Cell & Gene Therapy Bioprocessing & Commercialization

Sector Overview

Janet Lambert, CEO

September 12, 2019

Alliance for Regenerative Medicine

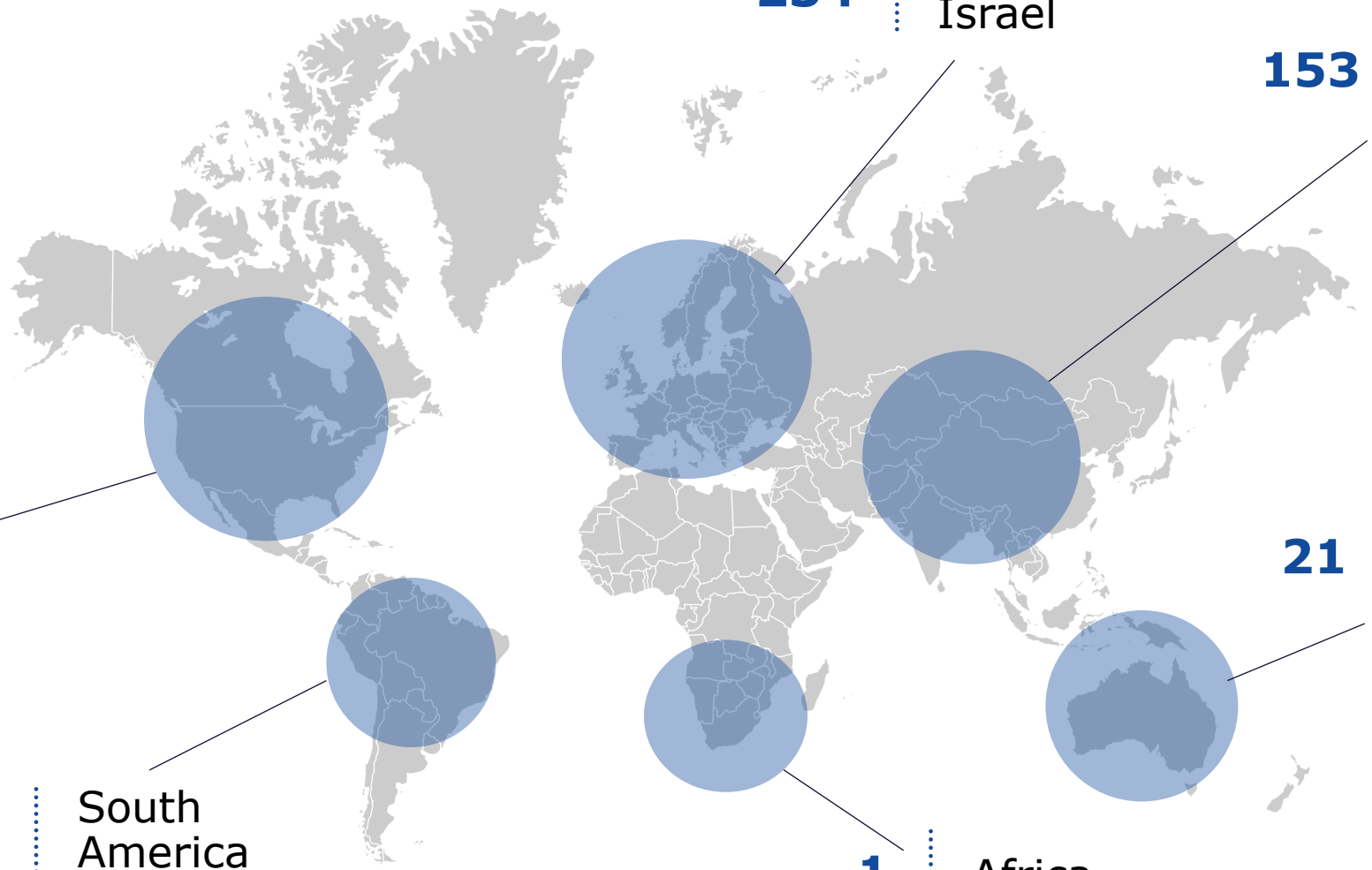
About ARM

- **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
  - Conducting key stakeholder outreach, **communication**, and education
  - Facilitating sustainable access to **capital**

Alliance *for* Regenerative Medicine

Current Global Sector Landscape

932+
Regenerative Medicine Companies Worldwide, including Gene and Cell Therapies, and Tissue Engineering Therapeutic Developers



234 Europe & Israel

153 Asia

510 North America

21 Oceania
Australia, New Zealand, Marshall Islands

13 South America

1 Africa

Source data provided by: informa

Patient Impact of Recently Approved Products

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Therapy Name	Product Developer	Response
Kymriah	Novartis	• **40%** of patients with R/R DLBCL treated experienced a complete response • **60%** of patients with R/R B-Cell ALL treated experienced a complete response
Yescarta	Kite Pharma, a Gilead company	• **58%** of patients with R/R B-Cell NHL treated experienced a complete response
LUXTURNA	Spark Therapeutics	• **55%** of patients treated showed an improvement of 2+ light levels darker after treatment
Zolgensma	AveXis / Novartis	• **93%** of patients SMA Type 1 treated were alive without permanent ventilation at 24 months post-treatment
Zynteglo	bluebird bio	• **75%** of patients with TDT without β0/β0 genotype treated achieved transfusion independence

