CIRM Manufacturing in California Workshop Summary
April 14, 2021 (Virtual)

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Background

The California Institute for Regenerative Medicine (CIRM) is dedicated to the acceleration of effective treatments and cures to patients. With $5.5B in new funding approved by California voters in November 2020, CIRM is now poised to build on its 14-year experience and accelerate development of innovative regenerative medicine approaches and ensure equitable access to patients with unmet medical needs.

The manufacturing of cell and gene therapies is a complex and ever-evolving process. As the regenerative medicine field rapidly grows, the science and clinical development of innovative cell and gene therapy candidates often outstrips the pace of their manufacturing development. In recent years, regulatory approvals of several clinically promising cell and gene therapy candidates were either delayed or completely stalled due to chemistry, manufacturing and controls (CMC) related deficiencies in the regulatory submissions. Manufacturing bottlenecks also represent a significant source of milestone delays in CIRM's translational and clinical projects portfolio. These challenges are further compounded by the nature of the manufacturing infrastructure in California, where several world-leading Good Manufacturing Practice (GMP) facilities support manufacturing for early clinical trials but few options exist for late-stage clinical and commercial manufacturing. Finally, there is a critical need to develop a diverse, highly skilled manufacturing workforce to help these challenges and bottlenecks in the California cell and gene therapy ecosystem.

CIRM convened an all-day virtual workshop of over 50 leaders in cell and gene therapy manufacturing to help it define collaborative solutions to the manufacturing and workforce needs in California. The workshop was also attended by CIRM ICOC board members and CIRM team members. The three sessions of the workshop focused on best practices for cell and gene therapy development projects, considerations for building a California public-private manufacturing network, and on collaborative approaches for building a diverse California manufacturing workforce.

Workshop Participants

Session Panelists & Presenters	Institution/Company
Jens Vogel, PhD	Bayer
Chris McClain, MBA	Be The Match
Tara Greene, MS	BioEthicA
Terri Quenzer, PhD Keau Wong, MS	California Community Colleges
Boro Dropulic, PhD	Caring Cross
Joseph Gold, PhD	City of Hope
Katy Spink, PhD	Dark Horse Consulting
Melissa Carpenter, PhD Michael Paglia, MS	ElevateBio
Wen Bo Wang, PhD	Fate Therapeutics
Krishnendu Roy, PhD	Georgia Tech, CMaT
Sue Behrens, PhD	Keck Graduate Institute
PJ Brooks, PhD	NCATS
John Balchunas, MS	NIIMBL
Tony Khoury	Project Farma
David DiGiusto, PhD Rahul Singhvi, ScD	Resilience
James DeKloe	Solano College
Maria Grazia Roncarolo, MD J Fraser Wright, PhD	Stanford University
Fyodor Urnov, PhD	UC Berkeley
Donald Kohn, MD	UCLA
Amy DuRoss, MBA	Vineti
CIRM ICOC	
Judith Gasson, PhD	
Stephen Juelsgaard, DVM, JD	
James Kovach, MD, JD	
Linda Malkas, PhD	
Jonathan Thomas, PhD, JD	
Art Torres, JD	
Kristiina Vuori, MD, PhD	

Participants	Institution/Company
Rajesh Ambasudhan, PhD	Allele Biotechnology
Tom Bollenbach, PhD	ARMI
Dhruv Sareen, PhD	Cedars Sinai Biomanufacturing
Parker Donner, MBA Shannon Eaker, PhD Fiona Plows, PhD	Cytiva
Anthony Davies, PhD Donald Fink, PhD	Dark Horse Consulting
Joerg Ahlgrimm	Discovery Labs
Eugene Brandon, PhD	IQVIA
Mark Lutgen, MBA Lauren Collison, PhD Nicolas Taquet, MS	KBI Biopharma
Chris Austin, MD Ilyas Singec, MD, PhD	NCATS
Kelvin Lee, PhD	NIIMBL
Jerrod Denham	Ology Bioservices
Chad Clark	Precision for Medicine
James Adams, MBA	Sonoma Therapeutics
Robert Deans, PhD	Synthego
Frank Jing, MS	Tenaya Therapeutics
Gerhard Bauer	UC Davis
Sujna Raval-Fernandez, PhD	UCLA
Dan Kaufman, MD, PhD	UCSD
Alan Ashworth, PhD Jonathan Essensten, MD, PhD Qizhi Tang, PhD	UCSF
Bruce Levine, PhD	University of Pennsylvania
Mohamed Abou-el-enein, PhD	USC

