Gene Therapy Sector Overview

The Art of Gene Therapy Summit

Janet Lambert, CEO

July 28, 2020

Alliance *for* Regenerative Medicine

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

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ARM is the Voice of the Sector

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360+ Members Across 25 Countries

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

Benefits of Membership

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Information
Access proprietary industry data and sector news

Sector Partners
Engage with patient advocacy groups & research institutions

Network
Meet commercial RM leaders and potential partners

Fundraising
Gain exposure to the investment community

Exposure
Present your work at influential ARM events

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

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

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

EOY 2019

State of the Sector Pre-COVID-19

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2019 Global Sector Landscape

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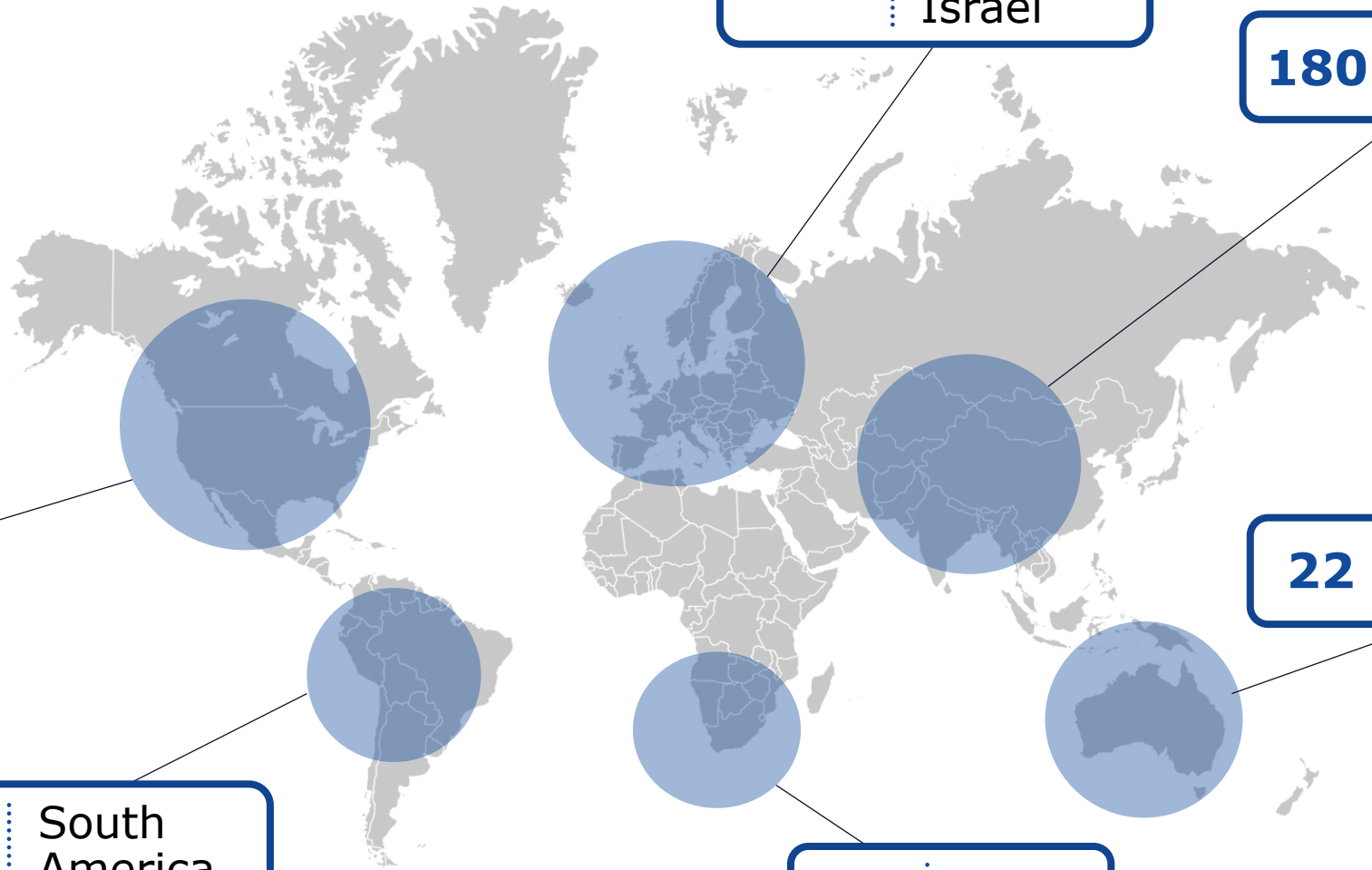
987+
Regenerative Medicine Companies Worldwide



