PROCESS ECONOMICS EVALUATION OF ADENO-ASSOCIATED VIRAL VECTOR (AAV) MANUFACTURING

Annabel Lyle, Department of Biochemical Engineering, UCL, UK and AstraZeneca, Cambridge, UK
annabel.lyle.16@ucl.ac.uk
Christos Stamatis, Department of Biochemical Engineering, UCL, UK
Martyn Hulley, Purification Process Sciences, BioPharmaceuticals Development, R&D, AstraZeneca, UK
Thomas Linke, Purification Process Sciences, BioPharmaceuticals Development, R&D, AstraZeneca, US
Albert Schmelzer, Cell Culture & Fermentation Sciences, BioPharmaceuticals Development, R&D, AstraZeneca,US
Richard Turner, Purification Process Sciences, BioPharmaceuticals Development, R&D, AstraZeneca, UK
Suzanne Farid, Department of Biochemical Engineering, UCL, UK

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With two products currently approved for gene therapy purposes, adeno-associated virus (AAV) manufacturing has seen consistent pressure to develop scalable strategies, particularly during cell culture and purification. Traditionally, cell culture in adherent mode and gradient density-based polishing steps have been adopted for AAV processing. However, these technologies rely on scale-out strategies to increase capacity in a commercial environment, thereby incurring large costs and facility footprints. This presentation presents insights from an advanced economics analysis using a decisional tool developed at UCL to identify the most cost-effective route for large-scale manufacture of AAV. A cost of goods (COG) comparison will be presented between adherent and suspension cell culture, as well as anion-exchange chromatography versus batch ultracentrifugation at the base case. This provides benchmark COG values, the savings that can be achieved moving to more scalable technologies and the contributions of materials, labour, QC and facility-related costs. A stochastic cost comparison is used to reveal the impact of key input uncertainties (e.g. productivities) on the robustness of each strategy and the likelihood of achieving target COG values. Next, the case study looks at a broad range of USP (e.g. multi-layer cell factories, fixed-bed reactor, single-use stirred tank bioreactor) and DSP (e.g. packed-bed chromatography, batch and continuous ultracentrifugation) technology options and uses an optimisation algorithm to identify the optimal flowsheet for AAV manufacture in terms of both cost-effectiveness and meeting purity targets. This analysis highlights how the optimal flowsheet will change depending on the purity target that needs to be met, with specific focus upon HCPs, DNA and empty capsids Finally, the presentation will highlight how the optimal solutions change for different combinations of demand, batch size and AEX yield, highlighting the trade-off between achieving high yields and purities, whilst opting for scalable technologies. These insights help make better decisions early on in development to facilitate successful commercialisation.