Gene Therapy Sector Overview

The Art of Gene Therapy Summit

Janet Lambert, CEO
July 28, 2020
About ARM

• Leading international advocacy organization representing the regenerative medicine and advanced therapies sector

• Dedicated to realizing the promise of gene, cell, and tissue-based therapies for patients in need

• Priorities:
  • Clear, predictable, and harmonized regulatory pathways
  • Enabling market access and value-based reimbursement policies
  • Addressing industrialization and manufacturing hurdles
  • Compile sector data, educate media and other stakeholders
**Gene Therapy**
- Abeona Tx
- AGTC
- AskBio
- Astellas/Audentes
- BioMarin
- bluebird bio
- Caribou Biosciences
- CRISPR Tx
- Editas Medicine
- Genentech
- GlaxoSmithKline
- Intellia Tx
- Orchard Tx
- Pfizer
- PTC
- Sangamo Tx
- Sanofi
- Sarepta
- Spark Tx
- UltraGenyx
- UniQure
- Voyager Tx

**Cell Therapy**
- Atara Bio
- Athersys
- Autolus
- Bellicum
- BlueRock Tx
- BMS
- Celyad
- CSL Behring
- Gilead/Kite
- Iovance
- Johnson & Johnson
- Kiadis Pharma
- Lyell
- Mesoblast
- MilliporeSigma
- Novartis
- Pluristem Tx
- ReNeuron
- Semma Tx
- Takeda Pharma
- Thermo Fisher
- Tmunity Tx

**Tissue Engineering**
- Ankasa Regen Tx
- Aspect Biosystems
- Avita Medical
- Avery Tx
- AxoGen
- BioStage
- Castle Creek Bio
- CDI/Fujifilm
- Enzyvant
- Histogen
- MEDIPOST America
- MiMedx
- Miromatrix Medical
- Novadip Biosciences
- PolarityTE
- Sigilon
- STEL Technologies
- StemBioSys
- Theradaptive
- Verigraft
- Videregen

**Non-Profit & Academic Institutions**
- AABB
- Baylor Medicine
- CCRM
- CG Therapy Catapult
- CIRM
- City of Hope
- CureDuchenne
- FARA
- Fondazione Telethon
- Fraunhofer Institute
- Fred Hutch
- GENETHON
- Global Genes
- Leukemia & Lymphoma Society
- Missouri Cures
- M.J. Fox Foundation
- MSK Cancer Center
- Northwestern Univ.
- NYSCF
- Texas Heart Institute
- Univ. of Pennsylvania

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*ARM is the Voice of the Sector*

*360+ Members Across 25 Countries*
Benefits of Membership

**Sector Partners**
Engage with patient advocacy groups & research institutions

**Fundraising**
Gain exposure to the investment community

**Science & Technology**
Work with other manufacturing and technology experts to reduce barriers to product development and scale

**Information**
Access proprietary industry data and sector news

**Network**
Meet commercial RM leaders and potential partners

**Exposure**
Present your work at influential ARM events

**Sector initiatives**
Help shape sector-wide initiatives, policy priorities, and policy positions

**Influence**
Collectively engage with lawmakers and key government agencies in the US and EU
EOY 2019

State of the Sector Pre-COVID-19
2019 Global Sector Landscape

496+ Gene Therapy Developers Worldwide

North America: 271

South America: 2

Europe & Israel: 109

Asia: 107

Oceania: 7

Australia, New Zealand, Marshall Islands
## Patient Impact of Recently Approved Products