237 Europe & Israel

180 Asia

534 North America

22 Oceania

Australia, New Zealand, Marshall Islands

13 South America

1 Africa

2019 Global Sector Landscape

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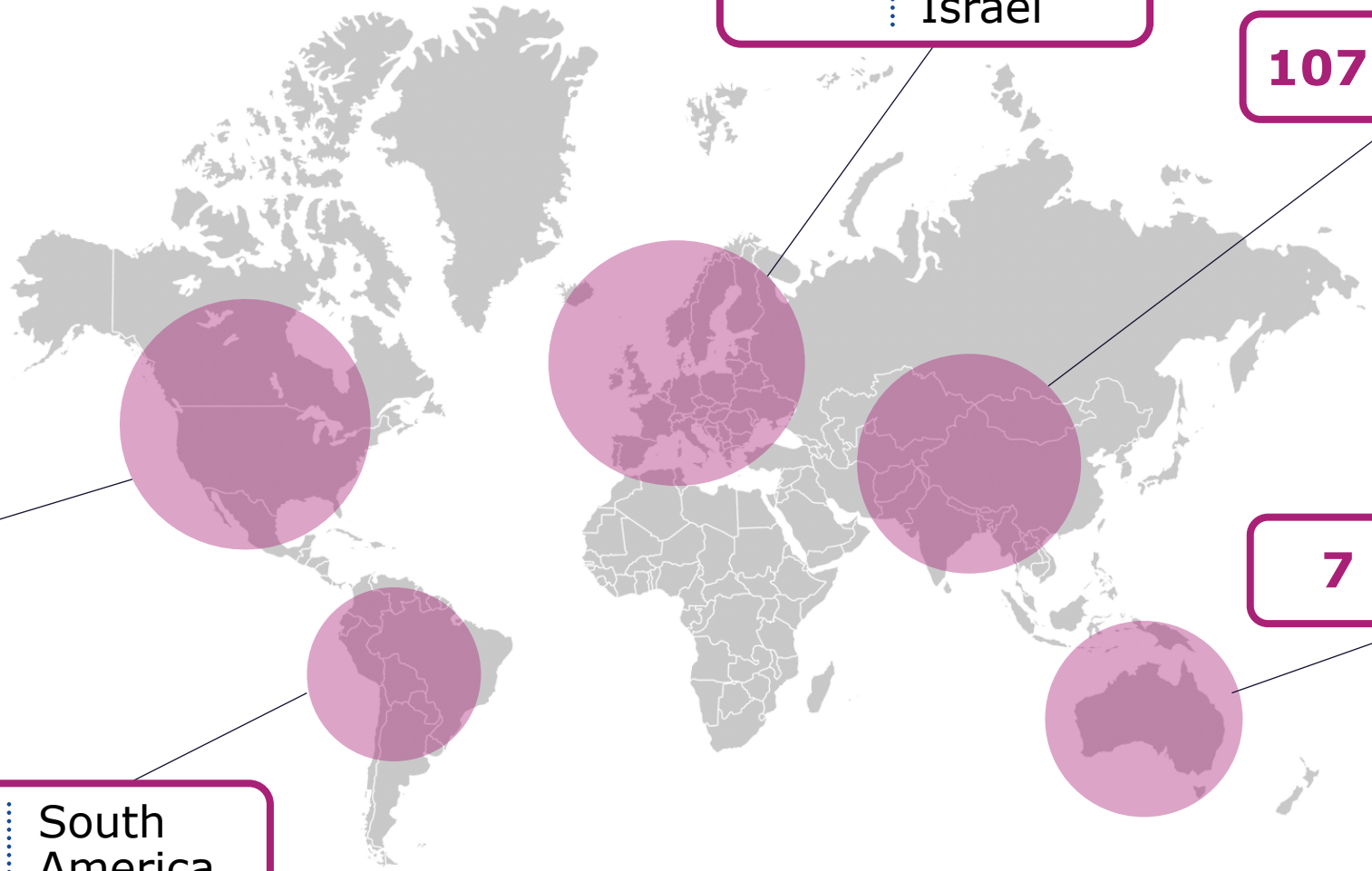
496+
Gene Therapy Developers Worldwide