Session 1 - Incorporating Practical QbD Principles in Cell and Gene Therapy Manufacturing Development

The objective of this session was to identify feasible early-stage manufacturing mitigation steps to reduce the manufacturing risks that delay clinical development and approval of cell and gene therapy candidates. To drive the conversation, CIRM posed that incorporation of select Quality by Design (QbD) principles early in translational development will improve both the quality of initial process development as well as manufacturing scale-up at later stages of clinical development. The session began with a series of panelist presentations on QbD and its applications in cell and gene therapies as well as roadblocks and best practices for early and late stages of manufacturing development. Following the presentations, the session was opened up to a Q&A involving all participants, where a rich discussion ensued on how CIRM can best support manufacturing development at very early stages of translation.

Critical Elements of the Manufacturing Quality by Design Framework Can and Should be Prioritized Early in Translational Development of Cell and Gene Therapies

QbD is a development framework rooted in science and risk management principles that defines an iterative data-driven approach toward deep understanding of the quality of the drug product, and the associated manufacturing and analytical processes. In the context of therapeutic development, the QbD framework emphasizes thorough understanding of the critical quality attributes (CQA) of the drug product, of the critical process parameters (CPP) of the manufacturing process, and of the control strategies that ensure quality of the product and manufacturing process. The FDA and international standards and regulatory agencies have been driving QbD adoption in small molecule and protein biologics manufacturing over the past two decades, and it is only a matter of time before it becomes a regulatory expectation for cell and gene therapies.

Today, QbD is not consistently adopted in cell and gene therapy development and, when it is, it is largely in later stages of clinical development. The primary challenges for widespread adoption of QbD in cell and gene therapies are that the CQAs and CPPs for the product and process are (1) myriad, (2) often unique to the product, technology or disease indication and (3) often not measurable by current standard analytical assays. In other words, the bespoke nature of cell and gene therapies that defines their value proposition as transformative therapies also makes them incredibly difficult to manufacture. The panelist presentations included a case study of applying QbD principles to AAV gene therapy platform development where the purity, potency and safety of the vector product are a function of vector design, process design and process controls. The presentations described how gene therapy platforms are more amenable to QbD approaches given that their characteristics, manufacturing processes and analytical methods skew closer to protein-based biologics. The presenters advocated for concerted efforts to establish QbD-driven gene therapy technology platforms, which can accelerate and de-risk development of a portfolio of gene therapy candidates each encoding different protein products for a variety of diseases. This viewpoint was supported by several participants later in the discussion.

Cell therapies, on the other hand, are defined by an interaction of dynamic complex systems involving variable starting cell materials leading to a living cell product with 1000s of potential CQAs, the therapeutic function of which is highly modified by the unique tissue microenvironments of the diverse patient cohorts. Panelists proposed that these challenges may be overcome by coupling deep multi-omics characterization with artificial intelligence/machine learning (AI/ML)-driven data analytics to define CQAs and CPPs. In the ensuing discussion, several experts argued that the academic researchers who are the early innovators of cell and gene therapy products would be well suited to perform such deep characterization and analyses. The presenters also proposed a provocative vision of the future where dynamic, feedback-controlled manufacturing processes produce personalized cell therapies at scale.

The themes of iterative manufacturing risk management coupled with deep characterization of the drug product, manufacturing process and controls in these early QbD presentations were reinforced throughout the remainder of the session.

Empower Academic Early Innovators to De-Risk Manufacturing by Planning Ahead

In an ideal setting, a sustained effort of deep product and manufacturing process characterization would take root at the very early stages of translational development for a cell or gene therapy project. In reality, time, resource and capital considerations don't always make this a wise investment for individual projects at such an early stage while the science is still being established. In the context of the CIRM portfolio, early translational research is almost always conducted by early innovators such as academic labs or small companies, with the latter often still reliant on academic collaborators. A consistent theme in the session was to adequately empower the early academic innovators to plan ahead for critical manufacturing milestones in their translational research projects.

