Cross-Sector Efforts to Advance Gene & Cell Therapy Manufacturing

Michael Lehmicke

Director, Science & Industry Affairs

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Alliance *for* Regenerative Medicine

About ARM

- **International advocacy organization**
  - Dedicated to realizing the promise of safe and effective regenerative medicines for patients around the world
  - Cell and gene therapy, tissue engineering
- **350+ members**
  - Small and large companies, non-profit research institutions, patient organizations, and other sector stakeholders
  - Across 25 countries
- **Priorities:**
  - Clear, predictable, and harmonized **regulatory** pathways
  - Enabling market access and value-based **reimbursement** policies
  - Addressing industrialization and **manufacturing** hurdles
  - Conducting key stakeholder outreach, **communication**, and education
  - Facilitating sustainable access to **capital**

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Coming Wave of Regenerative Medicines

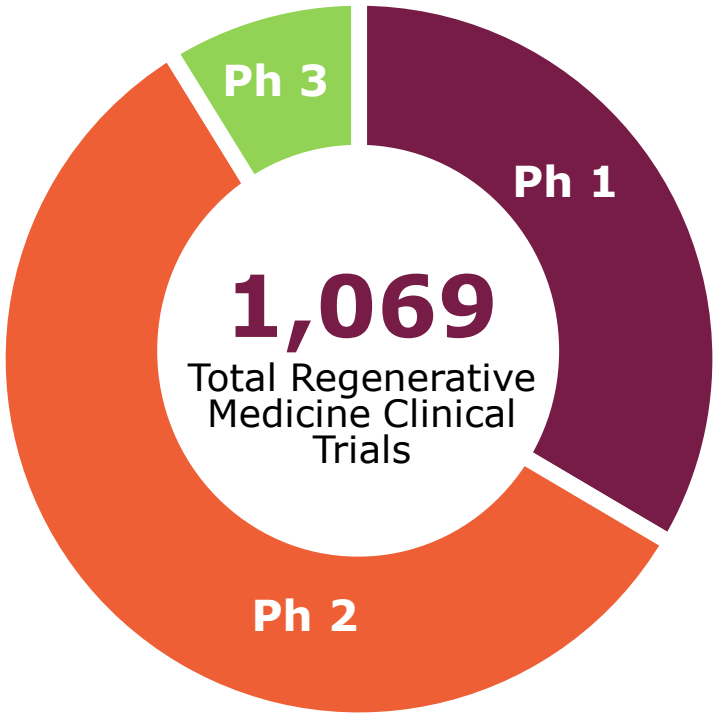
"We anticipate that by 2020 we will be receiving **more than 200 INDs per year** […] And by 2025, we predict that the FDA will be **approving 10 to 20 cell and gene therapy products a year** based on an assessment of the current pipeline and the clinical success rates of these products."

– Statement from FDA Commissioner Scott Gottlieb and CBER Director Peter Marks on new policies to advance development of safe and effective cell and gene therapies

"I had the opportunity to spend some time with my colleagues at the FDA and we've seen a steady growth in clinical trials. We **both expect to grow to 10 to 20 product approvals or submissions each year** within the next five years."

– Guido Rasi, Director General of the EMA, during his remarks at ARM's 2019 Meeting on the Mediterranean

Regenerative Medicine Clinical Trials by Phase and Technology Type



Phase 1: 358
across all tech types and indications

Gene Therapy: 117
Gene-Modified Cell Therapy: 187
Cell Therapy: 49
Tissue Engineering: 5

Phase 2: 617
across all tech types and indications

Gene Therapy: 219
Gene-Modified Cell Therapy: 207
Cell Therapy: 168
Tissue Engineering: 23

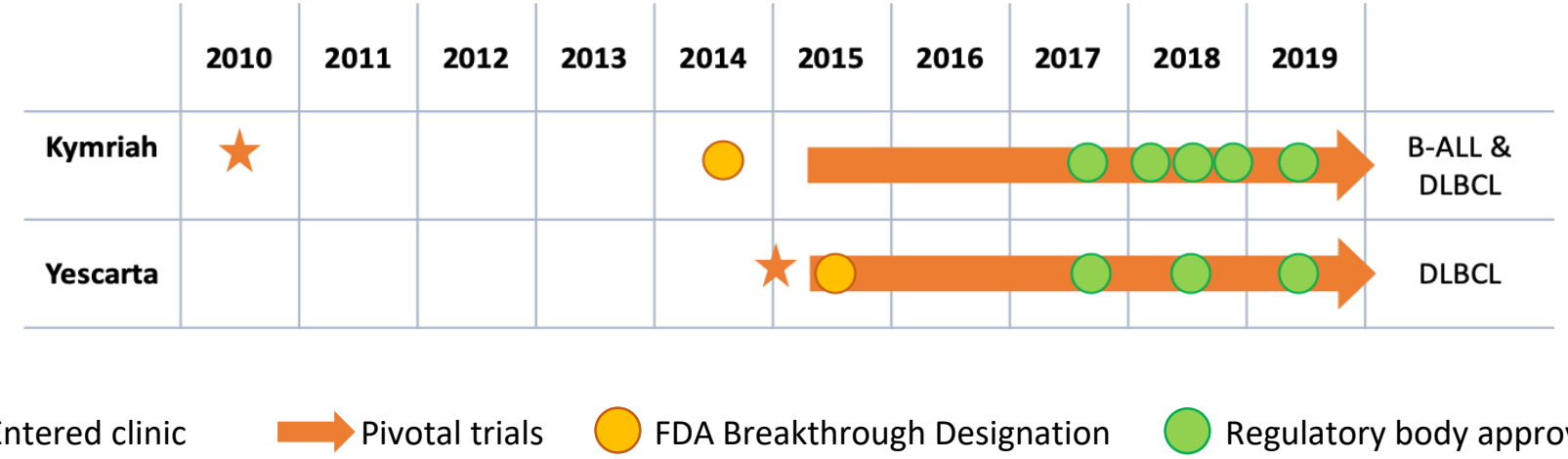
Phase 3: 94
across all tech types and indications