109 Europe & Israel

107 Asia

271 North America

7 Oceania

Australia, New Zealand, Marshall Islands

2 South America

Patient Impact of Recently Approved Products

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Therapy Name	Product Developer	Response
Zynteglo	bluebird bio	• **75%** of patients with TDT without β0/β0 genotype treated achieved transfusion independence
Zolgensma	AveXis, a Novartis company	• **93%** of SMA Type 1 patients treated were alive without permanent ventilation at 24 months post-treatment
LUXTURNA	Spark Therapeutics	• **93%** of patients treated showed an improvement of at least 1 light level from baseline
Yescarta	Kite Pharma, a Gilead company	• **58%** of patients with R/R B-Cell NHL treated experienced a complete response
Tecartus	Kite Pharma, a Gilead company	• **62%** of patients with R/R B-Cell mantle cell lymphoma treated experienced a complete response
Kymriah	Novartis	• **40%** of patients with R/R DLBCL treated experienced a complete response • **82%** of patients with R/R B-Cell ALL treated experienced complete remission or complete remission with incomplete hematologic recovery

- *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*

State of the Sector: 2019

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17

RM Products Granted RMAT, PRIME, and/or SAKIGAKE Designations in 2019

1,066

Ongoing RM/AT Clinical Trials

$9.8B

Raised in Global Financings in 2019

2019 was a significant year of growth for the regenerative medicine sector

Where are we now?

Sector Trends in H1 2020

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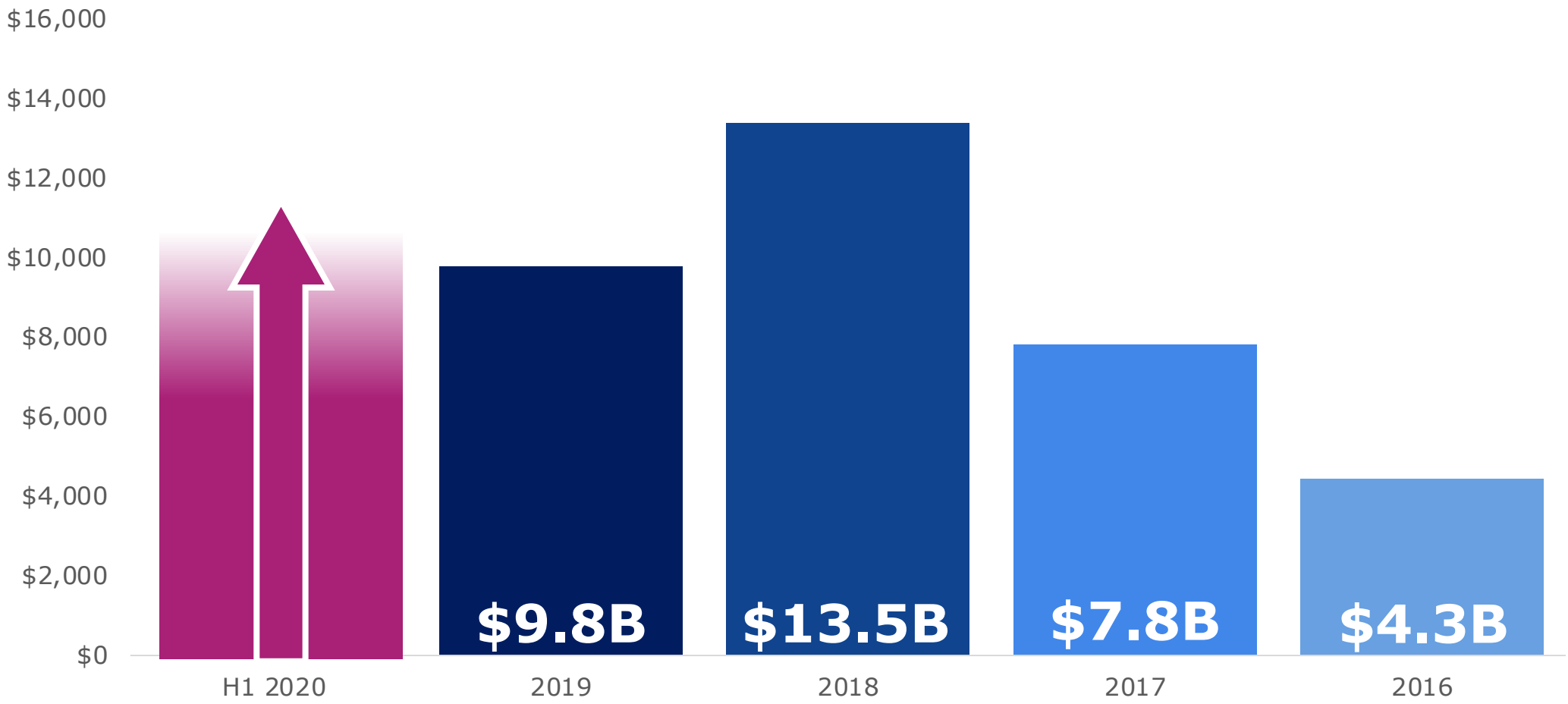
Total Global Financings by Year