This begins with educating and training the academic principal investigators (PIs) on the merits of QbD in manufacturing as well as on the basic requirements of current GMP (cGMP) requirements for eventual clinical testing. The participating CIRM-funded PIs noted that CIRM has already been doing this by virtue of its application requirements, award milestones and expert advisory panels for Translational and Clinical stage projects. The participants agreed that CIRM is well suited to further develop PI education resources and establish best practices. For example, it is feasible to expect Translational stage projects to initiate manufacturing risk assessment and quality target product profiles, both key items in the QbD framework. Participants also agreed that a sustained focus on development of CQAs and CPPs should start while the project is still in the academic labs. This would require the CIRM translational stage projects to invest more time and resources in thoroughly defining the product and process characteristics.

As articulated in panelist presentations and in the ensuing discussion, academic PIs should leverage the expertise at the academic GMP manufacturing facilities very early in translational development. For CIRM projects, this would start prior to submitting a Translational stage application and would continue throughout the Translational award. All GMP manufacturing facilities have readiness criteria that therapeutic development projects must meet before their manufacturing process can be transferred to the facility. High-demand facilities have algorithms that prioritize projects based on readiness, clinical impact and other criteria. The early and sustained interaction between the development teams and the GMP facility could ensure project readiness by defining the process development plan, identifying and mitigating supply chain and other manufacturing risks, and anticipating technology transfer challenges. This early collaboration between the academic PIs and the GMP manufacturing facilities will save time and costs and improve the quality of the manufacturing process.

Resource Academic Institutions to Support Early Clinical Manufacturing and to De-Risk Projects for Commercial Manufacturing

Academic research institutions play a central driving role in the discovery, preclinical development and early clinical development of cell and gene therapies. Academic early innovators leverage institutional resources to develop novel technology platforms that lead to discovery and early translational development of therapeutic candidates. The academic GMP manufacturing facilities support process development and manufacturing for the initial clinical trials. The previous sections have discussed how the academic PIs must be empowered to anticipate and mitigate manufacturing risks. The participants also discussed and advocated for CIRM to enhance the resources and expertise at the academic GMP manufacturing facilities to support QbD driven manufacturing development. In particular, the participants noted that the facilities should be adequately staffed to provide process development and regulatory CMC support to cell and gene therapy development teams at the early translation stages of their projects. The facilities should have access to proteomics, single cell sequencing, next generation sequencing and other "omics" technologies to support early development of CQAs and CPPs.

In a prelude to the next session's topic, participants also argued that individual facilities should specialize in specific manufacturing platforms and testing capabilities, and network with other institutions to cover the spectrum of cell and gene therapy platform needs. Finally, participants generally agreed that the data infrastructure should be modernized and digitized to enable more robust quality management systems, which in turn will enable efficient technology transfer to industry for late stage clinical and commercial

manufacturing. The digital data infrastructure would better facilitate inter-institutional sharing of best practices and establishment of standard processes and testing methodologies across a network.

Establish Regulatory Best Practices

The regulatory and quality experts in attendance translated the session's discussion into key regulatory best practices that CIRM should broadly support across its portfolio of projects. The experts provided practical tips for improving the quality and outcome of pre-IND and IND submissions. They encouraged development teams to present their manufacturing risk assessments in both pre-IND and IND submissions as further justification of their testing plans. While "omics" data is useful in demonstrating product and process characteristics, care must be taken to guide FDA reviewers on relevance of the data and analyses. Other recommendations elaborated on critical development milestones, including linking CQAs to meaningful patient outcomes and ensuring timely potency assay development by utilizing qualified activity assays in early clinical trials. Finally, building on general consensus, it was recommended that cell therapy developers collaborate with the FDA in determining how manufacturing QbD can best be applied to cell therapies.

Session 2 - Operationalizing a Public-Private CA Manufacturing Network

This session focused on the topic of building a unique network of diverse California stakeholders to support the manufacturing needs of CIRM's diverse portfolio of cell and gene therapy development projects. The presentations and discussions centered around identifying critical stakeholders in a CIRM public-private manufacturing network and mechanisms to incentivize deeper collaboration on manufacturing projects. To seed the discussion, CIRM had invited select grantees, Industry Alliance Program members and key stakeholders to briefly present their own collaborative and innovative approaches for supporting cell and gene therapy manufacturing. This was followed by a Q&A session with robust input from all participants.

Lightning Presentations

Bespoke Gene Therapy Consortium – PJ Brooks, NCATS
A proposal for a public-private partnership for developing a robust AAV gene therapy platform that streamlines plug and play AAV vector design, preclinical testing, manufacturing and clinical development of gene therapies for diseases of no commercial interest.