Gene Therapy: 30
Gene-Modified Cell Therapy: 16
Cell Therapy: 32
Tissue Engineering: 16

Source data provided by: informa

Why Is Manufacturing High Priority Now?

- Life-saving therapies are coming to fruition
- More therapies advancing to Phase 3 studies and commercialization via accelerated regulatory pathways such as RMAT
- Shorter timelines vs. small molecule drugs
- These successes are creating pressure to scale up manufacturing and build a robust supply chain



Manufacturing Challenges

- Many challenges exist related to scale up, and effectively validating and controlling processes
- A robust process should be scalable
  - Start planning early
  - What are the CMC guidelines?
  - Traditional pharma principles do not always apply
- Additional CMC guidance is needed
  - Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications; Guidance for Industry (DRAFT– scheduled for 2019 release)
  - Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Somatic Cell Therapy Investigational New Drug Applications (INDs) April 2008
- Best practices need to be established, best done collaboratively

ARM A-Gene Project

- A book of knowledge for best practices in gene therapy manufacture
- Application of quality by design principles to a case study of AAV5 vector manufacture
- Based on A-Mab model, a QbD approach to monoclonal antibody manufacturing (2009)
- 35 participants from 23 companies/organizations
- Q1 2020 completions

Participating organizations:

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ARM A-Cell Project

- The cell therapy-focused sister project to A-Gene
- 34 participants from 24 companies/organizations
- Q2-Q3 2020 completion

Participating organizations:

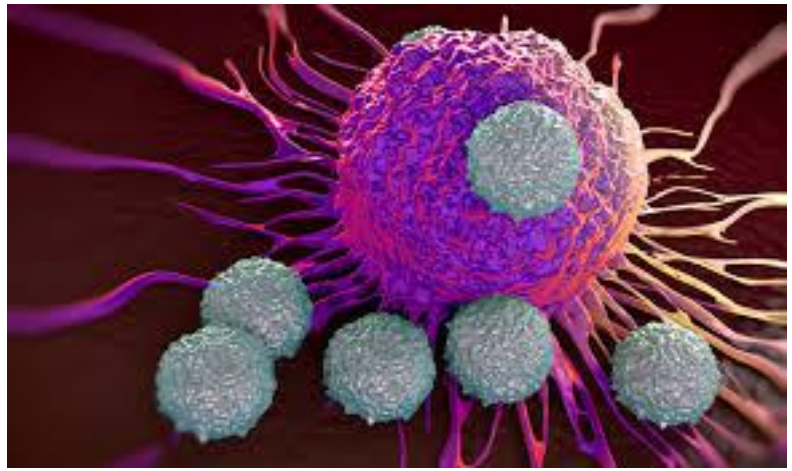
Table of Contents:

ARM CMC Workshops

- ARM and the U.S. Pharmacopeia (USP) co-hosted a workshop titled "Comparability in Cell and Gene Therapies" – May 31, 2019
  - 120+ participants
  - Speakers from the FDA and EMA/CAT
  - Full report (including presentations) available on ARM's web sit: https://alliancerm.org/manufacturing/
- An ongoing series:
  - The next CMC workshop will be held December 2019 in Raleigh-Durham, North Carolina.

Standards Coordinating Body:

Connecting the Regenerative Medicine Community to the Standards Development Process



- Launched in early 2017, SCB is an **independent 501(c)(3)** organization
- Occupies unique niche within field with **no vested interests in specific scientific, commercial, clinical or policy approaches**
- SCB is **not an SDO**, but rather **coordinates** the standards development process
- Serves as **communication vehicle** among all stakeholders, including government agencies, critical to the development of standards
- SCB works to **coordinate** standards activities, **engage** experts, and **educate** the regenerative medicine community.

