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Scale-up and scale-down challenges for a high density long-term perfusion suspension cell culture in large-scale single use bioreactors

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As part of efforts to develop a continuous processing platform for biologics manufacturing using single use bioreactors, we have been focusing on development of several initial unit operations: high density perfusion suspension cell cultures and early product capture steps, in order to realize its potentials of being flexible, improving product quality and lowering costs. These initial unit operations require large volumes and represent the most important part of this processing platform. By integrating these steps into a continuous operation, we can deliver the largest benefits of this processing platform. In this presentation, we will discuss our efforts towards continuous biologics manufacturing using a case study focusing on direct scale-up of an ATF (Alternating Tangential Flow) based high density perfusion cell culture, from 2L scale coupled with ATF2 to large single use bioreactors coupled with ATF6 or ATF10. Appropriate considerations of agitation and aeration rates, ATF operation parameters as well as bioreactor processing conditions resulted in successful scale-up of more than 100 folds. This high density long-term perfusion suspension cell culture was successfully implemented in large scale single use bioreactors. Results of large-scale manufacturing batches indicate highly consistent process performance, productivity and quality of directly captured products. Furthermore, a representative scale-down model based on ATF2 was established for manufacturing support and further process optimization.