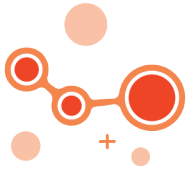
Patient Impact of Regenerative Medicine

59,575

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

Select Anticipated Near-Term Approvals (Global)

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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: late 2019 (US)

Zynteglo (bluebird bio)
- Beta thalassemia
- Expects to file: 2019 (US)

Valrox (BioMarin)
- Hemophilia A
- Expects to file: Q4 2019 (US & EU)

GS010 (GenSight Biologics)
- Leber hereditary optic neuropathy
- Expects to file: H2 2020 (US & EU)

AT132 (Audentes Therapeutics)
- X-linked myotubular myopathy
- Expects to file: 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)

Select Anticipated Near-Term Approvals (Global)

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Cell-Based Immuno-Oncology

Rivo-cel (Bellicum Pharmaceuticals)
- HSCT to treat blood cancers
- Expects to file: EOY 2019 (EU)

tab-cel (Atara Biotherapies)
- EBV-PTLD
- Expects to file: 2H 2019 (US)

liso-cel (Celgene)
- Diffuse large B-cell lymphoma (DLBCL)
- Expects to file: Q4 2019 (US)

ide-cel (bluebird bio / Celgene)
- Multiple myeloma
- Expects to file: 1H 2020 (US)

ATIR101 (Kiadis Pharma)
- HSCT to treat blood cancers
- Decision expected: 1H 2020 (EU)

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)

Select Anticipated Near-Term Approvals (Global)

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Cell Therapy

SB623 (SanBio)
- Traumatic brain injury
- Expects to file: January 2020 (Japan)

Remestemcel-L (Mesoblast)
- Acute graft versus host disease
- Decision expected: 2020 (US)

TEMCELL (Mesoblast / JCR Pharma)
- Epidermolysis bullosa
- Decision expected: 2020 (Japan)

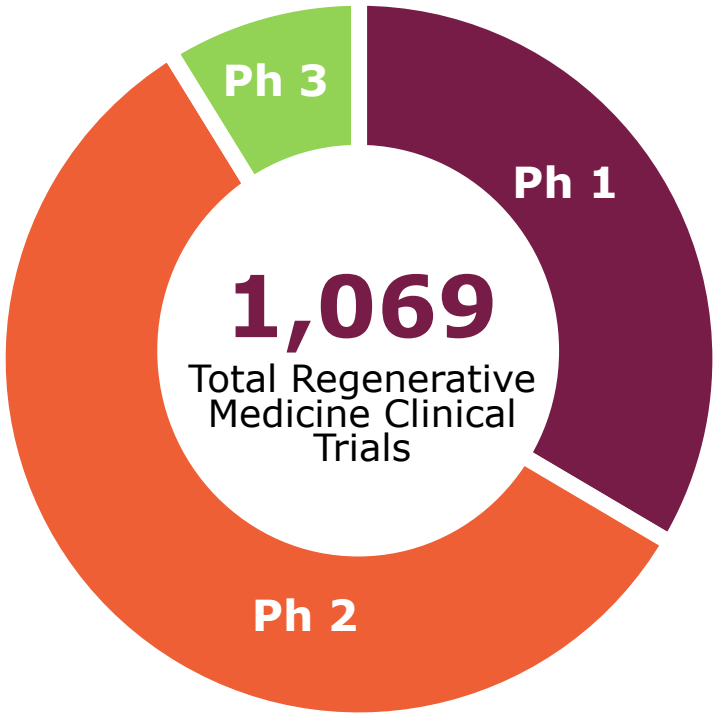
Tissue-Based

RVT-802 (Enzyvant Therapeutics)
- Complete DiGeorge 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: 358
across all tech types and indications

Gene Therapy: 117
Gene-Modified Cell Therapy: 187
Cell Therapy: 49
Tissue Engineering: 5

Phase 2: 617
across all tech types and indications

Gene Therapy: 219
Gene-Modified Cell Therapy: 207
Cell Therapy: 168
Tissue Engineering: 23

Phase 3: 94
across all tech types and indications

Gene Therapy: 30
Gene-Modified Cell Therapy: 16
Cell Therapy: 32
Tissue Engineering: 16

