American Society of Gene & Cell Therapy
Poster Presentation
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Development and Scalability of Transfection-Based Production and Purification of Novel Clade F Adeno-Associated Viruses Isolated from Human Hematopoietic Stem Cells (AAVHSCs)

Mercaldi M, Stanvick M, Gilmore D, Fieger M, Zhou S, Junaid Z, Burnham B, Gagnon J, McGivney J, Adamson Small L, Krantz D, Smith E, McGrath D, Yin J and Kelly T

Homology Medicines, Inc.

Homology Medicines is a clinical-stage genetic medicines company developing gene therapy and gene editing adeno-associated viral (AAV) therapeutics for the treatment of rare diseases. Using a proprietary dual platform based on the production of novel Clade F capsids derived from hematopoietic stem cells (AAVHSCs), we have developed a GMP manufacturing process that delivers high-quality gene therapy and gene editing product candidates. The platform has been linearly scaled up to meet current and future clinical and commercial supply demands. The AAV production utilizes suspension HEK293 cells in a serum-free, transfection-based bioreactor process. This process has been successfully scaled up from 2L to 2000L and has been executed over 400 times across more than 300 different constructs to produce consistent, high-quality product candidates. To enhance the platform process productivity, bioreactor optimization increased titer 1.5-3.5 times and our platform chromatography-based depletion of empty capsids was able to consistently deliver final product with > 90% nucleic acid containing capsids. To support clinical expansion, we have built a 25,000 square foot internal manufacturing facility, are currently operating three 500L bioreactors, and have successfully produced GMP material at the 500L scale for multiple pipeline candidates. Additionally, a 2,000L bioreactor scale is now confirmed. In summary, Homology has developed a scalable production and purification platform that has been utilized for external and internal manufacturing of AAVHSC vectors to support multiple product development and pipeline programs for both gene therapy and gene editing.