<table>
<thead>
<tr>
<th>Therapy Name</th>
<th>Product Developer</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zynteglo</td>
<td>bluebird bio</td>
<td>• 75% of patients with TDT without β0/β0 genotype treated achieved transfusion independence</td>
</tr>
<tr>
<td>Zolgensma</td>
<td>AveXis, a Novartis company</td>
<td>• 93% of SMA Type 1 patients treated were alive without permanent ventilation at 24 months post-treatment</td>
</tr>
<tr>
<td>LUXTURNA</td>
<td>Spark Therapeutics</td>
<td>• 93% of patients treated showed an improvement of at least 1 light level from baseline</td>
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<tr>
<td>Yescarta</td>
<td>Kite Pharma, a Gilead company</td>
<td>• 58% of patients with R/R B-Cell NHL treated experienced a complete response</td>
</tr>
<tr>
<td>Tecartus</td>
<td>Kite Pharma, a Gilead company</td>
<td>• 62% of patients with R/R B-Cell mantle cell lymphoma treated experienced a complete response</td>
</tr>
<tr>
<td>Kymriah</td>
<td>Novartis</td>
<td>• 40% of patients with R/R DLBCL treated experienced a complete response</td>
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<tr>
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<td>• 82% of patients with R/R B-Cell ALL treated experienced complete remission or complete remission with incomplete hematologic recovery</td>
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- 60,000+ patients to be enrolled in RM clinical trials
- 500,000+ patients treated with cell and gene therapies by 2030 in the US alone*

*MIT NEWDIGS estimate
2019 was a significant year of growth for the regenerative medicine sector.
Where are we now?

Sector Trends in H1 2020
Total Global Financings by Year

2020 is on track to surpass 2018 as the highest year on record for gene & cell therapy financing

Source data provided by: informa

**M&A not included**
Cell & Gene Therapy Financing Explodes

“From my perspective, the delays so far in the cell and gene therapy space have not been as meaningful as they could have been [...] What I do think is unappreciated is the ability for one-time treatments to actually mitigate some of these issues in the future, and that’s what gene therapy is all about. You treat a patient once and they’re done.”

Gbola Amusa, Partner, Director of Research & Head of Healthcare Research, Chardan

Despite COVID-19, it has been a strong first half for biotech fundraising:

- 5+ cell and gene therapy companies have gone public since the beginning of the year
  - 3 in the second quarter
- Strong public performance in the biopharma sector
- Numerous public and private financings raising $100M+
## $100M+ Financings: H1 2020

### INITIAL PUBLIC OFFERINGS

- Legend Bio – $487M (Jun 9)
- Passage Bio – $284M (Feb 3)
- Akouos – $244M (Jun 25)
- Generation Bio – $230M (Jun 12)
- Beam Tx – $207M (Feb 11)

### CORPORATE PARTNERSHIP (UPFRONT PAYMENTS ONLY)

- uniQure & CSL Behring – $450M (Jun 24)
- Biogen & Sangamo – $350M (Feb 27)
- bluebird & Bristol-Myers Squibb – $200M (May 11)
- UltraGenyx & Daiichi Sankyo – $125M (Mar 31)
- Fate Tx & Janssen – $100M (Apr 2)
- Regeneron & Intellia – $100M (Jun 1)

### PRIVATE FINANCINGS

- Sana Bio – $700M (Jun 23)
- Orca Bio – $192M (Jun 17)
- Elevate Bio – $170M (March 30)
- Legend Bio – $150M (Apr 1)
- Freeline Tx – $120M (Jun 30)
- Poseida Tx – $110M (Jun 25)
- Generation Bio – $110M (Jan 10)
- Akouos – $105M (March 3)
- JW Tx – $100M (June 9)

### FOLLOW-ON FINANCINGS

- Iovance – $604M (Jun 2)
- bluebird – $575M (May 18)
- Allogene – $550M (Jun 1)
- Adaptimmune – $259M (Jun 4)
- Editas – $216M (June 23)
- Atara Bio – $202M (Jun 24)
- Fate Tx – $201M (Jun 11)
- Adverum Bio – $150M (Feb 14)
- Krystal Bio – $125M (May 18)
- IVERIC bio – $125M (Jun 17)
- Intellia Tx – $115M (Jun 5)
- Replimune – $115M (Jun 8)
- AVROBIO – $100M (Feb 18)