Source data provided by: informa

Clinical Trials by Sub-Category – as of 1H 2019

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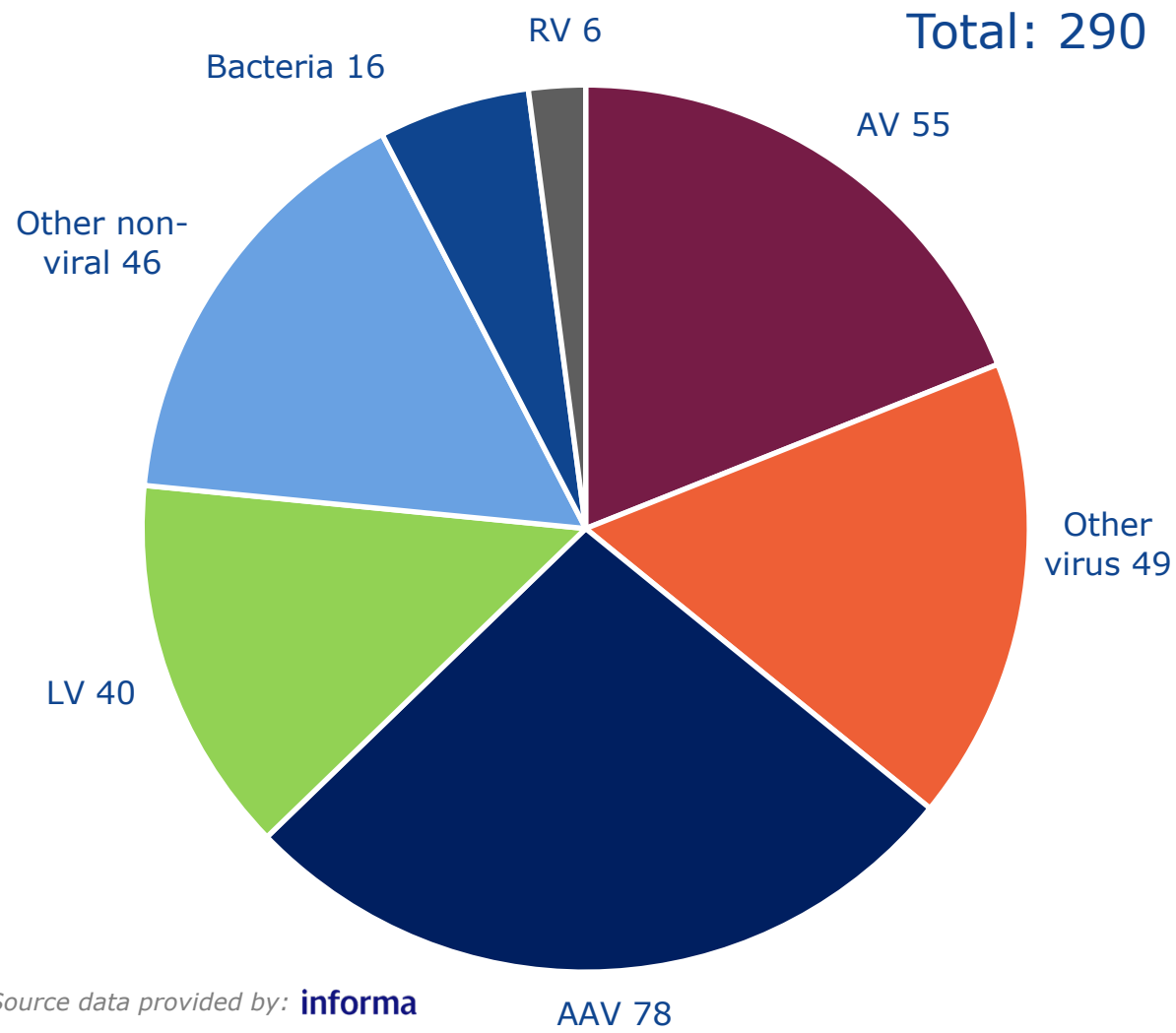
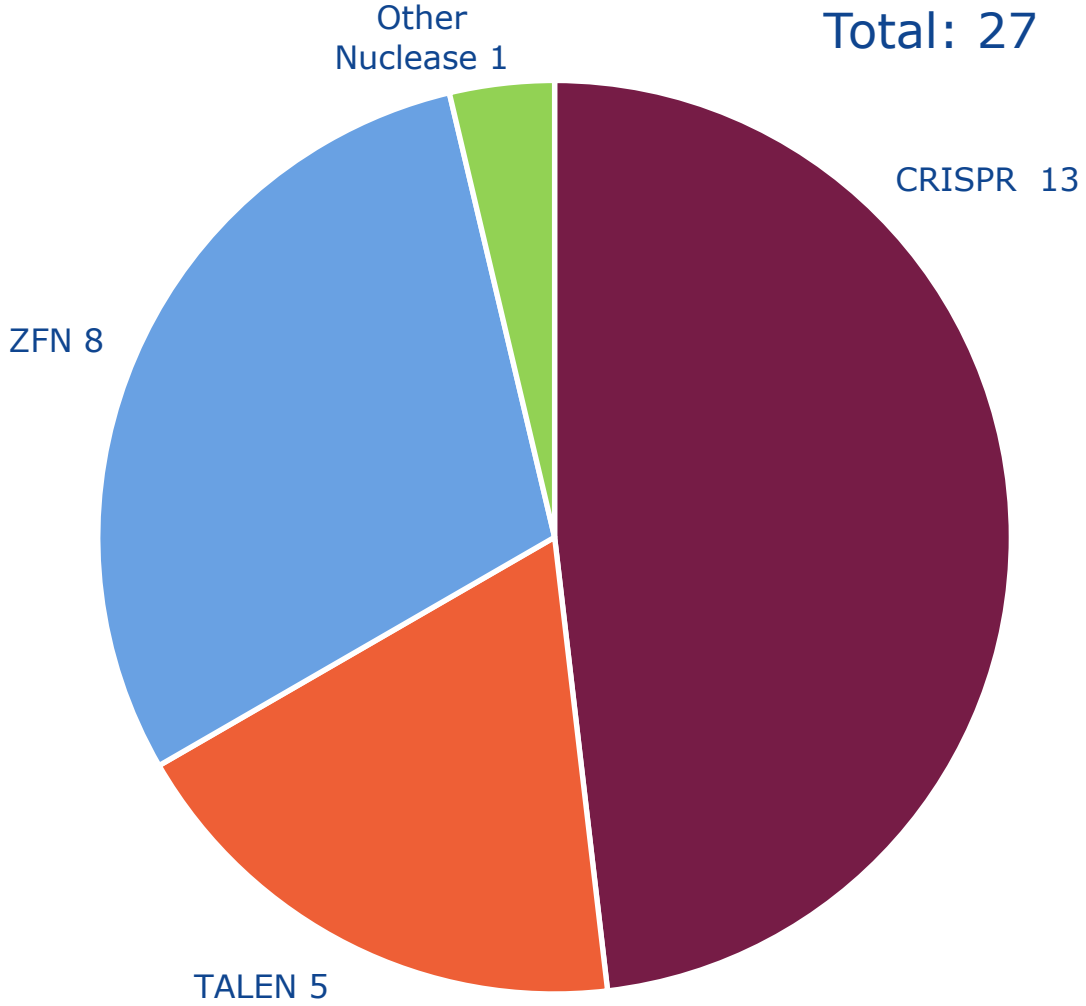
Gene Delivery Vectors
viral & non-viral

