SCALING UP AND INDUSTRIALIZATION THE PRODUCTION AND PURIFICATION OF VIRAL VECTORS FOR THERAPEUTIC USE: CHALLENGES AND PROGRESS

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Key Words: Virus production, scale up, adherent cell culture, bioreactor, manufacturing.

With several recent FDA approvals and a strong drug pipeline, gene therapy is coming of age. With this comes the requirement to ensure that there are robust manufacturing processes in place in order to scale with demand and to make these therapies readily accessible to those who need them. However, current manufacturing processes for gene therapies have often been developed with limited scalability in mind and large shifts in technology have to take place to enable industrialization. This also has to be done while keeping costs in mind. Here, we will present a case study which illustrates the challenges and solutions to scale both up and downstream process steps required to manufacture adenovirus. After implementation of a bioreactor, the bioreactor scale increased 125 fold, from 0.53m^2 to 66 m^2. With the implementation of several scalable unit operations on the downstream, this took 1 day as opposed to 3 – 4 days required for the entire optimized process generating purified viral vector for the successfully completion of a global in vivo toxicology study. Altogether, the practicalities around manufacturing virus to industrial scale.

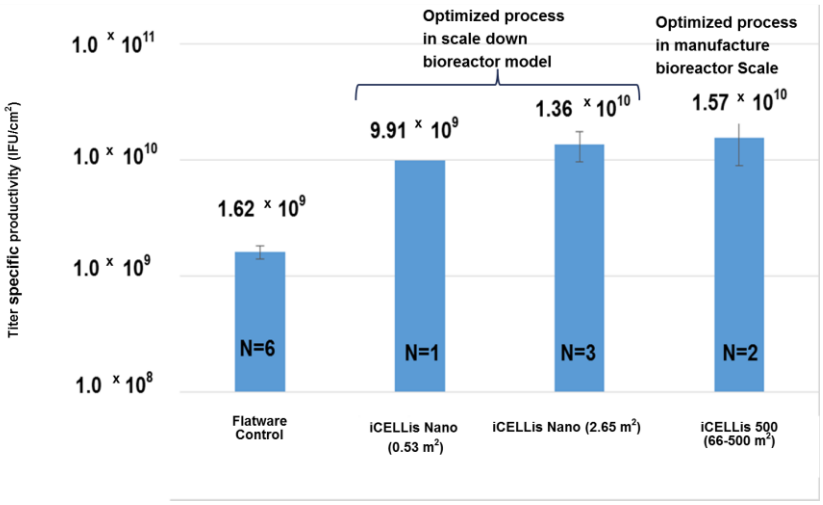

Figure 1 – Linear titer scalability: Process development from flatware to Manufacturing Scale