Business of Regenerative Medicine

Sector Overview

Janet Lambert, CEO
July 15, 2019
About ARM

• **International advocacy organization**
  • dedicated to realizing the promise of safe and effective regenerative medicines for patients around the world

• **330+ members**
  • Small and large companies, non-profit research institutions, patient organizations, and other sector stakeholders

• **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***
Current Global Sector Landscape

917+
Regenerative Medicine Companies Worldwide, including Gene and Cell Therapies, and Tissue Engineering Therapeutic Developers

502 North America

233 Europe & Israel

145 Asia

23 Oceania
Australia, New Zealand, Marshall Islands

13 South America

1 Africa

Source data provided by: informa
Total Targeted Enrollment of Patients in Current Regenerative Medicine Clinical Trials Worldwide

- **9,533** Target Enrollment of Phase I Clinical Trials
- **29,069** Target Enrollment of Phase II Clinical Trials
- **20,973** Target Enrollment of Phase III Clinical Trials

Source data provided by: informa
Patient Impact of Recently Approved Products

40% of patients with R/R DLBCL treated with Novartis’s Kymriah experienced a complete response

60% of patients with R/R B-Cell ALL treated with Novartis’s Kymriah experienced a complete response

55% of patients treated with Spark Therapeutics’ Luxturna showed an improvement of 2+ light levels darker after treatment

93% of patients with AveXis / Novartis’s SMA Type 1 treated with Zolgensma were alive without permanent ventilation at 24 months post-treatment

75% of patients with TDT without β0/β0 genotype treated with bluebird bio’s Zynteglo achieved transfusion independence
### Select Anticipated Near-Term Approvals (Global)

#### Gene Therapy
- **Zolgensma** (AveXis / Novartis)
  - Spinal muscular atrophy type 1
  - Decision expected: mid 2019 (EU & Japan)
- **GT-AADC** (PTC Therapeutics)
  - AADC deficiency
  - Expects to file: Q4 2019 (US & EU)
- **Zynteglo** (bluebird bio)
  - Beta thalassemia
  - Expects to file: 2019 (US)
- **Valoctocogene roxaparvovec** (BioMarin)
  - Hemophilia A
  - Expects to file: Q4 2019 (US & EU)
- **GS010** (GenSight Biologics)
  - Leber hereditary optic neuropathy
  - Expects to file: Q4 2019 (EU) / H2 2020 (US)
- **OTL-101** (Orchard Therapeutics)
  - ADA-SCID
  - Expects to file: 2020 (US)
- **OTL-200** (Orchard Therapeutics)
  - Metachromatic leukodystrophy
  - Expects to file: 2020 (US & EU)

#### Cell-Based IO
- **Rivo-cel** (Bellicum Pharmaceuticals)
  - HSCT to treat blood cancers
  - Expects to file: EOY 2019 (EU)
- **ATIR101** (Kiadis Pharma)
  - HSCT to treat blood cancers
  - Decision expected: 1H 2020 (EU)
- **Remestemcel-L** (Mesoblast)
  - Acute graft versus host disease
  - Decision expected: 2020 (US)
- **P-BCMA-101** (Poseida Therapeutics)
  - Multiple myeloma
  - Expects to file: 2020 (US)
- **Lifileucel** (Iovance)
  - Advanced metastatic melanoma
  - Expects to file: 2020 (US)
- **LN-145** (Iovance)
  - Advanced metastatic cervical cancer
  - Expects to file: 2H 2020 (US)

#### Cell Therapy
- **SB623** (SanBio)
  - Traumatic brain injury
  - Expects to file: January 2020 (Japan)
- **TEMCELL** (Mesoblast / JCR Pharma)
  - Epidermolysis bullosa
  - Decision expected: 2020 (Japan)

#### Tissue-Based
- **RVT-802** (Enzyvant Therapeutics)
  - Complete DiGorge anomaly
  - Decision expected: 2019 (US)
- **Humacyl** (Humacyte)
  - End stage renal disease
  - Expects to file: 2020 (US)
- **Stratagraft** (Mallinckrodt)
  - Deep partial thickness burns
  - Expects to file: 2020 (US)
Regenerative Medicine Clinical Trials by Phase and Technology Type