Total: 290



Gene Editing

Total: 27



Source data provided by: informa

Clinical Trials by Sub-Category – as of 1H 2019

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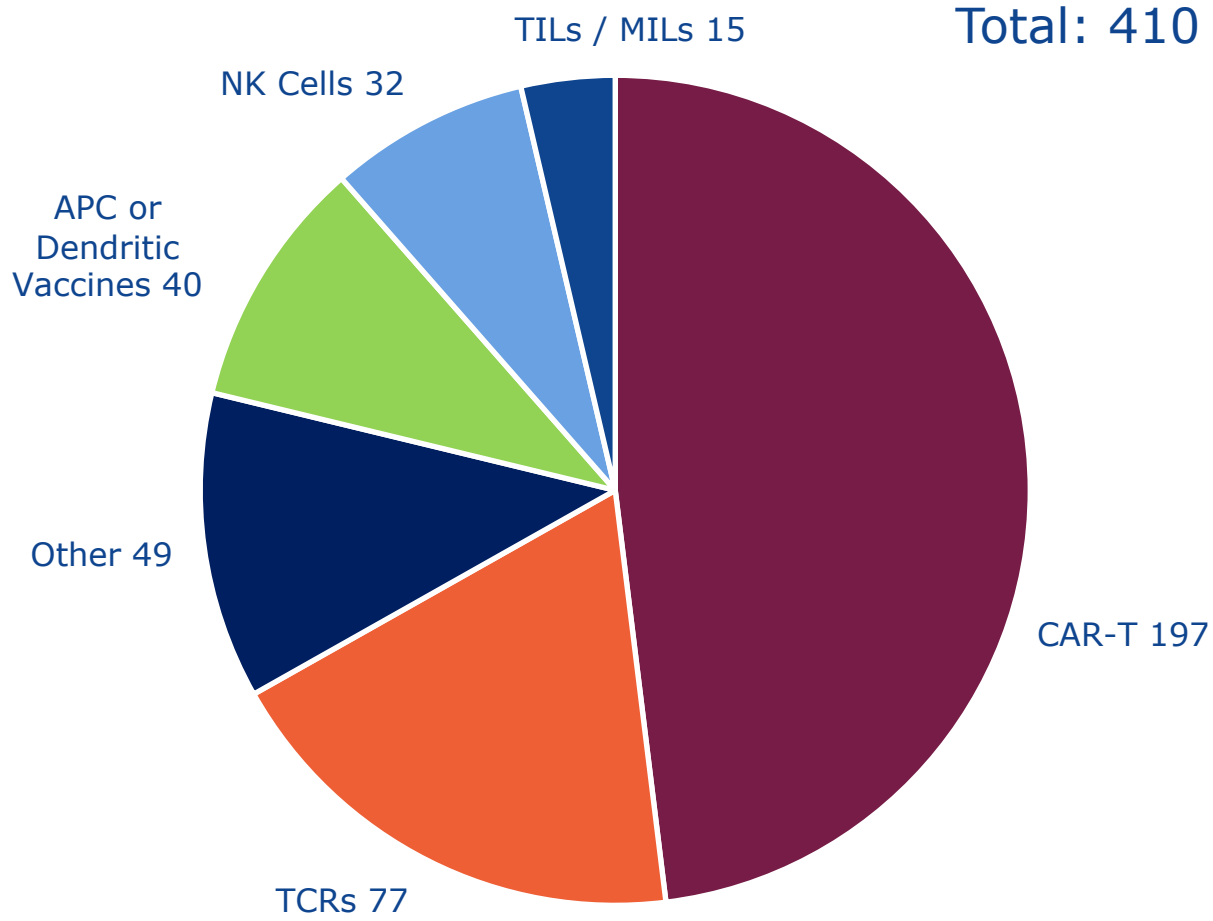
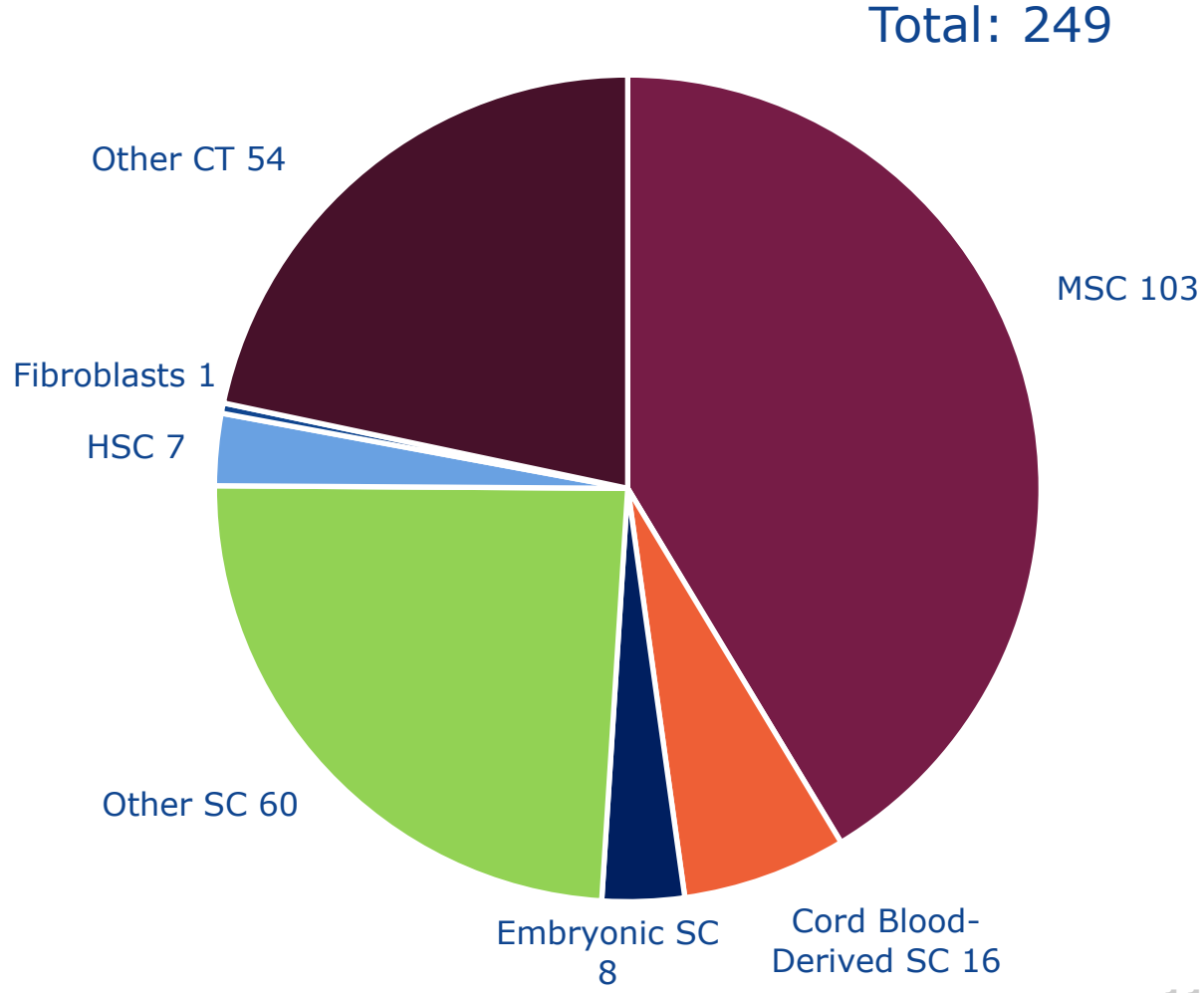
Gene-Modified Cell Therapy

