Landscape and Evolution of the Cell & Gene Therapy Marketplace:

Public Policy Considerations

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IO360

#IO360nyc

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@alliancerm

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
  - **Analysis, communication**, and education
  - Facilitating sustainable access to **capital**

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ARM Members Active in IO Include:

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- Adaptimmune Tx
- Adicet Bio
- Artiva BioTx
- Astellas Pharma
- Atara BioTx
- Autolus Tx
- Bellicum Pharma
- bluebird bio
- Cabaletta
- Carisma Tx
- Cartherics
- Celgene / BMS
- Cell Medica
- Cellect Bio
- CBMG
- CRISPR Tx
- Editas
- ElevateBio
- ExCellThera
- Fate Tx
- Gamida Cell Tx
- GammaDelta Tx
- Genprex
- GSK
- Intellia Tx
- Iovance BioTx
- Janssen (J&J)
- Kite / Gilead
- Legend Bio
- Magenta Tx
- MaxCyte
- Minerva Bio
- MolMed
- Mustang Bio
- NexImmune
- Nkarta
- Novartis
- Nkarta
- Novartis
- OncoSenX
- Oxford BioMedica
- PDC*line Pharma
- Pfizer
- Poseida Tx
- Precigen
- Precision Bio
- Sangamo Tx
- Takeda
- T-knife
- Tessa Tx
- Tmunity Tx
- Unum Tx
- WindMIL Tx
- Zelluna Immunotherapy
- Ziopharm Oncology

CAR-T, TCR, NK Cell, TILs/MILs, Gamma Delta, and More

Background

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- Cell, gene, and immunotherapies represent the future of treating and curing disease.
  - These technologies can significantly disrupt the way physicians treat patients.
- The manufacturing, distribution, and patient access experience is significantly different from many of the current processes and models.
- **Many government reimbursement methodologies are ill equipped to support appropriate access to these therapies** and adequately reimburse manufacturers for providing them.

Modernizing Current Reimbursement Methodologies

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- ARM supports market access policies that are **patient-focused while also stimulating and rewarding innovation**.
    - This is complicated by the current political and policy environment in Washington.
- Most IO therapies are accessed in the inpatient setting.
- Some therapies are administered in the outpatient setting (mainly clinical trials); a trend toward outpatient delivery is anticipated.
- The combination of the current environment and site of care presents different challenges and opportunities.

Key Policy Issues Facing ARM Members in 2020

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Inpatient Setting

- Providing equal access to CAR-T therapies.
  - Current add-on payment set to expire later in 2020.
  - ARM working on new bundled payment for providing CAR-T.

Outpatient Setting

- Create a Value Based Contracting process.
- Protect market-based pricing, oppose government price controls and/or the "importation" of a foreign price.

New Analysis of 10 Year Cost Impact of Cell & Gene Therapy

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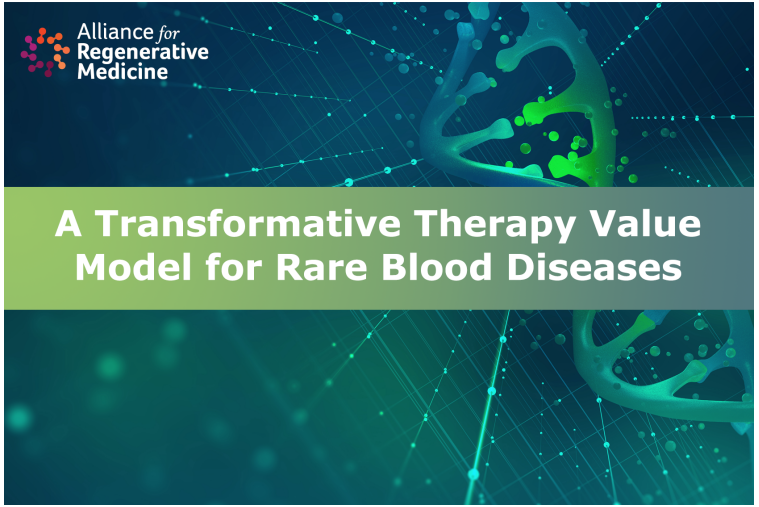

- A Transformative Therapy Value Model (TVM): a refined model developed to evaluate long-term value of regenerative medicines.
- Employs 10-year timeframe used by US Congressional Budget Office.
- Sickle cell disease, hemophilia A, and multiple myeloma are case studies.
- Conclusion: **cell and gene therapies could provide cost savings of 18-30% over a 10-year period** in these indications.

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Global Regulatory Issues

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Maintaining an effective regulatory framework

- In the US – Hundreds of unregulated stem cell clinics; strong FDA regulatory enforcement needed; regulation of novel and platform technologies.
- In Europe – Growing use of Hospital Exemption for commercial purposes; need to limit use of HE to research setting.

Refining guidance for CGTs

- CMC issues at play much earlier in the development process than with conventional therapies.
- January 2020 FDA CMC guidance – manufacturing, characterization, controls, process validation.
- CAR-T specific guidance expected in 2020.

Harmonization Across Major Markets

CGTs encompass a wide spectrum of products, each with their own concerns

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Autologous single product lot

Large scale allogeneic cell bank-based product

Common Concerns

Mechanism of action, material qualification, challenges establishing specifications, manufacturing facility, product shipping/handling, major manufacturing changes

Specific Concerns

- Product tracking and segregation
- High product variability (collection)
- Limited material or time for testing
- Short shelf life
- Manufacturing logistics
- Scale-out

- Donor eligibility
- Qualification of cell banks
- Reproducibility of replacement bank
- Stability of cell banks and intermediates
- Scale up

Slide from the US FDA

FDA vs. EMA – Disharmony?

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Areas of Significant Difference	Impact
1. Timing and extent of GMP implementation	Stage specific GMP program designed for US may not meet EU requirements
2. In the EU, a Potency Assay with Acceptance Criteria is required for Ph1/FIH trials	Delay to start of ph. 1 clinical trial in EU vs. US
3. In the EU, a Qualified Person must ensure GMP compliance and authorizes FP release	US sponsors must hire a QP. Logistical issues.
4. US Cleanroom Air Classification Standards differ from European Guidelines	EU requirement for Grade B vs. ISO 7 "background" disqualifies many US facilities
5. In the US, testing laboratories must be CLIA certified	Allogeneic cell line derived in EU not usable in US
6. Disease-specific donor testing requirements are not harmonized	Allogeneic cell lines

Source: IQVIA/ARM EU-US Regulatory Analysis Copyright © 2019 IQVIA.