

Workshop on Expanding AAV Manufacturing Capacity for Rare Disease Gene Therapies

Natcher Conference Center | NIH Campus | Bethesda, MD

January 28–29, 2020

Day 1 — Tuesday, January 28

- 8:00 a.m. Registration**
- 8:30 a.m. Welcome**
Christopher Austin, M.D.— Director, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH)
- 8:40 a.m. Introductory Remarks**
Peter Marks, M.D., Ph.D. — Director, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA)
- 8:50 a.m. AAV Manufacturing Landscape Overview**
Guangping Gao, Ph.D. — President, American Society of Gene and Cell Therapy (ASGCT); Professor, Microbiology and Physiological Systems; Penelope Booth Rockwell Professor in Biomedical Research; Co-Director, Li Weibo Institute for Rare Diseases; Research Director, Horae Gene Therapy Center and Vector Core; Scientific Director, UMass Medical School (UMMS)-China Program Office
- 9:00 a.m. Session 1: Overview of Current Manufacturing Formats/Technologies**
An overview of the three leading manufacturing formats/technologies (triple transfection, baculovirus, herpes simplex virus), including the relative advantages and challenges associated with each system.
- Moderator: *Guangping Gao, Ph.D.* — President, ASGCT; Professor, Microbiology and Physiological Systems; Penelope Booth Rockwell Professor in Biomedical Research; Co-Director, Li Weibo Institute for Rare Diseases; Research Director, Horae Gene Therapy Center and Vector Core; Scientific Director, UMMS-China Program Office
- Panelists: *Steven Gray, Ph.D.* — Associate Professor, Department of Pediatrics, UT Southwestern Medical Center
Barry Byrne, M.D., Ph.D. — Director, University of Florida Powell Gene Therapy Center; Professor, Pediatrics and Molecular Genetics and Microbiology, UF Health
Nathalie Clément, Ph.D. — Associate Director, University of Florida Powell Gene Therapy Center
Rob Kotin, Ph.D. — Professor, Microbiology and Physiological Systems, UMass Med Gene Therapy Center
- 10:15 a.m. Break**
- 10:30 a.m. Session 2: Major Logistical Bottlenecks**
A review of multiple bottlenecks to generating clinical grade AAV for trials. These include limited good manufacturing practice (GMP) facilities, limited supply of experienced personnel, upstream and downstream supply chain shortages (e.g., plasmids, media, plasticware), and delays and uncertainty of timing of release testing assays. The severity of each bottleneck may vary by project size, institution type, manufacturing format, or other factors.



Moderator: *Michael Lehmicke, M.S.* — Director, Scientific and Industry Affairs, Alliance for Regenerative Medicine

Panelists: *Gina Hann, M.B.A.* — Founder, President, and Treasurer, Batten Hope
Steve Kaminsky, Ph.D. — Professor, Research in Genetic Medicine;
Associate Director, Gene Therapy Core, Weill Cornell Medical College
Andrew Knudten, M.B.A. — Founder and Managing Consultant, Gene Therapy Consulting, LLC
Caroline Smith-Moore, Ph.D., M.B.A. — Assistant Director, Analytical, Golden LEAF Biomanufacturing Training and Education Center
Wei Wang, Ph.D. — Microbiologist, Division of Manufacturing and Product Quality, CBER, FDA

12:15 p.m. **Lunch** (on your own)

Rooms C1/C2 and F1/F2 are available for use for networking meetings.
Room D is reserved for 30-minute brown bag breakout sessions with patient advocates.

1:45 p.m. **The Looming Burden of AAV Manufacturing on a Community-Driven R&D Program**

Simon Frost, CPA — Founder, Hope for Annabel Foundation

2:00 p.m. **Session 3: Planning Ahead to Streamline Scale Transitions**

How to design manufacturing processes at each stage that avoid the need for extensive bridging studies, are compatible with vendor transitions, and support downstream transition to commercialization.

Moderator: *Denise Gavin, Ph.D.* — Chief, Gene Therapy Branch, Office of Tissues and Advanced Therapies (OTAT), CBER, FDA

Panelists: *Josh Grieger, Ph.D.* — Chief Technology Officer, AskBio
Richard Snyder, Ph.D. — Vice President, Science and Technology, Pharma Services, Viral Vector Services, Thermo Fisher Scientific
Robert Baffi, Ph.D., M.B.A. — President, Global Manufacturing and Technical Operations, BioMarin

3:30 p.m. **Break**

3:45 p.m. **Session 4: Master File Best Practices and Opportunities**

A review of master file best practices that can avoid risks and achieve maximal efficiencies and a discussion of opportunities to pool and consolidate existing manufacturing knowledge.