Total: 410



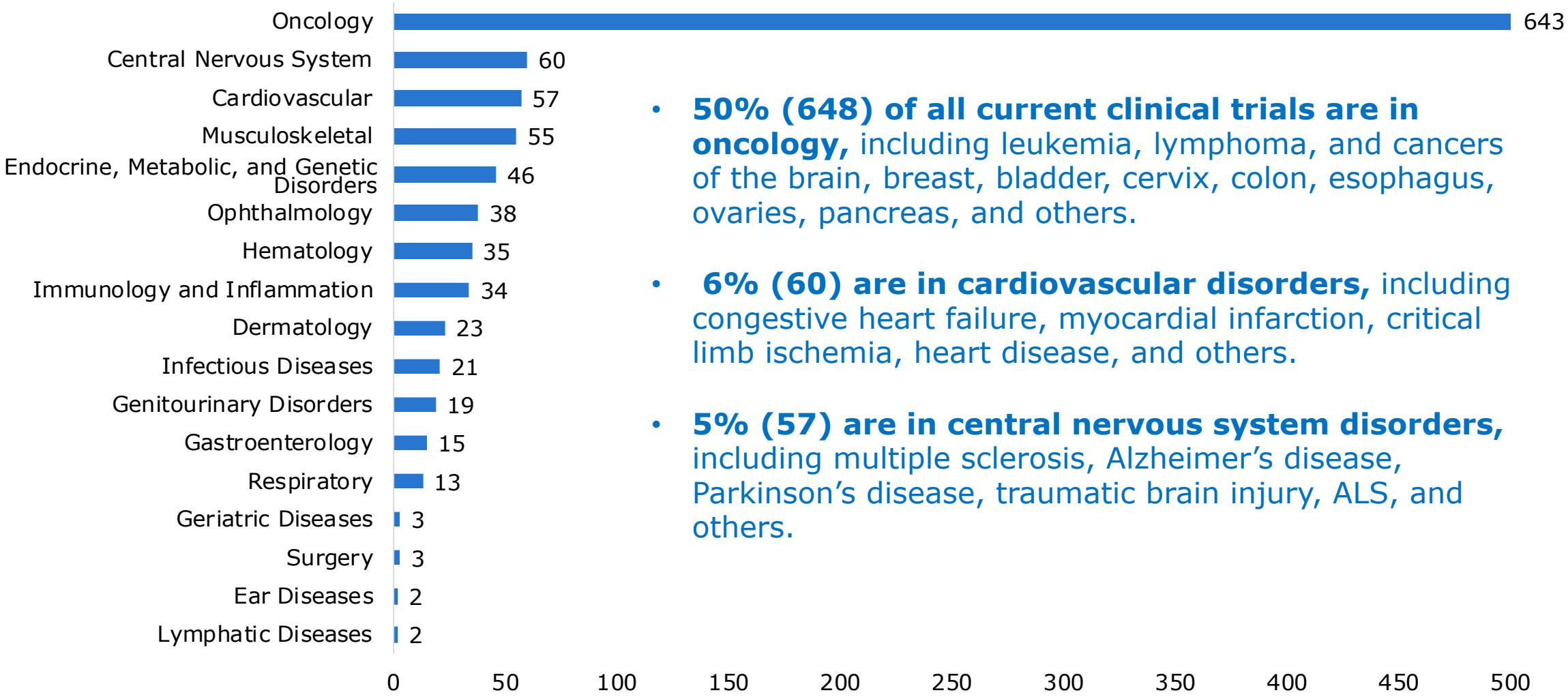
Cell Therapy

Total: 249



Source data provided by: informa

Regenerative Medicine Clinical Trials by Therapeutic Area



- **50% (648) 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% (60) are in cardiovascular disorders,** including congestive heart failure, myocardial infarction, critical limb ischemia, heart disease, and others.
- **5% (57) are in central nervous system disorders,** including multiple sclerosis, Alzheimer's disease, Parkinson's disease, traumatic brain injury, ALS, and others.

Source data provided by: informa

Total Global Financings: 1H 2019

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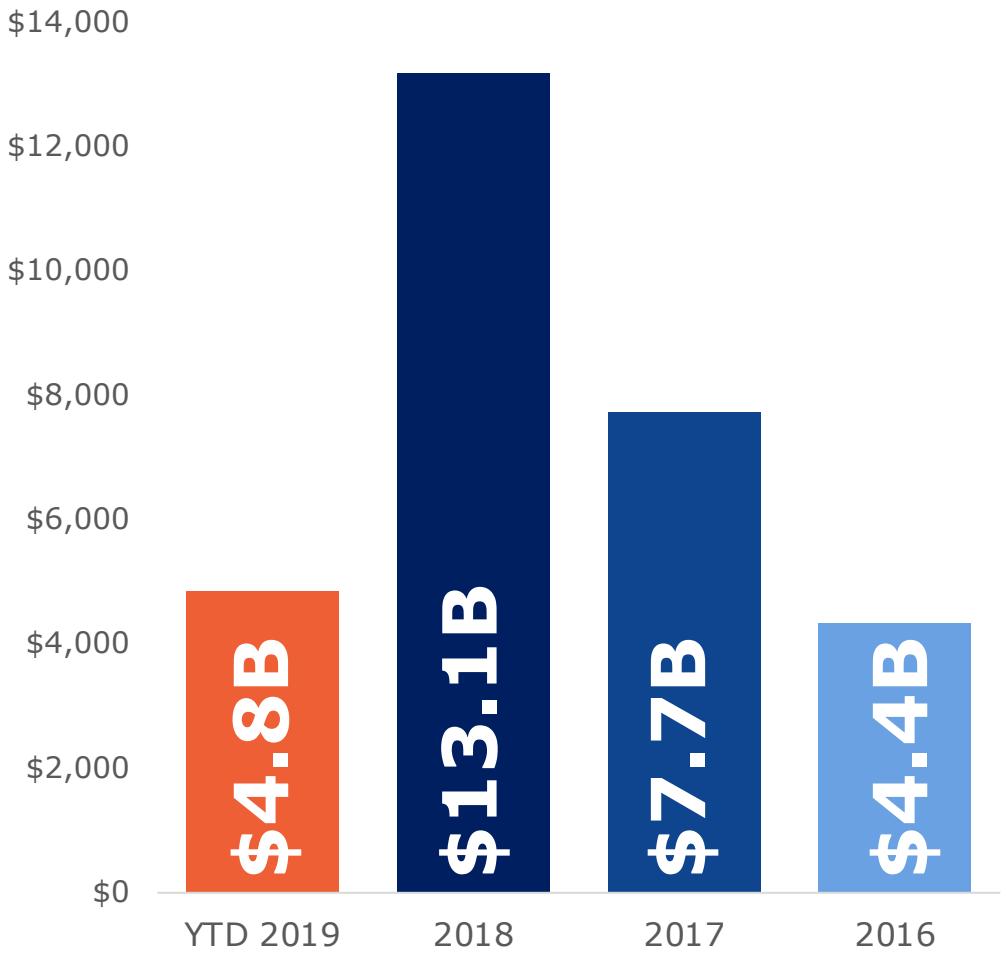
	Q2 2019	1H 2019
Total Global Financings	**$2.6B**	**$4.8B**
Gene-Based Therapies	**$2.2B**	**$4.3B**
Cell Therapy	**$691M**	**$1.5B**
Tissue Engineering	**$53M**	**$67M**