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**33 total $100M+ financings**

80% took place after states in the US began issuing stay at home orders
Gene Therapy Manufacturing in the Spotlight

- New and existing CMOs and CDMOs are ramping up production capabilities
- Pre-market companies establishing manufacturing capabilities early in the development timeline
- Appetite for industry standards and best practices to improve efficiency and standardization
- The use of viral vectors in certain COVID-19 vaccine development programs could lead to more demand for scaled-up manufacturing capabilities
- Manufacturing remains the key regulatory challenge for late-stage products

Tomorrow @ 2:45PM ET:

A-Gene: Applying Quality By Design Principles To The Development And Manufacture Of Gene Therapies

*Michael Lehmicke, Director, Science & Industry Affairs, ARM*
Gene-Editing Technologies Continue to Advance

Victoria Gray, the first sickle cell patient in the US to be treated with CRISPR

- June: CRISPR Therapeutics and Vertex showed that 9 months post-treatment with CRISPR therapy CTX001, the first sickle cell patient in the trial was free of VOCs, was transfusion independent

- May: Allogene Therapeutics and Gracell Biotechnology reported initial data from clinical trials of their respective gene-edited allogeneic CAR-T therapies

- April: Editas and Allergan announced the dosing of the first patient with an in vivo CRISPR-based therapy in a trial to Leber congenital amaurosis 10

- January: Locus Bio initiated the first clinical trial of a CRISPR-enhanced bacteriophage
Innovative Therapies Progress Towards the Market
Anticipated Near-Term Approvals

Gene Therapy

ValRox (BioMarin)
- Severe hemophilia A
- Filed for approval in US and EU in December 2019

OTL-200 (Orchard Therapeutics)
- Metachromatic leukodystrophy
- Filed for approval in the EU in December 2019

PT-AADC (PTC Therapeutics)
- AADC deficiency
- Filed for approval in the EU in January 2020

Cell-Based Immuno-Oncology (IO)

liso-cel (Bristol-Myers Squibb)
- Relapsed or refractory large B cell lymphoma
- Filed for approval in the US in December 2019

Tecartus (Kite Pharma / Gilead)
- Relapsed or refractory mantle cell lymphoma
- Filed for approval in the EU in January 2020

Yescarta (Kite Pharma / Gilead & licensees)
- Relapsed or refractory B-cell lymphomas
- Fosun Kite filed in China in February 2020
- Daiichi Sankyo filed in Japan in March 2020

JWCAR029 (JW Therapeutics)
- Non-Hodgkin lymphoma
- Filed for approval in China in July 2020

Tissue Engineering

RVT-802 (Enzyvant Therapeutics)
- Pediatric Congenital Athymia
- US filing accepted for review in June 2019

Stratagraft (Mallinckrodt)
- Deep partial thickness thermal burns
- Completed rolling BLA in the US in June 2020

Cell Therapy

Ryoncil (Mesoblast)
- Acute graft versus host disease
- Completed rolling BLA in US in January 2020
EOY 2019: Clinical Landscape for Regenerative Medicine

Phase 1: 381

- Gene Therapy: 111
- Cell-Based IO: 222
- Cell Therapy: 42
- Tissue Engineering: 6

Phase 2: 591

- Gene Therapy: 209
- Cell-Based IO: 215
- Cell Therapy: 144
- Tissue Engineering: 23

Phase 3: 94

- Gene Therapy: 32
- Cell-Based IO: 15
- Cell Therapy: 30
- Tissue Engineering: 17

1,066 Ongoing Regen Med Clinical Trials
EOY 2019: Clinical Landscape for Regenerative Medicine

- Oncology: 657
- Musculoskeletal: 60
- Central Nervous System: 57
- Endocrine, Metabolic and Genetic Disorders: 55
- Cardiovascular: 46
- Hematology: 35
- Ophthalmology: 33
- Immunology and Inflammation: 31
- Dermatology: 23
- Infectious Diseases: 20
- Genitourinary Disorders: 16
- Gastroenterology: 16
- Respiratory: 10
- Geriatric Diseases: 3
- Lymphatic Diseases: 2
- Ear Diseases: 1
- Surgery: 1
Regulating Cell & Gene Therapies Amidst COVID-19

International regulators recognize the importance of continued work to meet the unmet medical needs of thousands of patients with diseases and disorders unrelated to the COVID-19 pandemic.