The Regenerative Medicine Standards Landscape

Alliance for Regenerative Medicine

- Overview of existing regenerative medicine standards by sector

Community Perspectives: Needed Standards in Regenerative Medicine

- Overview of more than 30 needed standard areas identified and prioritized by over 250 regenerative medicine experts

Standards Advancement Projects

- SCB currently has over 15 standards advancement projects

Standards Education and Engagement

- SCB publishes newsletters, webinars, fact sheets & hosts workshops to educate and engage the community on regenerative medicine standards

FOR MORE INFORMATION VISIT www.standardscoordinatingbody.org OR CONTACT dhenke@regenmedscb.org

Existing USP Chapters

USP Chapter <1046> Cellular and Tissue-based Products

- Covers Quality Systems, qualification of source materials and components, manufacturing, technology transfer, analytical methods, stability, storage, shipping, and labeling of products.

USP <1047> Gene Therapy Products

- Guidance for development of gene therapy products, including vector design, characterization of cell and virus banks, manufacturing, purification and formulation. Best practices for analytical method development including in-process and release testing, setting specifications and validation.

USP <1043> Ancillary Materials for Cell, Gene and Tissue-Engineered Products

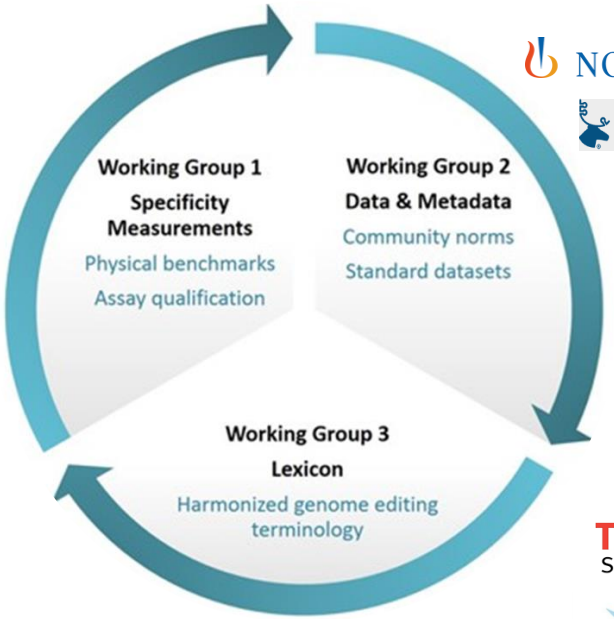
- Selection, characterization, vendor qualification, and QA/QC for ancillary materials used to produce cell and gene therapies. Provides a tiered system of risk classification incorporating information about the material, the degree of characterization, and the point of use in the process.

USP Development of Standards for Cell & Gene Therapy

- Overall strategy is to prioritize development of non-product specific performance standards and standards for raw materials
- USP is also seeking to develop general chapters to codify “best practices” in specific areas such as plasmid DNA or vector genome quantitation based on consensus from experts in the field
- USP will dedicate one expert committee to Cell and Gene Therapy products in the 2020-2025 cycle with applications from experts accepted until May 2020 (https://callforcandidates.usp.org/node)
- CGT standards under consideration for development:
  - AAV: vector genome quantitation, AAV9 standard, plasmid standards
  - Cell therapy: lentiviral vector copy number, cell type quantitation standards
- For more information: www.usp.org | jim.richardson@usp.org

NIST Genome Editing Consortium

NIST Genome Editing Consortium is a public-private partnership to address the measurements and standards needed to increase confidence of using genome editing technologies in research and commercial products



Member experts and recurring public workshops inform the work of three WGs (physical measurements, data/metadata, and lexicon)

NIST leads measurement WG, build upon highly successful NIST Genome in a Bottle (GIAB) standards; leading physical control material design and interlab studies.

32+ industry/academic member institutions; collaborating on measurement tools and standards; cost sharing formal membership mode.

Samantha Maragh, Leader, Genome Editing Program: samantha@nist.gov
Consortium website: https://g gov/xnV3

NIST Genome Editing Consortium

MISSION

Convene experts across academia, industry, non-profit & government to addresses the measurements and standards needed to increase confidence of utilizing genome editing technologies in research and commercial products.

CONSORTIUM GOALS

Qualify genomic assays used to evaluate genome editing outputs

Develop control materials

Develop reference data and standard metadata formats

Develop community norms for minimum information reporting

Generate a common genome editing lexicon

CONSORTIUM PARTICIPATION

Requires formal membership

Uses a cost sharing model

Participants contributes cash or non-cash *in-kind* contributions towards achieving the consortium goals

Samantha Maragh
Leader, Genome Editing Program
Samantha@nist.gov
Consortium website:
https://go.usa.gov/xnV3

For More

Upcoming webinar:

- Manufacturing Challenges Facing Cell & Gene Therapy
- September 19 – 11am ET
- Contact Lyndsey Scull to register - Lscull@alliancerm.org

Visit **www.alliancerm.org** to access additional resources, including:

- Quarterly sector data reports
- Upcoming near-term clinical trial milestones & data readouts
- Access to slides, graphics, and figures from ARM presentations
- Our weekly sector newsletter, a robust round-up of business, clinical, scientific, and policy news in the sector
- Commentary from experts in the field

For additional information, please contact:

- Michael Lehmicke, Director of Science & Industry Affairs
  mlehmicke@alliancerm.org

Thank You!

Alliance for Regenerative Medicine