CRISPR Therapies for Rare Diseases – Fyodor Urnov, UC Berkeley
A proposal for a non-profit led public-private partnership to enable the discovery, preclinical and clinical development, and delivery of personalized CRISPR gene therapies for "N-of-1" diseases.

Place-of-Care CAR-T Manufacturing – Boro Dropulic, Caring Cross
Description of the Caring Cross model for enabling global, decentralized place-of-care manufacturing of CAR-T cell therapies to reduce costs and increase patient access. The CIRM-funded clinical trial of a DuoCAR-T therapy for HIV is part of the test case for this decentralized manufacturing model.

Be The Match BioTherapies – Chris McClain, Be The Match
Description of Be The Match's 30 years of comprehensive support for bone marrow transplants and hematopoietic stem cell therapies including donor registry management, cell therapy supply chain management, clinical research support, and outcomes data tracking.

Jens Vogel, Bayer
Description of Bayer's focus on standardizing cell and gene therapy manufacturing by developing a modular platform concept, leveraging lessons learned from antibody biologics development and partnering with innovative cell and gene therapy companies.

Michael Paglia, ElevateBio
Description of ElevateBio's model of providing end-to-end centralized product development and manufacturing support for cell and gene therapy partners, whether they be academic labs, biotech or pharmaceutical companies.

David DiGiusto, Resilience National
Description of Resilience's goal to build a national network of facilities to support platform technology development, process development and manufacturing for a wide range of biologics, cell therapy and gene therapy partners.

Amy DuRoss, Vineti
Description of Vineti's software-based solutions for cell and gene therapy supply chain management. Vineti also collaborates with industry stakeholders to develop standards in supply chain management that protect patients and reduce complexity of healthcare delivery.

Following the lightning presentations, CIRM engaged all participants in a broad-ranging discussion on building a CIRM-supported public-private cell and gene therapy manufacturing network in California. The major takeaways are highlighted below.

Build a Broad Network That Charts Out the Path and Supports Projects From Early Translation to Commercialization

Participants agreed that a vision for a comprehensive California manufacturing network should begin with the end in mind and account for projects' needs across the spectrum from early translation through early commercialization. The network will need to account for capacity and expertise in core elements such as: process development, early and late-stage manufacturing, analytical testing, manufacturing supply chain and logistics, and workforce development. A critical requirement for all network participants will be to have demonstrated expertise in cell and gene therapy platforms. On that note, individual participants may best serve the network by specializing on specific platforms rather than trying to serve all needs.

The California cell and gene therapy manufacturing ecosystem poses an infrastructure problem. California has a broad network of academic and for-profit manufacturing facilities serving early-stage project needs but lacks significant infrastructure in late-stage manufacturing. Growth in large-scale manufacturing infrastructure will require, at a minimum, commitment from investors, engineering firms, construction firms, and contract manufacturing organizations to build in California.

Support Collaborative Manufacturing & Analytical Technology Development

Participants recommended that CIRM support collaborative development of novel manufacturing and analytical technologies by enabling its grantees to coordinate with national efforts of the Advanced Regenerative Manufacturing Institute (ARMI), National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) and the NIH. These networks combine resources and expertise of academic labs, small companies and large biopharmaceutical companies on multiple technology development projects ranging from analytical assay development for cell characterization through automation technology for closed manufacturing systems. Such technology development consortia generally have intellectual property sharing provisions to encourage broad adoption of the technologies. The consortia can also be used as vehicles for education and training of the participating stakeholders. Participants described training programs ranging from virtual seminars to multi-day workshops with hands-on training and demonstrations, which could be utilized for training on QbD and cGMP manufacturing principles.

Enable Academic Competency Hubs and Academic GMP Manufacturing Centers of Excellence

Building on previous comments on the importance of specialization, public-private collaboration, and sharing of data and best practices, the participants coalesced around the concept of building competency hubs. Competency hubs would be anchored by academic institutions that each specialize in specific aspects of cell and gene therapy development. Using gene therapies for rare diseases as an example, participants described a competency hub consisting of gene editing platform developers, manufacturing facilities, clinical trial sites and analytical cores that together specialize in small-scale manufacturing and clinical testing of many gene therapy candidates for rare diseases. The experience gained from iteration combined with the aggregated datasets would effectively inform CQAs and CPPs for the gene editing technology platform. In this model, the industry stakeholders function as resource, capital, and expertise partners in the effort but are also the ultimate consumers of the aggregated data output. Similar competency hubs could be setup and interconnected to support various cell and gene therapy technology platforms.

