Novel AAV Drug Product Formulation Achieving Long-Term Liquid State Stability (2-8°C) and High Titer Preparations (>E15vg/mL)

Kelly Walsh, Tyler Peters, Lori Karpes, Michael Mercaldi, Tim Kelly

Oxford Biomedica Solutions, Bedford, MA

ABSTRACT

Oxford Biomedica Solutions has a proprietary plug-and-play Process and Manufacturing Platform to develop and manufacture AAV gene therapies. As part of our proven ability to create commercial-ready programs, we have a strong focus and understanding on Drug Product development. This includes a comprehensive formulation development capability to enable long term storage and shipping at liquid storage temperatures (2-8°C), robustness to multiple freeze-thaw cycles, ability to stabilize very high titer presentations, all leading to improved ease for clinical use.

AAV products have a long-held reputation as both difficult to produce and store, which presents a significant challenge for distribution and administration. To address this, we have developed a novel drug product development system and proven platform formulation that can successfully deliver long term liquid phase stability, which has now been established out to 12 months.

With our proprietary platform formulation, stability was achieved at concentrations greater than 1E14 vg/mL for at least 1 year at 2-8°C or -80°C and 3 months at 25°C.

Furthermore, our proprietary platform formulation has been demonstrated to be stable at extremely high concentrations in excess of 1E15vg/mL, also in the liquid state at 2-8°C. Our platform has also demonstrated compatibility across multiple serotypes, eliminating the need for a serotype-specific formulation.

This data highlights the value that an early and thorough focus on Drug Product sciences can bring to an AAV product by providing long shelf-life, reduced administration volumes, 2-8°C supply chains, and clinical and commercial ready products. These Drug Product innovations will ultimately allow for a much simpler commercial supply chain to support high volume and globalization of Gene Therapy products.

CONTACT

Partner with us:
Visit www.oxbsolutions.com to learn more or scan the QR code.

INTRODUCTION

Drug Product Understanding is Critical to the Development of Stable AAVs

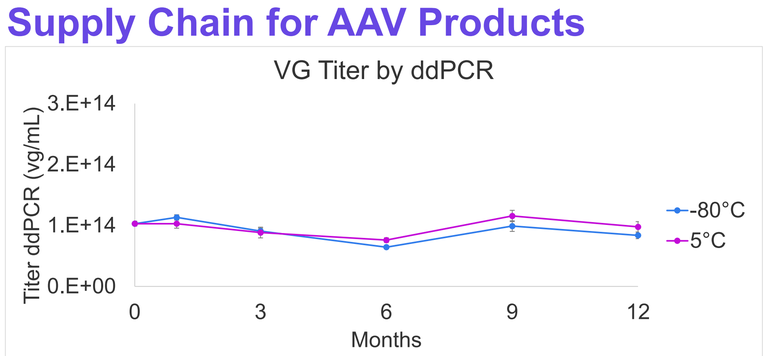
Active Vector
Buffer (pH)
Excipients
Surfactant
Primary Container

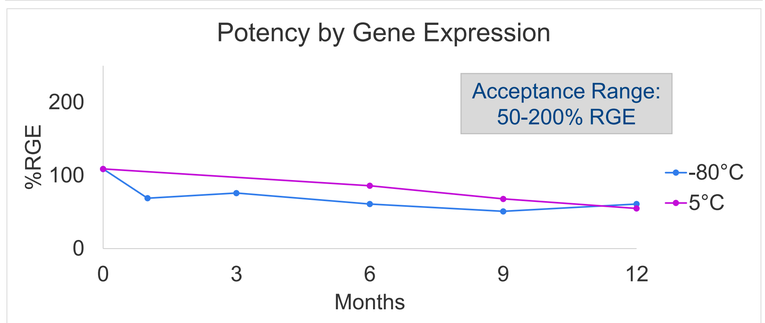
Stable Drug Products Enable Long Shelf Life

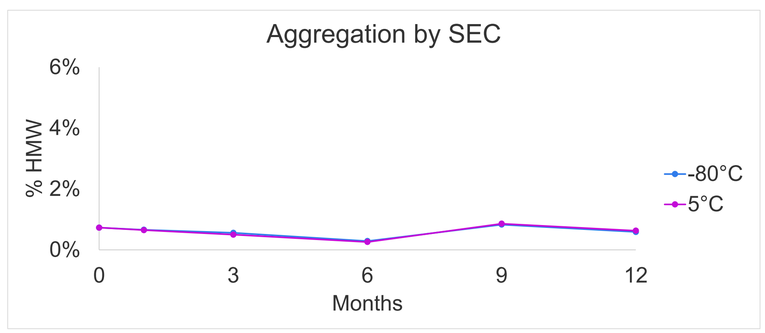
Implementation of drug product understanding early in a product's lifecycle is crucial to developing a safe and effective therapy. Early formulation development and thorough understanding of degradation pathways allows for the drug product to have a long shelf life. Further, drug product understanding can influence other parts of the organization and development process.