Source data provided by: informa

**both Gene-Based Therapies & Cell Therapy categories include financings from companies active in developing gene-modified cell therapies*

Total Global Financings: YTD 2019



2018 was a watershed year for regenerative medicine financings.

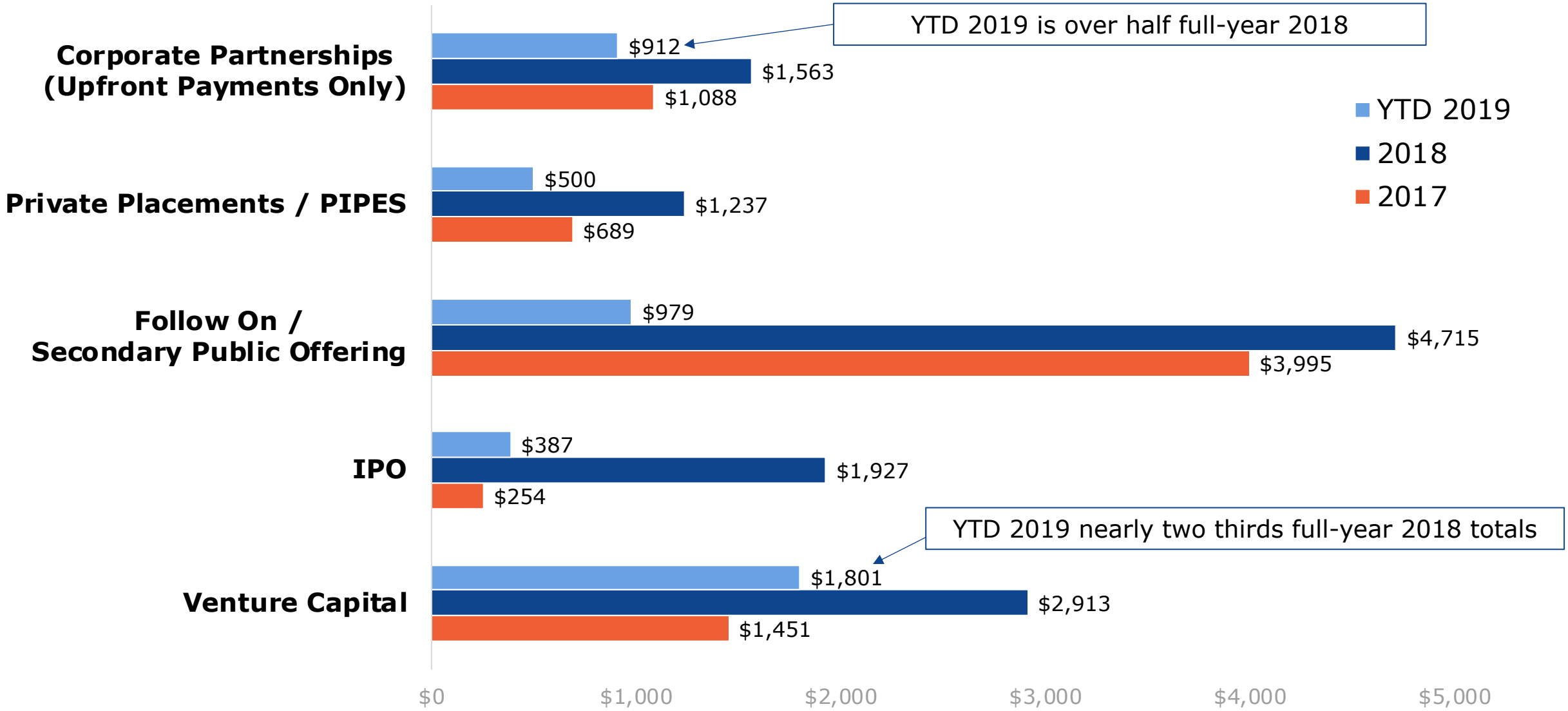
- Highest total financings raised in recent years
- In 2018, there were **eight IPOs** for regenerative medicine companies that raised **$100M+**
- The public performance averages for all RM/AT companies, cell-based IO companies, and gene therapy companies were higher than the Nasdaq Index and Nasdaq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