In the same vein, academic GMP manufacturing centers are the competency hubs for early cell and gene therapy process development and manufacturing. Building on the previous session's discussion on augmenting the resources and capabilities of the academic GMP manufacturing centers, this session's

discussion focused on networking the facilities to enable platform data sharing as well as establishment of best practices and standards. Participants had several specific areas of standardization and collaboration in mind for such a network. They also discussed how the CIRM network of academic and industry stakeholders could integrate with national efforts in standardization of cell and gene therapy manufacturing.

Leaders of academic GMP manufacturing facilities were broadly supportive of sharing and co-development of standard operating procedures (SOPs) for manufacturing platforms, analytical method development and validation, facilities controls and monitoring, etc. Several participants particularly noted that the network could reduce time and cost of development, and streamline regulatory submissions, by aligning on use of specific analytical methods. The coordination between academic GMP facilities would enhance the value of individual projects, the value of the network, and would contribute to standards-setting in the field. Despite the enthusiasm, several leaders cautioned that CIRM would need to address intellectual property policies at the institutional level to effectively enable sharing and co-development of SOPs.

Industry stakeholders would need to effectively integrate with academic institutions in a CIRM public-private manufacturing network. Industry participants noted that they have existing or planned collaborations with California academic institutions for manufacturing technology platform development, workforce training and co-location of GMP manufacturing sites. Such academic-industry relationships should be further solidified and broadly extended in a California manufacturing network. With respect to support of CIRM-funded projects, industry stakeholders would be providers of materials, resources, and expertise for earlier stage projects supported by the network. Ultimately, industry partners would be responsible for driving late stage clinical and commercial manufacturing for commercially viable projects.

Participants mentioned several ways that academic-industry collaborations could help streamline therapeutic development and accelerate standard-setting. Collaborative establishment of common databases and templates across manufacturing facilities would greatly improve the efficiency of manufacturing technology transfer both in and out of the academic GMP facilities. Biopharmaceutical industry partners could leverage their experience from protein biologics manufacturing to help develop cell and gene therapy manufacturing standards. Finally, the functionality of this network would be enhanced with targeted integration with national efforts such as technology development consortia (NIIMBL, ARMI, etc.) and standards setting efforts (i.e. the Alliance for Regenerative Medicine's A-Cell and A-Gene case study-based reference guides for QbD in cell and gene therapy manufacturing).

Session 3 - Training a Diverse Manufacturing Workforce

The intent of this session was to discuss how to leverage CIRM funding to provide education, training and certification of a diverse California manufacturing workforce. Workshop participants were asked to present and discuss industry workforce demands, collaborative scaling of education programs in community colleges and universities, and development of specialized training for a diversity of career pathways. The session began with a presentation on the California labor market for skilled technical positions in cell and gene therapies. The data spanning from the last 10 years showed a 4X increase in job postings over the time period. However, the presentation and the ensuing broader discussion highlighted a number of challenges facing cell and gene therapy workforce development in California. These challenges include:

1. Limited exposure of undergraduate students (including community college and 4-year university students) to various career pathways in research and biomanufacturing.
2. Limited opportunities for undergraduate student training/internships in specific areas of research and biomanufacturing, both in the academic and industry settings. Over 20% of community college students already have BS degrees, suggesting that they're returning for career skills training that they did not receive in their undergraduate education.
3. A prevalent employer mindset about employment and promotion of candidates with a minimum of a BS degree, which results in limited upward mobility for associates-degree holders even when they have received specialized training. Community colleges such as Solano College and Mira Costa college developed BS in biomanufacturing programs to provide a low-cost education to address this issue. However, these programs don't yet provide hands-on training in cell and gene therapy manufacturing.
4. High, and likely unsustainable, turnover rates at academic GMP manufacturing facilities due to industry competition.