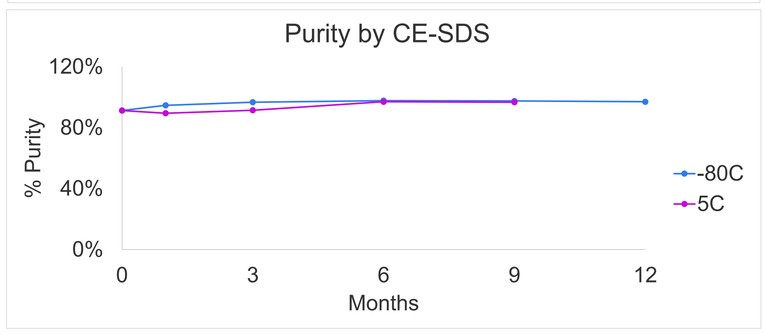
RESULTS

Novel Formulation Offers Refrigerated Supply Chain for AAV Products



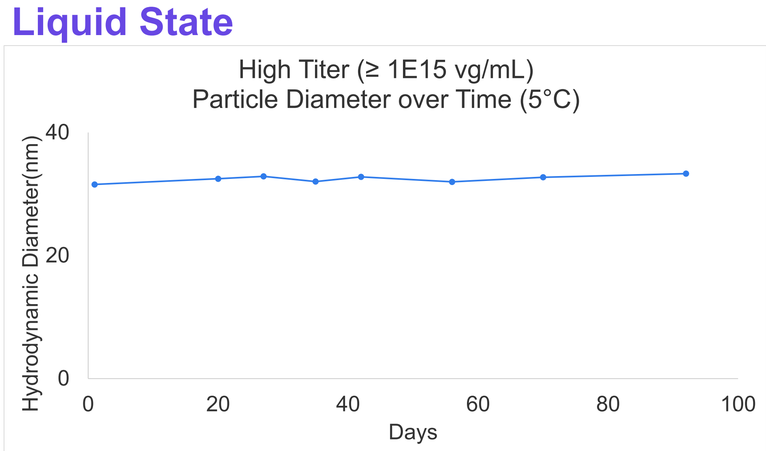


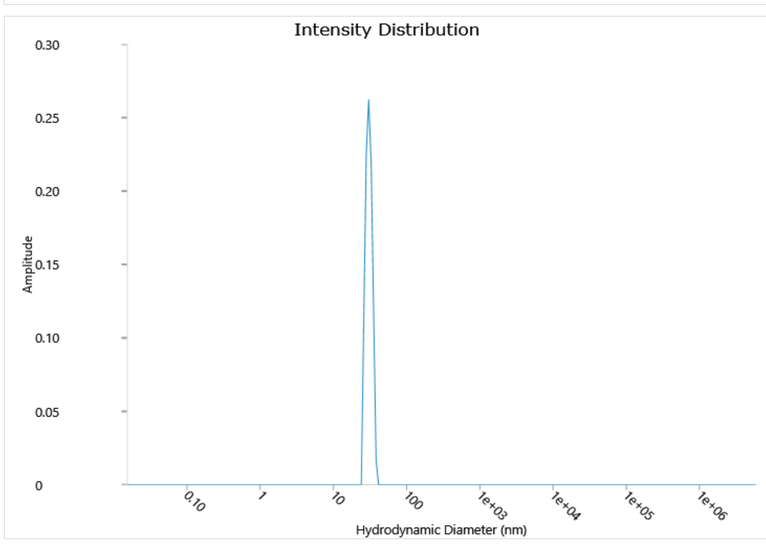




Stability data demonstrates 12 months of stability at -80°C and 5°C. Comparable stability profiles at -80°C and 5°C can enable a refrigerated supply chain for AAV products, eliminating the high costs associated with a frozen supply chain and easing clinical storage demands.

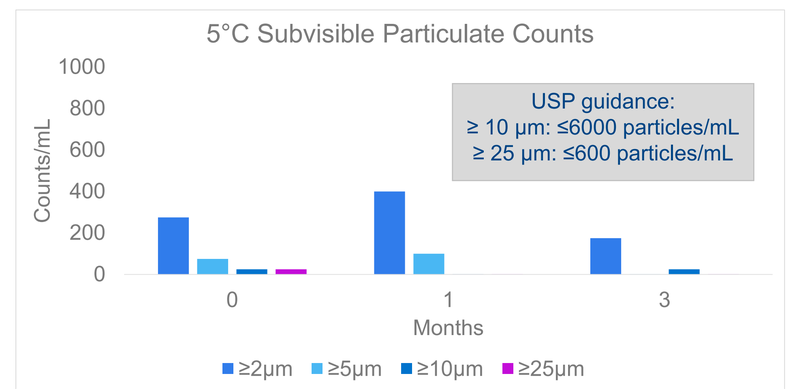
Very High Titer Preparation Stabilized in Liquid State