Phase 1: 349 across all tech types and indications
- Gene Therapy: 123
- Gene-Modified Cell Therapy: 160
- Cell Therapy: 55
- Tissue Engineering: 11

Phase 2: 618 across all tech types and indications
- Gene Therapy: 217
- Gene-Modified Cell Therapy: 197
- Cell Therapy: 182
- Tissue Engineering: 22

Phase 3: 93 across all tech types and indications
- Gene Therapy: 32
- Gene-Modified Cell Therapy: 17
- Cell Therapy: 31
- Tissue Engineering: 13

Total Regenerative Medicine Clinical Trials: 1,060

Source data provided by: informa
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#### Regenerative Medicine Clinical Trials by Therapeutic Area

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Number of Trials</th>
</tr>
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<tbody>
<tr>
<td>Oncology</td>
<td>618</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>67</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>60</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>56</td>
</tr>
<tr>
<td>Endocrine, Metabolic, and Genetic Disorders</td>
<td>44</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>38</td>
</tr>
<tr>
<td>Dermatology</td>
<td>36</td>
</tr>
<tr>
<td>Immunology and Inflammation</td>
<td>36</td>
</tr>
<tr>
<td>Hematology</td>
<td>35</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>21</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>15</td>
</tr>
<tr>
<td>Genitourinary Disorders</td>
<td>14</td>
</tr>
<tr>
<td>Respiratory</td>
<td>10</td>
</tr>
<tr>
<td>Surgery</td>
<td>3</td>
</tr>
<tr>
<td>Lymphatic Diseases</td>
<td>3</td>
</tr>
<tr>
<td>Geriatric Diseases</td>
<td>2</td>
</tr>
<tr>
<td>Ear Diseases</td>
<td>2</td>
</tr>
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</table>

- **58% (618)** of all current clinical trials are in **oncology**, including leukemia, lymphoma, and cancers of the brain, breast, bladder, cervix, colon, esophagus, ovaries, pancreas, and others.

- **6% (67)** are in **cardiovascular disorders**, including congestive heart failure, myocardial infarction, critical limb ischemia, heart disease, and others.

- **60 (6%)** are in **central nervous system disorders**, including multiple sclerosis, Alzheimer’s disease, Parkinson’s disease, traumatic brain injury, ALS, and others.
# Total Global Financings: Q2 2019

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Global Financings</th>
<th>Q2 2019</th>
<th>YTD 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Global Financings</td>
<td>$2.5B</td>
<td>$2.2B</td>
<td></td>
</tr>
<tr>
<td>Gene-Based Therapies</td>
<td>$2.2B</td>
<td>$4.3B</td>
<td></td>
</tr>
<tr>
<td>Cell Therapy</td>
<td>$691M</td>
<td>$1.5B</td>
<td></td>
</tr>
<tr>
<td>Tissue Engineering</td>
<td>$53M</td>
<td>$67M</td>
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</table>

*YTD financings calculated as of the end of Q2 2019
*Both Gene-Based Therapies & Cell Therapy categories include financings from companies active in developing gene-modified cell therapies

Source data provided by: informa
2018 was a watershed year for regenerative medicine financings.

- Highest total financings raised in recent years
- In 2018, there were **eight IPOs** for regenerative medicine companies that raised **$100M+**
- The public performance averages for all RM/AT companies, cell-based IO companies, and gene therapy companies were higher than the Nasdaq Index and Nasdaq Biotech Index for the majority of the year.