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

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33 total $100M+ financings
80% took place after states in the US began issuing stay at home orders

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)

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)

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

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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

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-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

Cell Therapy

Ryoncil (Mesoblast)
- Acute graft versus host disease
- Completed rolling BLA in US in January 2020

EOY 2019: Clinical Landscape for Regenerative Medicine

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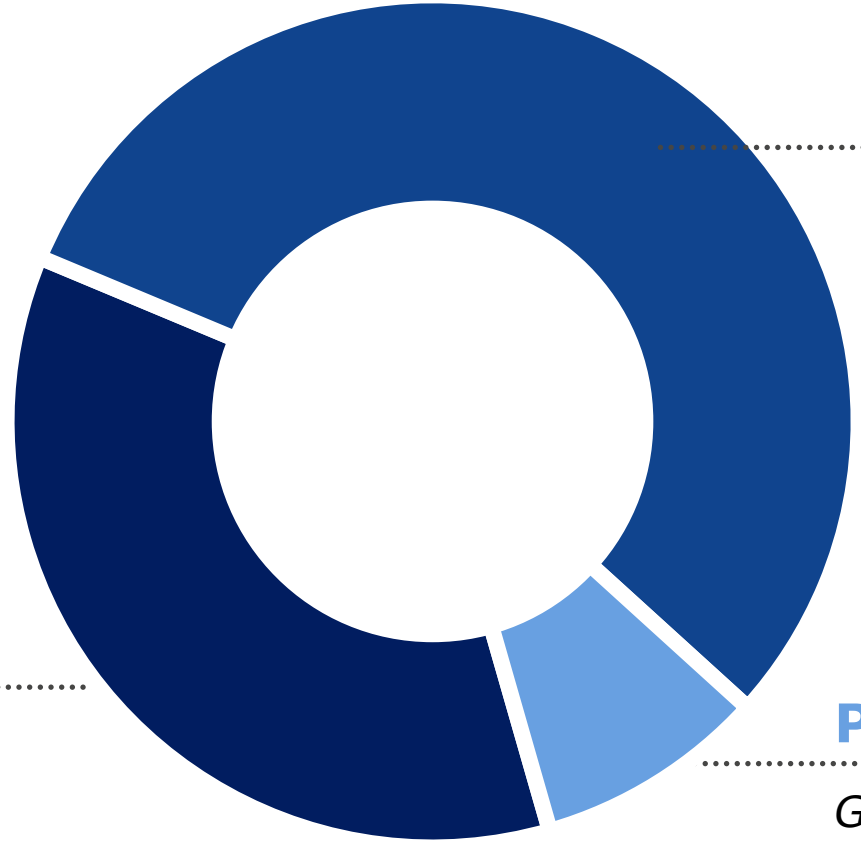
1,066
Ongoing Regen Med Clinical Trials