Moderator: *Andrew Harmon, Ph.D.* — Reviewer, Cell and Gene Therapy Chemistry, Manufacturing, and Controls (CMC), Division of Cellular and Gene Therapies (DCGT), CBER, FDA

Panelists: *Rajesh Thangapazham, Ph.D.* — Head, Regulatory Strategy and Innovation - Cell and Gene Technologies, Lonza Pharma Biotech & Nutrition
Johannes C. M. van der Loo, Ph.D. — Director, Clinical Vector Core, Children's Hospital of Philadelphia (CHOP)

4:45 p.m. **Open Floor Recap of Day 1 Themes and Opportunities**

5:00 p.m. **Adjournment**

Day 2 — Wednesday, January 29

- 8:00 a.m. Registration**
- 8:45 a.m. Welcome and Overview of Day 2 Topics**
Anne Pariser, M.D. — Director, Office of Rare Diseases Research (ORDR), NCATS, NIH
- 8:55 a.m. Perspectives on AAV Manufacturing**
R. Jude Samulski, Ph.D. — President, Chief Scientific Officer, and Co-Founder, AskBio;
Professor, Pharmacology, UNC School of Medicine Gene Therapy Center
- 9:15 a.m. Session 5: Analytics and Lot Release Testing**
Robust and efficient analytic methods for yield, potency, and purity lag behind clinical development of AAV gene therapies. Overall, obtaining accurate quantitation is a major challenge, as is aligning analytical development with the overall product and clinical development timeline.
- Moderator: *Zenobia Taraporewala, Ph.D.* — Acting Team Lead, CMC, DCGT, CBER, FDA
Panelists: *James Wilson, M.D., Ph.D.* — Director, Gene Therapy Program; Rose H. Weiss Professor and Director, Orphan Disease Center; Professor, Medicine and Pediatrics, Department of Medicine, University of Pennsylvania
Mark Galbraith, M.S. — Head, Quality Control and Analytical Sciences, Spark Therapeutics
Herbert Runnels, Ph.D. — Research Fellow, BioTherapeutics Pharmaceutical Sciences, Pfizer
- 10:45 a.m. Break**
- 11:00 a.m. Collaborating for Innovation**
Scott Dorfman — Chief Executive Officer, Odylia Therapeutics
- 11:15 a.m. Session 6: Innovative and Late-Breaking Approaches**
A selection of innovative and/or late-breaking approaches for expanding AAV manufacturing capacity.
- Chair: *Nicole Paulk, Ph.D.* — Assistant Professor, Gene Therapy, University of California San Francisco
- Talks: “Scalable rAAV production based on stable producer cell lines”
Nicole Faust, Ph.D., M.B.A. — Chief Executive Officer, CEVEC
“High Density Cell Respirator for Production Cell Growth”
Yuman Fong, M.D. — Sangiacomo Chair and Chairman, Department of Surgery, City of Hope Medical Center
“Making Gene Therapy Affordable and Accessible”
Audrey Greenberg — Executive Managing Director, The Discovery Labs, LLC
- 12:30 p.m. Lunch (on your own)**
Rooms C1/C2 and F1/F2 are available for use for networking meetings.
Room D is reserved for 15-minute brown bag breakout sessions with patient advocates.

- 1:30 p.m.** **Session 7: Prospects for Innovation and Barriers to Innovation and/or Uptake**
Given the number and severity of issues with current manufacturing formats, what are the prospects for outside-the-box innovations that dramatically increase efficiency?
- Moderator: *Andrew Byrnes, Ph.D.* — Chief, Gene Transfer and Immunogenicity Branch, CBER, FDA
- Panelists: *Jonathan Appleby, Ph.D.* — Chief Scientific Officer, Cell and Gene Therapy Catapult
Kelvin Lee, Ph.D. — Director, National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL); Gore Professor of Chemical and Biomolecular Engineering, University of Delaware
Otto-Wilhelm Merten, Ph.D. — Gene Therapy and Vector Manufacturing Specialist, Miltenyi Biotec
J. Fraser Wright, Ph.D. — Professor, Pediatrics, Center for Definitive and Curative Medicine, Stanford University School of Medicine
- 3:15 p.m.** **Break**
- 3:30 p.m.** **Open Floor Discussion with Q&A for Panelists**
- 4:15 p.m.** **Adjournment**