*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

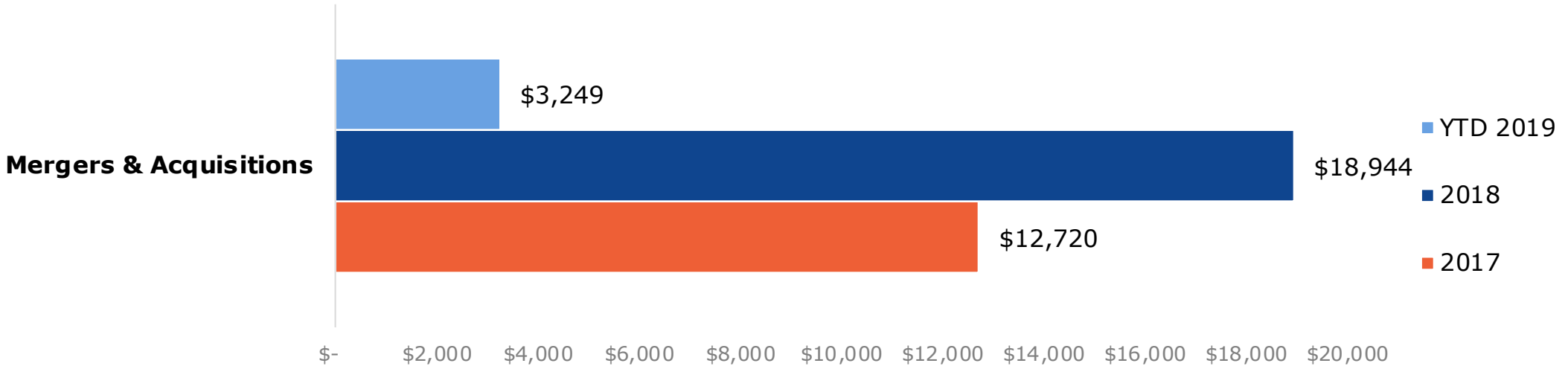
Source data provided by: informa

Total Financings by Type, by Year



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).*

Source data provided by: informa

Select Corporate Partnerships & Public Financings YTD 2019

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Corporate Partnerships: (Upfront Payments)

- Genentech/Roche signs $300M upfront agreement with Adaptive Biotechnologies – January 4
- Vertex signs $175M upfront agreement with CRISPR Tx – June 6
- Neurocrine Biosciences completes $115M upfront agreement with Voyager Tx – January 29
- Janssen signs $100M upfront agreement with MeiraGTx – January 31
- Astellas signs $80M upfront agreement with Frequency Therapeutics – July 17, 2019*

Private Placements & Venture Financings:

- Century Therapeutics launches with $250M – July 1, 2019*
- 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
- Juvenescence raises $100M in Series B – August 19*
- Gracell raises $85M in Series B – February 25
- MeiraGTx raises $80M in private placement – February 27

Public Offerings: (IPOs & Follow-Ons)

- Atara raises $150M in follow-on offering – July 23*
- 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
- AVROBIO raises $138M in follow-on offering – July 19*
- 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

** Financing closed in Q3 2019 and is not included in 1H 2019 totals.*

Market Access Landscape

As of September 2019

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Kymriah ★ ✓

Yescarta ★ ✓

Luxturna ★

Alofisel ★ ✓

Imlygic ✓

Kymriah ★ ✓

Luxturna ✓

Strimvelis ✓

Yescarta ★ ✓

Zalmoxis ★ ✓

Holoclar ★ ✓

Imlygic ★ ✓

Kymriah ★ ✓

Strimvelis ★ ✓

Yescarta ★ ✓

Luxturna ★ ✓

Holoclar ★ ✓

Imlygic ★ ✓

Strimvelis ★ ✓

Zalmoxis ★ ✓

Kymriah ★ ✓

Yescarta ★ ✓

Imlygic ★ ✓

Kymriah ★ ✓

Luxturna ★ ✓

Yescarta ★ ✓

Zolgensma ★ ✓

Kymriah

CADTH Assessment: Would be cost effective if price lowered

Yescarta ★ ✓

Kymriah ✓

Kymriah ★ ✓

Collategene ★ ✓

★ *Positive HTA/Payer Opinion* ✓ *Reimbursed*

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

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- Upcoming near-term clinical trial milestones & data readouts
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- Commentary from experts in the field

Thank You!

Alliance for Regenerative Medicine