2019 is on track to reach or exceed 2018 venture capital financings and upfront payments from corporate partnerships.
Total Financings by Type, by Year

Corporate Partnerships (Upfront Payments Only)
- YTD 2019: $912
- 2018: $1,563
- 2017: $1,088

Private Placements / PIPES
- YTD 2019: $500
- 2018: $1,237
- 2017: $689

Follow On / Secondary Public Offering
- YTD 2019: $979
- 2018: $4,715
- 2017: $3,995

IPO
- YTD 2019: $387
- 2018: $1,927
- 2017: $254

Venture Capital
- YTD 2019: $1,801
- 2018: $2,913
- 2017: $1,451

YTD 2019 is over half full-year 2018
YTD 2019 nearly two thirds full-year 2018 totals

Source data provided by: informa
Total M&A Transactions Values, By Year

*Does not include Roche’s planned $4.3B acquisition of Spark Therapeutics (expected to close by EOY 2019).
Select Corporate Partnerships & Public Financings in 1H 2019

Corporate Partnerships: (Upfront Payments)
• Adaptive Biotechnologies signs $300M upfront agreement with Genentech/Roche – January 4
• Vertex signs $175M upfront agreement with CRISPR Tx – June 6
• Neurocrine Biosciences completes $115M upfront agreement with Voyager Tx – January 29
• MeiraGTx signs $100M upfront agreement with Janssen – January 31
• Voyager Tx $65M upfront agreement with AbbVie – February 22

Private Placements & Venture Financings:
• Maze Tx raises $191M in venture funding – February 28
• Poseida raises $142M in Series C – April 22
• Beam Tx secures $135M in Series – March 6
• AlloVir raises $120M in Series B – May 22
• Passage Bio raises $115.5 Million in Series A – February 15
• Talaris Tx raises $100M in Series A – April 18
• Gracell raises $85M in Series B – February 25
• MeiraGTx raises $80M in private placement – February 27
• Inovio raises $70M in private offering – February 19
• Oxford Biomedica raises $68M in private placement – May 28

Public Offerings: (IPOs & Follow-Ons)
• Sangamo raises $145M in follow-on offering – April 8
• Precision Bio raises $145M in IPO – April 1
• Homology raises $144M in follow-on offering – April 12
• Orchard Tx raises $128M in follow-on offering – June 3
• Prevail Tx raises $125M in IPO – June 24
• Autolus raises $115.9M in follow-on offering – April 15
• Krystal Bio raises $115M in follow-on offering – June 24
• Rocket Pharma raises $91M in follow-on offering – April 19
• TCR2 Tx raises $86.25M in IPO – February 19
<table>
<thead>
<tr>
<th>Country</th>
<th>Products</th>
<th>HTA/Payer Opinion</th>
<th>Reimbursed</th>
</tr>
</thead>
<tbody>
<tr>
<td>France (TC/CEESP)</td>
<td>Alofisel</td>
<td>★</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Yescarta</td>
<td>★</td>
<td>✓</td>
</tr>
<tr>
<td>Germany (IQWIG/G-BA)</td>
<td>Holoclar</td>
<td>★</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Imlygic</td>
<td>★</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Kymriah</td>
<td>★</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Luxturna</td>
<td>★</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Strimvelis</td>
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<td></td>
<td>Yescarta</td>
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<td>✓</td>
</tr>
<tr>
<td></td>
<td>Zalmoxis</td>
<td>★</td>
<td>✓</td>
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<tr>
<td>UK (NICE/SMC)</td>
<td>Holoclar</td>
<td>★</td>
<td>✓</td>
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<tr>
<td></td>
<td>Imlygic</td>
<td>★</td>
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</tr>
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<td></td>
<td>Kymriah</td>
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<td></td>
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<td>✓</td>
</tr>
<tr>
<td></td>
<td>Yescarta</td>
<td>★</td>
<td>✓</td>
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<tr>
<td>Italy (AIFA/regional)</td>
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<td>✓</td>
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<td>Imlygic</td>
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<td>Zalmoxis</td>
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<td>Netherlands (ZIN/CVZ)</td>
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<td></td>
<td>Kymriah</td>
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<td>Yescarta</td>
<td>★</td>
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<td>U.S. (CMS)</td>
<td>Holoclar</td>
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<td></td>
<td>Zalgensma</td>
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Zynteglo, which was approved in Europe in June 2019, is currently working with payers in UK, Italy, Germany, France for its initial commercial rollout in 2020.
For More

This presentation will be available on our website and shared via Twitter at @alliancerm

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- 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
Thank You!