Regenerative Medicine: New Paradigms

Emile Nuwaysir, Chair
Janet Lambert, CEO

January 10, 2022
In 2021, we challenged the constraints, and the scientific dogma:

<table>
<thead>
<tr>
<th>Constraint:</th>
<th>Challenged By:</th>
</tr>
</thead>
<tbody>
<tr>
<td>“CAR-Ts are a last line of defense.”</td>
<td>CAR-T outperforms 2nd line SoC</td>
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<td>“Immune rejection will limit allogeneic cell utility.”</td>
<td>Allo-edited CAR-T cells match auto cells</td>
</tr>
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<td>“<em>In vivo</em> gene editing is in the future, not now.”</td>
<td>Curative <em>in vivo</em> CRISPR editing in liver</td>
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<td>“Genetic medicines change DNA sequence.”</td>
<td>The promise of altering the genome “memory”</td>
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<td>“Damage that has already occurred can’t be reversed.”</td>
<td>“Reversible” damage from AADC deficiency?</td>
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<td>“Complex, polygenic diseases are out of reach.”</td>
<td>Cell therapy can restore lost function in diabetes</td>
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</table>
Pushing the Frontier

- Moving earlier in the patient journey, with durable cures
- Broadening accessibility
- Medicines that blur the line between prevention and cure
2021 Highlights & Looking Ahead to 2022
ARM is the Global Voice of the Sector

Representing 400+ members worldwide

Promote Clear Regulation
Enable Innovative Reimbursement
Address Manufacturing Barriers
Educate Stakeholders
The next era of regenerative medicine
Investment Landscape
Long-term growth and short-term volatility

- Record breaking investment
- Gene editing rising in prominence
- Venture capital ascendant
- Down year for public equities
$23.1B raised in 2021
↑16% from 2020
$23.1B raised in 2021
↑ 16% from 2020

- $10.6B RAISED IN GENE THERAPY
  14% increase YoY
- $10.1B RAISED IN CELL IO
  26% increase YoY
- $2.0B RAISED IN CELL THERAPY
  15% decrease YoY
- $341M RAISED IN TISSUE ENGINEERING
  10% increase YoY
$23.1B raised in 2021
↑ 16% from 2020

$18.0B RAISED BY US DEVELOPERS
53% increase YoY

$3.3B RAISED BY EUROPEAN DEVELOPERS
8% decrease YoY

$2.2B RAISED BY APAC DEVELOPERS
4% decrease YoY
Gene Editing Gains Prominence

The proportion of gene therapy financings raised by companies active in gene editing increased from 38% to 45% over the past 3 years.
Venture Capital Drives Record-Breaking Investment

- **VC**: $9.8B (↑73% YoY)
- **IPO**: $4.8B (↑30% YoY)
- **Follow On Financing**: $3.7B (↓38% YoY)
- **Corporate Partnerships**: $2.3B (↓23% YoY)
- **Private Placement / PIPEs**: $1.9B (↑50% YoY)
- **SPAC**: $566M (Increase from 0)

**Year-Over-Year Changes:**
- $2B
- $4B
- $6B
- $8B
- $10B
Market Factors Depress Public Equity Performance
Commercial & Clinical Landscape
Approvals of New Products in 2021

**Breyanzi** (US)
CAR-T Therapy
DLBCL
BMS

**Abecma** (US & EU)
CAR-T Therapy
Multiple myeloma
bluebird bio & BMS

**Stratagraft** (US)
Tissue Therapy
Severe burns
Mallinckrodt

**Skysona** (EU)
Gene Therapy
Cerebral ALD
bluebird bio

**Carteyva** (China)
CAR-T Therapy
LBCL
JW Therapeutics

**Rethymic** (US)
Tissue Therapy
Congenital Athymia
Enzyvant

* RMAT designated product
2,261 Ongoing Global Clinical Trials in Regenerative Medicine

