A Versatile Suspension-Based Platform for the Manufacturing of AAVs

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Abstract

Recombinant adeno-associated virus (rAAV) is the most widely used viral vectors for gene therapy. However, rAAV manufacturing remains a challenge as the demand for high quality AAV vectors is far greater than the available capacity, hence manufacturers tend to scale up the process which impacts the costs as well as the quality of the AAV produced. Additionally, manufacturing processes vary from one AAV serotype to another and show dependency on vector length and molecular configuration, increasing the time for process development, scale-up and therefore time to clinic.

We have developed a robust modular suspension platform process that minimizes batch variability and builds quality into the product by design. By using high-throughput scale-down models this process decreases complexity, increases the flexibility for scale-up, and thereby decreases the cost of goods (COGs).

Our platform is an end-to-end process solution, composed of multiple unit operations that are differentiated from the industry. This process platform was optimized for vector yield at best possible quality, to align with the stringent, continuously evolving regulatory requirements, while allowing for flexibility and adaptability to specific customer program needs.

We present here yield and product-related impurity data for the most frequently clinically applied AAV serotypes at different bioreactors scales using our proprietary split two plasmid platform. We are continuously expanding our database to show universal applicability of our modular platform over various AAV serotypes.

The modularity of our platform and our continuous efforts in understanding process dependencies requiring specific solutions offers the necessary flexibility to quickly adapt the manufacturing process to specific product needs which streamlines overall process development and scale-up and reduces overall development costs. We continue to innovate AAV gene therapy with a major focus on CMC to support the field in making AAV gene therapy accessible to patients suffering from more common diseases with higher risk benefit profiles and accordingly high regulatory bars. Our commitment is to develop the safest possible products for our clients and their patients.

A differentiated end-end platform, backed by powerful analytics to drive high product yield, potency and quality

Cassette/capsid optimization, & lead selection

Split 2-Plasmid Transfection

Bioreactor cultivation

Cell Lysis & Clarification

Affinity Column Chromatography

Viral clearance

AEX F/T mode

Optional Full / Empty Separation

Viral clearance, TFF & Formulation

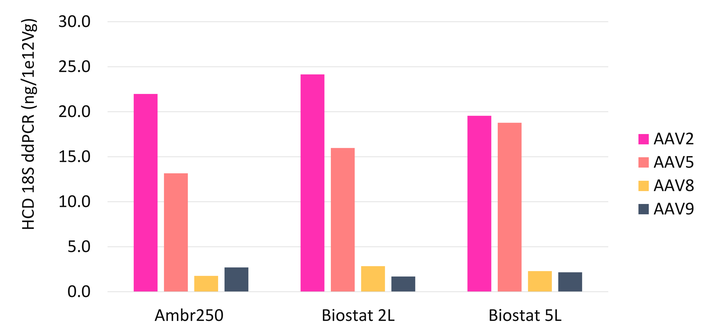
Split 2-plasmid transfection system drives **yield and quality improvements**

Chromatography steps support a **scalable downstream process**

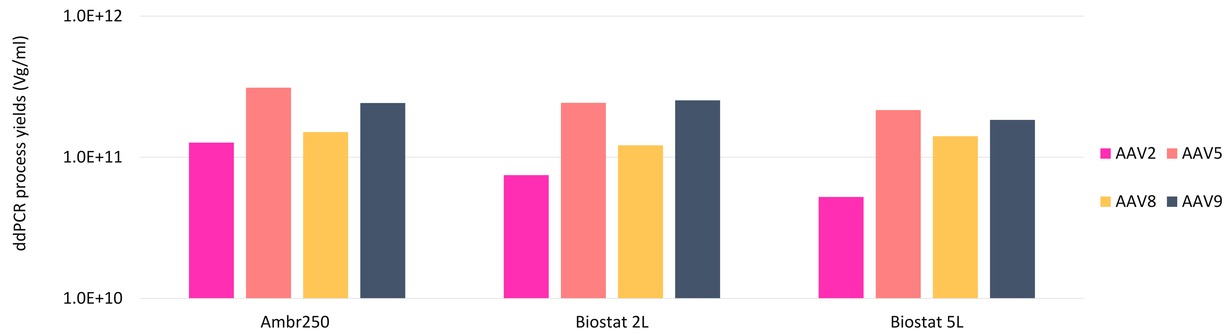
Comprehensive and proprietary analytical methods **limit developmental risks** at every stage of the process

Differentiated versus industry standard offering

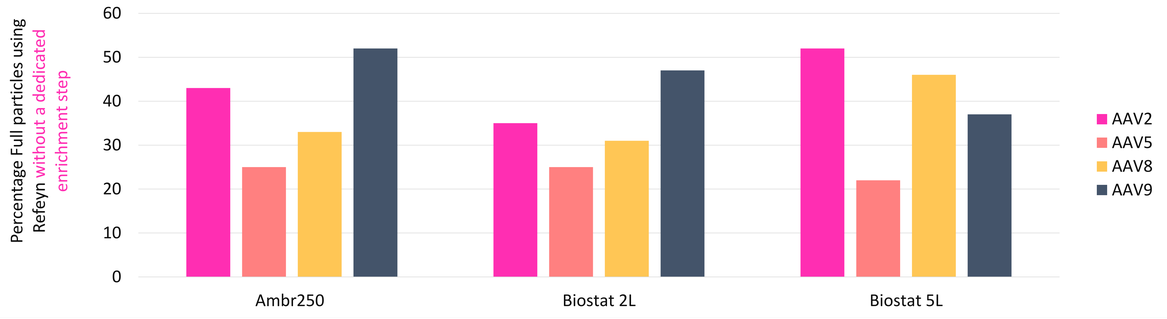
Comparable quality at different scales



Comparable yields at different scales



Comparable quality at different scales



Summary

To meet our clients' needs across a product life cycle in a fast-developing field, we have developed a strong and scalable platform that is intended to produce high yields of multiple serotypes while keeping the best possible product quality in mind. To serve our clients with their unique product development needs, our manufacturing technology is supported by an industry-leading analytical platform offering, our in-depth knowledge of AAV biology, gene therapy product development and CMC regulatory expertise. We continuously improve our modular platform through innovation and optimization in several areas, including formulation, analytical and process development, as well as starting materials (plasmid evolution and cell engineering), allowing our clients to easily integrate and take advantage of next-generation advancements. Depending on a client's product demands, our platform can be customized to diligently balance yield and quality, adjust to varying risk/benefit profiles of a certain indication, or make applicable to a particular route of administration .

Please refer to Poster #561 for additional details regarding the vast array of AAV serotypes that are compatible with our platform.

See Poster #522 for additional details regarding our platform scalability up to a 200L scale.

Aim higher

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