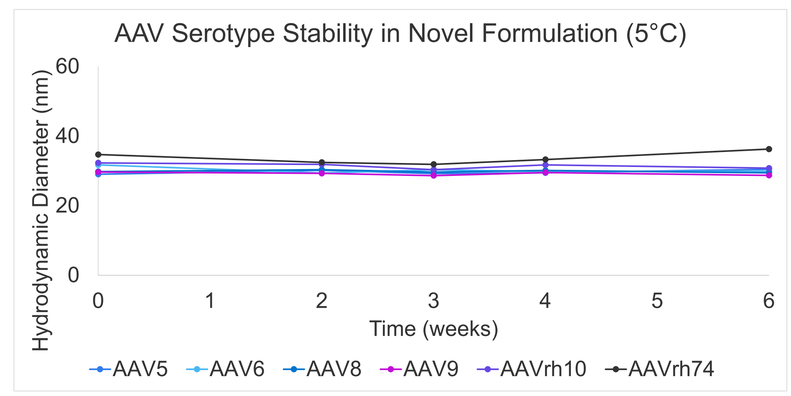
AAV with titer exceeding 1E15 vg/mL demonstrated early stability at refrigerated conditions, evaluating particle diameter by dynamic light scattering (DLS). A sample DLS image shows a single distribution of particle diameters centered at 30 nm, indicating that the sample is largely comprised of monomeric species. Monitoring the particle diameter over time shows that the high titer preparation maintains a monomer-based size distribution demonstrating high titer stability (>1E15 vg/mL) out to 90 days at refrigerated storage conditions.

Novel Formulation Prevents Sub-Visible Particle Formation



Implementation of sub-visible particle monitoring on stability has demonstrated that OXB Solutions' novel formulation protects against sub-visible particle formation over time. Typical sources of sub-visible particles include product aggregation.

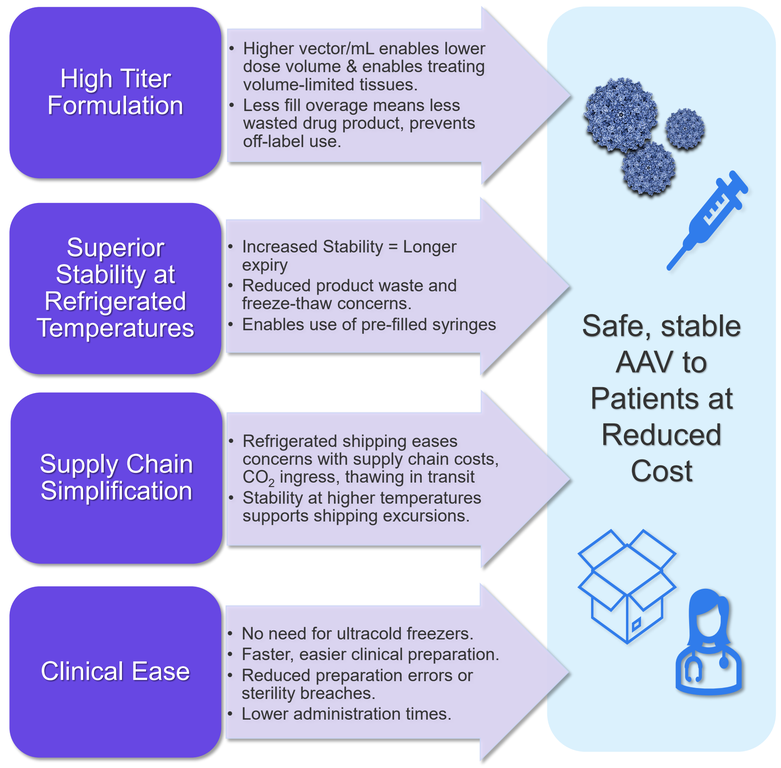
Proof of Concept Stability of Multiple Serotypes in Novel Formulation



Various AAV serotypes were purified through affinity chromatography and evaluated for stability in OXB Solutions' novel formulation at 5°C. Stability was monitored using ddPCR, capsid-specific ELISA, and aggregation by SEC (data not shown). Dynamic light scattering (DLS) was used to track the hydrodynamic diameter of the particles in solution. All serotypes evaluated maintained monomeric distributions (~30 nm) over 6 weeks at 5°C and 25°C storage.

High Titer Liquid Formulations Offer Patient Convenience and Reduced Cost

A deep and thorough understanding of drug product sciences in the AAV space can bring a wide range of benefits to the patient's experience. OXB Solutions' approach to drug product development examines how the combination of high titer formulation, refrigerated supply chain, and an optimized product presentation can improve the patient's experience to deliver the best possible AAV therapy possible.



CONCLUSIONS

- OXB Solutions has a novel formulation that can support refrigerated supply chain out to 12 months.
- Novel formulation protects from aggregation and other pathways of degradation.
- OXB Solutions' novel formulation is applicable to many serotypes, including AAV5, AAV6, AAV8, AAV9, AAVrh10, and AAVrh74. Accelerated stability confirms early compatibility. Additional serotypes are also currently under evaluation.
- An early investment in drug product development offers different levers to enable the safest patient experience.

Presented at ESGCT, October 2022, Edinburgh, Scotland