Leverage CIRM Education Programs to Broadly Enhance On-Ramps for Hands-on Training and Micro-Credentialing of Students

Students in associate and bachelor's degree programs at community colleges and/or 4-year universities have limited exposure to hands-on training in cell and gene therapy manufacturing. Workshop participants noted their individual efforts to provide such training opportunities at their own GMP manufacturing facilities. CIRM's Bridges and SPARK programs are designed to educate and train diverse college and high school student cohorts, respectively, across the state of California in cell and gene therapy research careers. Participants noted that some Bridges grantees have facilitated manufacturing training by partnering with a few academic of biotech GMP manufacturing facilities. Similarly, companies described partnering with community colleges to offer internships in GMP manufacturing and quality as a pathway to employment. Other participants suggested that even short exposures such as boot camps would provide valuable hands-on training for students. CIRM could build on these efforts by broadly facilitating bootcamp or internship partnerships with community colleges, academic GMP facilities and biotech companies in its existing SPARK and Bridges programs. Community colleges participants noted an effort in developing micro-credentialing, which could be beneficial to Bridges students for career placement opportunities in cell and gene therapy manufacturing. The SPARK high school students would have early exposure to career opportunities in cell and gene therapy manufacturing. Participants strongly recommended that the internship opportunities broadly expose students to the breadth of manufacturing, quality and regulatory career pathways. They also emphasized that the training programs should demonstrate the unique connection between manufacturing personalized cell and gene therapy medicines and patient treatments and outcomes.

The SPARK and Bridges programs could incorporate community colleges in several ways. The grantee institutions could leverage the hands-on training at community colleges to build general biomanufacturing skills. Community colleges can also be Bridges grantees and partner with institutions and companies to provide hands-on cell and gene therapy research and manufacturing training for their students. This would give community college students a valuable opportunity to build specialized cell and gene therapy skills on top of their biomanufacturing training.

Facilitate the Development & Adoption of Certificate Programs to Enable Specialization and Career Progression

A consistent theme throughout the session was CIRM's opportunity to facilitate partnerships between manufacturing facilities and education programs for strengthening and expanding certificate programs. CIRM could leverage its education funding programs along with the potential public private manufacturing network to support specialization and career progression in cell and gene therapy manufacturing. Certificate programs could provide 1-2 year hands-on training at GMP manufacturing facilities to build specialized skills in cell and gene therapy manufacturing. Importantly, the students would be directly contributing to the operations of the facility while enrolled in the certificate programs.

Such programs could help overcome several challenges for all stakeholders. Firstly, if designed to meet the qualification requirements of employers, the certificates would rapidly train the workforce in specialized skills for manufacturing and process development, quality and regulatory career pathways. The certificate programs could help address the challenge of increasing diversity, equity and inclusion in the manufacturing workforce by providing efficient on-ramps for participation in these career pathways. The workshop participants also described a common challenge facing manufacturing technicians interested in career advancement where their employers would first require completion of science degree programs.

Finally, leaders of academic GMP manufacturing facilities noted a shared challenge of high employee turnover due to their inability to match industry compensation packages. The academic facilities expend significant effort training personnel only to have them depart to industry after a short period of productive contribution. Certificate programs could increase retention and extend productive contribution of trained personnel at the academic facilities. The programs would also establish the academic facilities as critical partners in the development of a highly skilled and diverse manufacturing workforce in California. Thus, the certificate programs would create more accessible, affordable and efficient pathways for diverse California populations in developing career skills that are ultimately more relevant to employers.

Appendix: Workshop Agenda

Session 1 - Incorporating Practical QbD Principles in Cell and Gene Therapy Manufacturing Development

Panelists:
Melissa Carpenter
David DiGiusto
Joseph Gold
Tara Greene
Krishnendu Roy
Wen Bo Wang
J Fraser Wright

Description:
This session will help define the practical considerations and milestones for QbD-driven cell and gene therapy manufacturing development plans. Panelists will present an introduction to QbD principles as well as key lessons learned from early and late stage manufacturing development of cell and gene therapies. This will be followed by a Q&A session where the moderators will engage panelists and all participants in a discussion of the critical elements of a QbD-driven manufacturing project.

CIRM encourages and expects all participants to contribute to the session discussion.

Session Agenda (120 minutes)

1. Panelist Presentations (1 hour)

Brief Primer on QbD-Driven Cell and Gene Therapy Manufacturing Development.
Tara Greene & Krishnendu Roy (5-10 minutes Presentation, 5-minute Q&A)

Manufacturing Lessons Learned from Developing and Commercializing In Vivo Gene Therapies.
J Fraser Wright (10 minutes Presentation, 5-minute Q&A)

Best Practices for Early Stage Manufacturing Development.
Joseph Gold (10 minutes Presentation, 5-minute Q&A)

Mitigating Manufacturing Risks at Later Stages of Clinical Development.
David DiGiusto (10 minutes Presentation, 5-minute Q&A)

2. Q&A Session with Panelists & All Participants (1 hour)
Moderated by Sohel Talib & Shyam Patel (CIRM)

What essential QBD elements should an early translational stage project account for in formulating its manufacturing development project plan?

