufacturing process for a current clinical trial and IND amendment, AgonOx and Providence began to look for products to close and streamline key portions of the established manufacturing process for a shared project. It was imperative to find products that would maintain established levels of cell recovery, viability, and efficacy.

AgonOx and Providence had started their clinical trial when discussions with the ScaleReady team began. Critical stages of the cell therapy manufacturing process were still being completed using open and manual processing steps. The team wanted automation to address the following concerns:

1. **Risk of contamination:** open systems are susceptible to contamination, which in the downstream stages of a cell therapy manufacturing process can lead to production delays, increased costs, and rejection of unsafe products.
2. **Consistency and reproducibility:** Variability in the environment and operator practices can lead to inconsistent yields. This variability can hinder the chances of demonstrating product safety and efficacy in a clinical trial.
3. **Time of manufacturing process:** Long processing times increases the cost of labor. The desire was to have automation decrease the amount of time needed to complete these processing steps.
4. **Comparability with historical data:** Cell recovery, health, and outcomes needed to be comparable to the historical data generated from this team.

Given these concerns, ScaleReady outlined a process using key products to close and streamline critical downstream processing steps.

Methods

During the initial discussion with the AgonOx team, ScaleReady gained an understanding of their current manufacturing process and the need for urgency to comply with established timelines. Since ScaleReady has a wide range of customers at various stages of development, the team was able to quickly define the critical stages where the process needed to be closed to progress through the planned regulatory filings. The proposed process improvements were presented and compared to the established SOPs of the manufacturing team. It was important to ensure the final cell product function would be maintained so previously collected data could still be used for the amendment.

The timeline from initial discussion to completion of engineering runs as follows:

The ScaleReady team recommended the use of the G-Rex500M-TF unit to replace the G-Rex 500M unit that had previously been validated for the process. The G-Rex500M-TF unit allows for sterile welding to containers, which closes the harvest process while maintaining the same cell yields and quality that had been previously established. Because of the linear scalability and consistency between open and closed G-Rex systems, the team was able to seamlessly replace the 500M open system with the 500M-TF closed system with no change to the initial validation of G-Rex as the culture vessel used in this process. After the culture duration completes, the ScaleReady team suggested the use of the GatheRex Liquid Handling & Cell Harvest Pump to reduce the volume of each culture vessel and then harvest the cell suspension from the bottom of the G-Rex unit into a transfer pack. For cell washing, the ScaleReady team recommended to then use the Lovo Cell Processing System to effectively wash and concentrate the cell product into fresh buffer to prepare for eventual freeze. Lovo can be used at the low end of the cell yield scale as well as the high end of the expected range. The proposed process from ScaleReady provided a solution to close critical stages of AgonOx's cell therapy manufacturing process, as well as shortened manufacturing time, decreased raw material usage, and provided for automated consistency for their process.

Results

Three engineering runs were successfully completed to evaluate the proposed manufacturing process. The yields from the G-Rex500M-TF units were comparable to historical data. Average processing times were cut down by approximately 40%. The viable cell recovery at the end of the process were comparable to historical data with a lower standard deviation. The graph on the right shows the viable cell recovery post processing. Table 1 below shows the average processing time comparison between the manual and automated process.

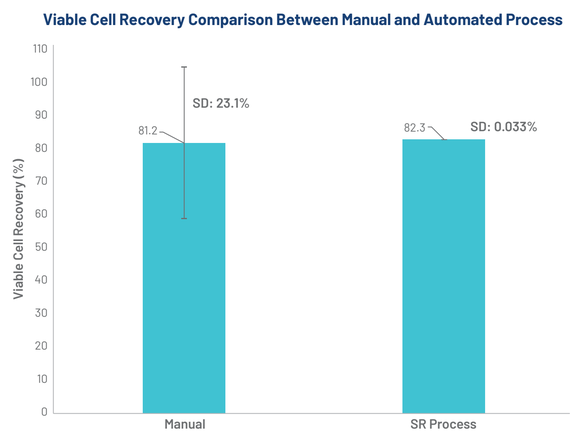

Table 1: Average Processing Time Comparison Between the Manual and Automated Process

	Average Processing Time	Total Number of Runs
Manual	5 hours	23
SR Process	3 hours	3

Testing completed within the 2-month timeline and culminated in the inclusion of the G-Rex 500 M-TF, GatheRex, and Lovo Cell Processing system into a current ACT clinical trial and future IND amendment.

Conclusions

ScaleReady products can be used to close and automate cell therapy manufacturing stages without impacting cell yield, health, and functionality. Additionally, these products can assist in decreasing processing times.

- **Closed System Processing: ScaleReady products** mitigate contamination risks by allowing for sterile tube welds to the system.
- **Decreasing Processing Times: ScaleReady products** can be integrated to decrease operator intervention and processing times.
- **Automation to Drive Consistency:** By standardizing and automating processes, ScaleReady's products can enhance the consistency and reproducibility of cell therapy production.
- **Maintaining Cell Health, Yields, and Functionality:** ScaleReady products are designed to be flexible and customizable to meet the specific needs of different cell therapy manufacturing processes. This adaptability allows for the integration of these products while maintaining cell outcomes established by previous testing.

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ScaleReady is a Joint Venture formed by Bio-Techne, Fresenius Kabi, and Wilson Wolf. Combining selected offerings from the three partners, the ScaleReady manufacturing platform combines tools and technologies for cell culture, cell activation and expansion, gene editing, and cell processing.

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