AAV ANALYTICAL

CHARACTERIZATION WORKSHOP

HOSTED BY

Alliance for Regenerative Medicine

IN PARTNERSHIP WITH

usp™

DAY 1 · Wednesday, March 8, 2023

7:30 – 8:30 AM

Registration & Breakfast

8:30 – 8:50 AM

Opening Remarks

Josephine Lembong, Manager, Science and Industry Affairs, Alliance for Regenerative Medicine (ARM)

Diane McCarthy, Senior Director, Biologics, US Pharmacopeia (USP)

8:50 – 9:30 AM

How GC Titer, Full-Empty Profile and Potency Correlate and What We Know about Clinical Relevance

Khandan Baradaran, Vice President, Regulatory CMC, Ultragenyx

- What are the methods for characterization of full and empty capsids?
- How do GC titer, capsid profile, and potency correlate?
- Which attributes are clinically relevant?

9:30 – 10:00 AM

USP Roadmap for AAV: Current Activities, Collaboration, and Future Directions

Jerome Jacques, Principal Scientist, USP

- Review of USP activities on reference standards for AAV gene therapy
- NIIMBL-NIST-USP collaboration study on analytical methods for Full-to-Empty particle
- Discussion of future developments of reference standards

10:00 – 10:30 AM

Removal of Empty AAV Capsids to Undetectable Levels Using Orthogonal Purification Steps – Product Quality and Process Robustness Considerations

Rahul Sheth, Senior Scientist 2, Purification Process Development, BioMarin Pharmaceutical

- Higher dose AAV therapies and evolving regulatory expectations necessitates more scrutiny of AAV product quality
- Empty capsids are heterogenous and may carry other impurities. They should be reduced to lowest possible levels
- Combination of Anion Exchange Chromatography and Zonal Ultra Centrifugation provides a robust purification scheme for removal of empty capsids to undetectable levels

DAY 1 · Wednesday, March 8, 2023

10:30 – 11:00 AM

Characterization of Defective - Interfering Particles through Next-Generation Sequencing

Lauriel Earley, Senior Scientist, Shape Therapeutics

- Description of Defective - Interfering (DI) particles and their potential impact on gene therapy outcomes
- Overview of NGS platforms for DI characterization
- Published and representative cases of DI Characterization

11:00 – 11:15 AM

Morning Break

11:15 – 11:45 AM

Evaluating PTMs in Relation to AAV Capsid Integrity

Adriana Kita, Associate Director, Analytical Development, Ultragenyx

11:45 AM – 12:30 PM

Panel Discussion

Moderator: *Khandan Baradaran*

Panelists: *Andrew Byrnes (U.S. FDA), Jerome Jacques, Rahul Sheth, Lauriel Earley, Adriana Kita*

12:30 – 1:15 PM

Lunch Break

1:15 – 1:45 PM

Setting Up for Success: Meeting Regulatory Expectations for Potency Assays

Christopher Miyake, Sr. Director, Regulatory Affairs CMC, Sarepta Therapeutics

- Importance of addressing potency assay development early
- Potency assay expectations through the stages of development
- Agency guidance and thoughts on potency assays for ATMPs

1:45 – 2:15 PM

Development of a Functional Potency Assay for the Characterization of a Novel Krabbe Gene Therapy

Erandi De Silva, Co-founder & Senior Vice President, Product Development, Forge Biologics

- Overview of potency assay requirements
- Potency assay development and qualification
- Considerations for functional potency assessment

DAY 1 · Wednesday, March 8, 2023

2:15 – 2:45 PM

Multi-Attribute Potency Assay for AAV Gene Therapy Drug Product

Connie Tsai, Associate Director, Analytical Development Bioassay, Novartis Gene Therapies

- Approaches to potency assay development: Common fit-for purpose matrix approach and our approach
- Platform technology for AAV relative potency, infectivity, and characterization

2:45 – 3:15 PM

Success Story of Luxturna Potency Assay Development and Validation

Ravindra Kumar, Director, Bioassay Lead, Analytical Sciences and Quality Control, Spark Therapeutics

- Approval timeline (phase I to BLA)
- Importance of potency assay to support MoA
- Potency assay development/validation and implementation strategy/FDA feedback
- Life-cycle management of potency assay

3:15 – 3:30 PM

Afternoon Break

3:30 – 4:15 PM

Panel Discussion

Moderator: *Josephine Lembong*

Panelists: *Denise Gavin (U.S. FDA), Christopher Miyake, Erandi De Silva, Connie Tsai, Ravindra Kumar*