“Pandemic workload does get priority. But there are many other serious and life-threatening diseases out there, and we’ve got to pay attention to those as well.”

Wilson Bryan, Director, Office of Tissues and Advanced Therapies (OTAT), Center for Biologicals Evaluation and Research (CBER), FDA

“I am confident that we will be able to successfully overcome the challenge of COVID-19 and also continue to meet our mission to protect public and animal health during this quickly evolving crisis.”

Guido Rasi, Executive Director, European Medicines Agency (EMA)
**FDA & EMA Continue to Promote Accelerated Pathways**

The FDA has granted **7 RMAT designations** and the EMA has granted **2 PRIME designations** in H1 2020, on par with recent years.

<table>
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<tr>
<th><strong>RMAT DESIGNATIONS</strong>*</th>
<th><strong>PRIME DESIGNATIONS</strong></th>
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| **CRISPR Tx / Vertex – CTX001** | **MeiraGTx & Janssen – AAV-RPGR**  
Gene-editing therapy for inherited hemoglobinopathies  
**Immunicum – Ilixadencel**  
Cell therapy for kidney cancer  
**Novartis – Kymriah**  
CAR-T therapy for r/r follicular lymphoma  
**TissueTech – TTAX02**  
Tissue product for spina bifida  
**Tessa Tx – CD30 CAR-T**  
CAR-T therapy for Hodgkin lymphoma |
| **AlloVir – Viralym-M**  
Cell therapy for viral infection following HSCT |

**In total:**
- 53 product candidates granted RMAT designation
- 27 granted product candidates granted PRIME designation

* An additional 2 products granted RMAT designation this year have not been publicly announced
Policy Successes on Key ARM Issues

In the United States:

• CMS released a proposal that would allow state Medicaid programs to enter value-based payment contracts for gene and cell therapies (June)

• CMS’ FY21 IPPS draft rule includes a proposed new DRG for CAR-T therapies, ensuring appropriate reimbursement for providers (May)

In Europe:

• The EC proposed relaxing GMO requirements for vaccines and therapies targeting COVID-19 – a potential first step in creating a dialogue towards streamlining clinical trial requirements for gene therapies (June)
Looking Ahead

What to Expect in H2 2020 & Beyond
A Year Like No Other

- Development pipeline and company formation are being super charged by tremendous levels of investment
- Continued expansion of manufacturing capabilities and facilities
- Important clinical progress in gene editing and elsewhere; robust pipeline
- Despite efforts to provide flexibility in clinical trial protocols, COVID-19 trial disruptions will delay some clinical development
- Policy progress will continue alongside COVID realities, new EMA head
- FDA RMAT guidances for neurodegenerative diseases, genome editing, and CAR-T therapies, and the “N of 1” therapies for ultra-rare disorders effort, likely slowed
- Several anticipated approvals as early as 2H 2020
Advancing Innovation During COVID-19

ARM’s latest sector report will be published **Wednesday, August 5**

The report will include:
- H1 2020 financing totals
- An update on the clinical landscape
- Commentary from investors, payors, and other sector experts on the effects of COVID-19 on the sector
- An overview of cell therapy approaches to treating COVID-19
- A look at the European ATMP sector

Visit www.alliancerm.org & sign up for ARM updates to receive ARM’s H1 report straight to your inbox.
Thank You!

Visit [www.alliancerm.org](http://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

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