**CANCER**
Including leukemias, lymphomas, breast cancer, brain cancer, lung cancer, prostate cancer, & others

**NEUROLOGICAL**
Including disorders such as Alzheimer’s, Parkinson’s, ALS, multiple sclerosis, cerebral palsy & others

**DIABETES**
Including Type 1 & Type 2, as well as related conditions such as diabetic kidney failure

**CARDIOVASCULAR**
Including damage caused by heart attack and vascular disease

**RARE DISEASES**
Including many fatal diseases that affect infants and children

**STROKE**
Including stroke recovery and paralysis due to stroke

*Data as of Q3 2021*
1,129 Industry-Sponsored Clinical Trials

Gene Therapy: 222
- Ph 1: 43
- Ph 2: 132
- Ph 3: 47
- Total: 225

Cell-Based IO: 465
- Ph 1: 31
- Ph 2: 209
- Ph 3: 225
- Total: 465

Cell Therapy: 424
- Ph 1: 62
- Ph 2: 130
- Ph 3: 6
- Total: 424

Tissue Engineering: 18
- Ph 1: 1
- Ph 2: 11
- Ph 3: 6
- Total: 18

1,132 Academic & Government Sponsored Trials

Gene Therapy: 84
- Ph 1: 3
- Ph 2: 57
- Ph 3: 24
- Total: 84

Cell-Based IO: 377
- Ph 1: 3
- Ph 2: 187
- Ph 3: 187
- Total: 377

Cell Therapy: 656
- Ph 1: 67
- Ph 2: 156
- Ph 3: 433
- Total: 656

Tissue Engineering: 15
- Ph 1: 1
- Ph 2: 6
- Ph 3: 8
- Total: 15

Data by GlobalData. *Data as of Q3 2021
Looking Ahead: 2022+

• 2022 is a big year for rare disease approvals...
• ... amid an evolving shift in focus to more prevalent diseases in coming years
# Upcoming Cell & Gene Therapy Regulatory Decisions

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<td><strong>uniQure/CSL</strong>&lt;br&gt;Hemophilia B</td>
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- **Janssen/Legend**: Multiple Myeloma
- **BioMarin**: Hemophilia A
- **PTC Therapeutics**: AADC Deficiency
- **GenSight Bio**: LHON
- **Atara Bio**: EBV+ PTLD
- **Krystal Bio**: Epidermolysis Bullosa
- **uniQure/CSL**: Hemophilia B
- **bluebird bio**: Beta thalassemia, Cerebral ALD
- **bluebird bio**: Sickle Cell Disease
- **CARsgen**: Hemophilia B
- **CRISPR / Vertex**: Sickle Cell & Beta Thal
- **Adaptimmune**: MLD
- **Orchard**: Wiskott-Aldrich

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**Regions**: United States, Europe

**Decisions**: BLA/MAA submitted, BLA/MAA planned
Late-stage data readouts
• Pfizer, BioMarin, Solid Bio

Early data in prevalent disorders
• Vertex

Gene editing continues march to the clinic
• ViaCyte/CRISPR, Beam, Verve begin trials
• Data from Caribou, Intellia, & others
Beyond 2022

Evolution from rare monogenetic diseases and cancers to more prevalent 10-20 approvals a year by 2025?

Examples of Ph 3 Industry Trial Indications:

- Bladder Cancer
- Breast Cancer
- Cartilage Defects
- Cirrhosis
- Congestive Heart Failure
- Critical Limb Ischemia
- Diabetic Foot Ulcers
- Diabetic Neuropathy
- Esophageal Cancer
- Glioblastoma
- Head & Neck Cancer
- Leukemia & Lymphoma
- Lung Cancer
- Macular Degeneration
- Myocardial Infarction
- Osteoarthritis
- Ovarian Cancer
- Prostate Cancer
- Refractory Angina
Jayla Turner

Jayla was born in 2007 and diagnosed with complete DiGeorge syndrome

Without treatment, life expectancy is 2-3 years

She received the therapy now known as Rethymic in 2008

Jayla is now 14 years old in the 9th grade

She enjoys gymnastics, cheering, & volleyball and is an honor roll student
Visit us at www.alliancerm.org!

Slides & a recording of this presentation will be made available at bit.ly/2022-SOTI

Stay up-to-date with ARM’s newsletter, *The Sector Vector*: bit.ly/ARM-SV

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Alliance for Regenerative Medicine
2022: A Banner Year for Rare Genetic Disease Therapies?