4:15 – 4:30 PM

Concluding Remarks

Josephine Lembong, Manager, Science & Industry Affairs, ARM

DAY 2 · Thursday, March 9, 2023

7:30 – 8:30 AM

Registration & Breakfast

8:30 – 8:40 AM

Opening Remarks

Josephine Lembong, Manager, Science & Industry Affairs, ARM

8:40 – 9:10 AM

Manufacturing Yields and Impact to Patient Access

Pierre Caloz, Chief Operating Officer, uniQure

- Patient access criteria: the costs
- Cost structure in Biotech: the role of R&D costs and manufacturing yield
- Platform approach to improve speed, reduce costs and optimize quality
- The uniQure example of platform for development and manufacturing
- Other challenges for patient access

9:10 – 9:40 AM

Quality of AAV Vectors: Impact on Induction and Detection of Immune Responses

Roberto Calcedo, Vice President, Preclinical and Immunology, Affinia Therapeutics

- Overview of preexisting and induced immune responses to AAV vectors (capsid and transgene)
- Effect of empty AAV particles on induction of humoral and cellular immune responses
- Effect of empty of AAV particles on detection of antibodies to AAV

9:40 – 10:10 AM

The Current and Future State of Choosing qPCR vs ddPCR in AAV Analytics

Matthew Hewitt, Vice President, Technical Officer CGT & Biologics, Charles River Laboratories

- qPCR and ddPCR method overview
- Method application in AAV analytics
- Considerations when qualifying and validating methods
- Future implications on program advancement to clinical and commercial

DAY 2 · Thursday, March 9, 2023

10:10 – 10:40 AM

Product Comparability and the Transition from qPCR to ddPCR for Characterization of a Novel Krabbe Gene Therapy

Adam Davis, Vice President, Analytical Development, Forge Biologics

- Overview of ddPCR methods
- ddPCR assay qualification
- Comparability when transitioning from a qPCR-based quantification to ddPCR
- Special considerations for ddPCR use for viral vector quantification

10:40 – 11:00 AM

Morning Break

11:00 – 11:30 AM

Moving from Vector Genome Titer to Quantification of Vector Genome Integrity by Multiplex dPCR

David Dobnik, Co-founder and Chief Scientific Officer, Niba Labs

- Vector genome integrity is becoming more and more important
- Current vector genome titer methods overestimate the number of full-length genomes
- Advanced multiplex dPCR approaches can help in quantification of genome integrity

11:30 AM – 12:00 PM

Benefits and Challenges of qPCR vs. ddPCR vs. Total Particle Titer Methods

Andrea Hamilton, Associate Director of Quality Control, Gyroscope Therapeutics

- Overview of qPCR and ddPCR as AAV genomic titer methods
- Consideration of total particle methods to determine AAV titers
- Highlighting Gyroscope's experience with development of ddPCR and total titer methods

12:00 – 12:40 PM

Lunch Break

DAY 2 · Thursday, March 9, 2023

12:40 – 1:10 PM

Regulatory Considerations for AAV Vector Genome and Capsid Titer Determination

Andrew Harmon, Lead Biological Reviewer, Gene Therapy CMC, U.S. Food and Drug Administration (FDA)

- Regulatory considerations for AAV dose determining assays before Phase 1 (assay qualification)
- Regulatory consideration for AAV dose determining assays before pivotal (assay validation)
- Dosing based on nominal Vg titer in pivotal studies (when dosing based on weight)
- Regulatory considerations for Capsid titer determination

1:10 – 1:50 PM

Panel Discussion

Moderator: *Matthew Hewitt*

Panelists: *Pierre Caloz, Roberto Calcedo, Adam Davis, David Dobnik, Andrea Hamilton, Andrew Harmon*

1:50 – 2:00 PM

Concluding Remarks

Josephine Lembong, Manager, Science & Industry Affairs, ARM

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Thank you for attending!

STAY ENGAGED

Research & Publications:

A-Gene:
https://alliancerm.org/manufacturing/a-gene-2021

A-Cell:
https://alliancerm.org/manufacturing/a-cell-2022/

Upcoming ARM Events:

Meeting on the Med
April 12-14, 2023 in Barcelona, Spain

Cell and Gene Congressional Fly-In
May 9-10, 2023 in Washington, DC

Meeting on the Mesa
October 10-12, 2023 in Carlsbad, CA

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