

IMPLEMENTING CONNECTED PROCESSES AT-SCALE – CHALLENGES AND OPPORTUNITIES FOR STREAMLINING OPERATIONS

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Key Words: Media Concentrates, Multi-column Chromatography, Single-Use, Connected, Scale-Up

In response to increased demands placed on biopharmaceutical manufacturers to diversify portfolios and to reduce costs, bioprocesses are being intensified to allow for significant protein production in $\leq 2,000$ L single-use bioreactors. Many biopharmaceutical manufacturers are maturing continuous bioprocessing platforms to meet these demands. Hardware, which was once thought to be novel and high-risk for failure, is now being proven as robust at-scale. When coupled with single-use technology, these processes enable biomanufacturing facilities to be built faster at a lower cost, with more flexibility for reconfiguration and support of regional manufacturing. Many challenges remain to achieving this final vision including liquid management for large-scale perfusion operations, overcoming product sieving decay often encountered in filtration-based cell retention devices, and bioburden control for long duration operations.

In a collaborative case study, Merck & Co., Inc. and Just Biotherapeutics will demonstrate a strategy leveraging fully single-use equipment and connected operations for an extended duration at manufacturing-scale (500L). This presentation will highlight bioreactor performance with the deployment of media concentrate technology to ease the logistical, staffing and space constraints of a traditional perfusion process, as well as implementation of large-scale microfiltration membranes for cell retention with consistently high protein transmission. In addition, data will be presented not only on the performance of a linked continuous multi-column protein A chromatography capture step, but also bioburden monitoring from multiple points in the process. Advancements implemented during this campaign as well as valuable lessons learned will open the door to further expanding the continuous boundary of connected operations and continuous bioprocessing.