What are the critical manufacturing development milestones as cell and gene therapy candidates progress through the stages of clinical development?

What are the critical resources, expertise, and services needed by the academic and small biotech start up companies in order for them to incorporate QBD manufacturing principles in their product development plan?

Questions from panelists & participants

Session 2 - Operationalizing a Public-Private CA Manufacturing Network

Panelists:
PJ Brooks
Amy DuRoss
Tony Khoury
Donald Kohn
Chris McClain
Michael Paglia
Katy Spink
Jens Vogel

Description:
This session will discuss building a unique network of diverse California stakeholders to support the manufacturing needs of CIRM's broad cell and gene therapy development project portfolio. The session will start with lightning presentations describing collaborative non-profit and industry manufacturing models and how they may fit in a broader public-private manufacturing network. This will be followed by a broader discussion between all participants on building a public-private manufacturing network in California, incentivizing the stakeholders and establishing short-term and long-term success criteria.

CIRM encourages and expects all participants to contribute to the session discussion.

Session Agenda (120 minutes)

1. Lightning Presentations (30 minutes)

Collaborative Non-Profit Manufacturing Approaches (3 minutes each)

- Bespoke Gene Therapy Consortium - PJ Brooks, NCATS
- CRISPR Therapies for Rare Diseases - Fyodor Urnov, UCB IGI
- Place-of-Care CAR-T Manufacturing - Boro Dropulic, Caring Cross
- Be The Match Biotherapies - Chris McClain

Collaborative Industry Manufacturing Approaches (3 minutes each)

- Bayer - Jens Vogel
- ElevateBio - Michael Paglia
- Resilience - Rahul Singhvi
- Vineti - Amy DuRoss

2. Q&A Session with Panelists & Participants: Building a California Public-Private Manufacturing Network. (90 minutes)
Moderated by Sohel Talib & Shyam Patel (CIRM)

What are the critical participants in a public-private cell and gene therapy manufacturing network? (Initial responses from panelists then open to all participants)

How can network participants be incentivized to collaborate along the lifecycle of a cell and gene therapy development project? (Initial responses from panelists then open to all participants)

What are potential 2-year, 5-year and 10-year success criteria for an operational public-private manufacturing network? (Initial responses from panelists then open to all participants)

Questions from participants

Session 3 - Training a Diverse Manufacturing Workforce

Panelists:
John Balchunas
Sue Behrens
James DeKloe
Terri Quenzer
Maria Grazia Roncarolo
Keau Wong

Description:
This session will discuss the education, training and certification of a diverse manufacturing workforce. Workshop participants will discuss meeting the industry workforce demands, collaboratively scaling education programs in community colleges and universities, and providing specialized training for cell and gene therapy manufacturing.

CIRM encourages and expects all participants to contribute to the session discussion.

Session Agenda (120 minutes)

1. California's Regenerative Medicine Manufacturing Workforce Needs (30 minutes)

Presentation: Training the Skilled Technical Workforce for Cell and Gene Therapy
James DeKloe (5-10 minutes)

Participant discussion: The Workforce Needs & Training Programs of Academic GMPs, CDMOs, Companies, and Vendors/Service Providers. (20 minutes)

2. Q&A Session with Panelists & Participants: Building Collaboration between academia and industry to educate and train a diverse, highly skilled CAGT workforce (90 minutes)
Moderated by Kelly Shepard & Shyam Patel (CIRM)

Manufacturing & Quality Technician Positions: How can the community college infrastructure be enhanced via academic & industry collaborations to incorporate cell and gene therapy specialization?

Advanced career pathways (analytical development, process development, QA, managerial roles): What are collaborative models for education and hands-on training for these career pathways at the undergraduate, certification and advanced degree levels?

How can workforce education curricula and hands-on training programs be future-proofed to ensure that the workforce meets the demands of the rapidly evolving cell and gene therapy industry?

How can all stakeholders collaborate to enhance diversity, equity and inclusion in cell and gene therapy manufacturing careers?

Questions from panelists and participants