Phase 2: 591

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

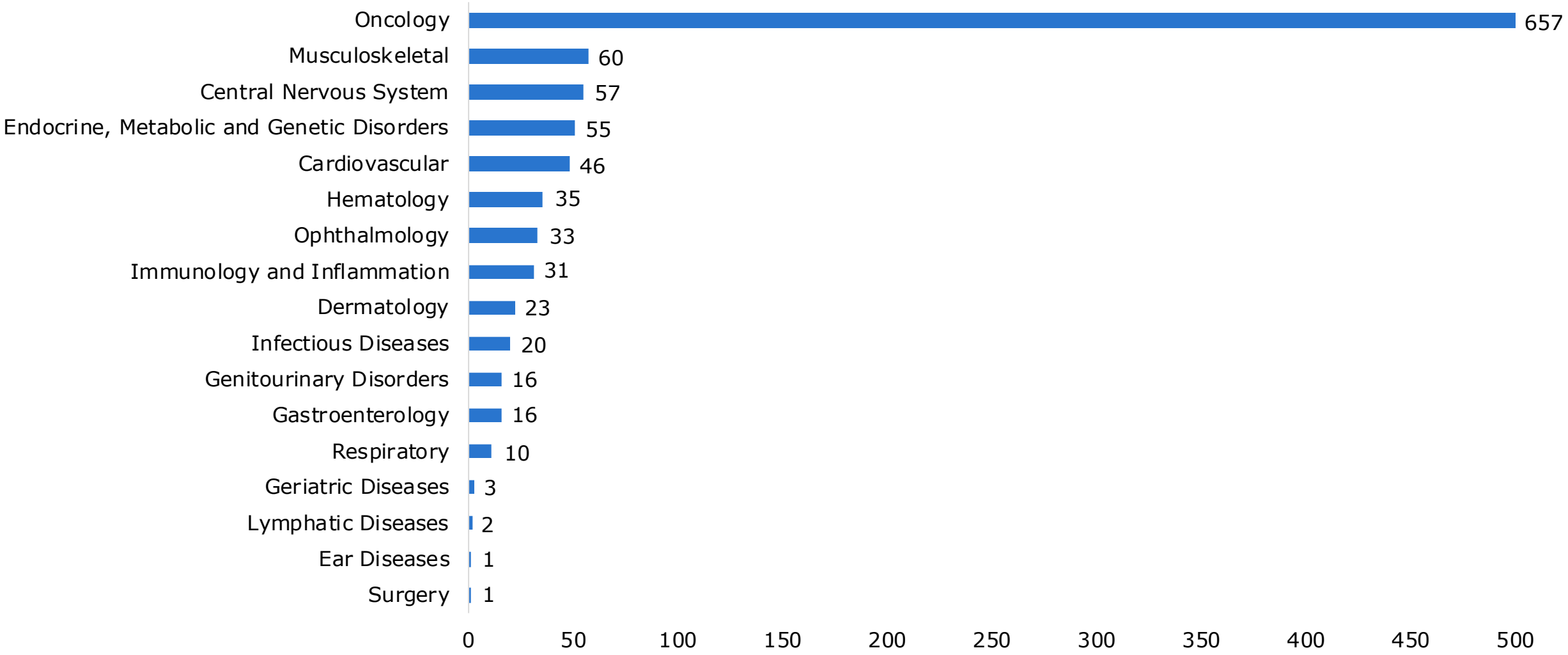
Phase 1: 381

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

Phase 3: 94

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

EOY 2019: Clinical Landscape for Regenerative Medicine



Regulating Cell & Gene Therapies Amidst COVID-19

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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

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

RMAT DESIGNATIONS*

CRISPR Tx / Vertex – CTX001
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

PRIME DESIGNATIONS

MeiraGTx & Janssen – AAV-RPGR
Gene therapy for X-linked retinitis pigmentosa

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)

ARM members meet with Congressional representatives to discuss value-based payment models for cell and gene therapies

Looking Ahead

What to Expect in H2 2020 & Beyond

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A Year Like No Other

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- 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.

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Thank You!

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

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