



# Alliance *for* **Regenerative Medicine**

REGENERATIVE MEDICINE SECTOR OVERVIEW

## 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
  - Compile sector data, **educate** media and other stakeholders

# 350+ ARM Members

*\*\*Members in bold are publicly traded companies*



4BIO Capital 4D Molecular Tx AABB **Abeona Tx** Accelerated Bio ACF Bioservices **Adaptimmune** Adicet Bio **Adverum Bio** **AGTC** Aivita Biomedical Akouos Akron Bio Albiomedix Aldevron Alpha-1 Foundation Ambys American Association of Tissue Banks American Gene Technologies International American Society of Plastic Surgeons **Amicus** Andalusian Initiative for Advanced Therapies ANEMOCYTE Angiocrine Bio apceth Biopharma Archbow Consulting Artiva Bio Aruvant Aseptic Technologies ASGCT AskBio Aspect Biosystems Asset Management Company Association of Clinical Research Organizations **Astellas** **Atara Bio** **Athersys** **Audentes Tx** AusBiotech **Autolus** Avectas Avery Tx **Avita Medical** AVM Bio **AVROBIO** **AxoGen** **Axovant** B-MoGen Barkey Baylor College of Medicine Be the Match Biotherapies **Bellicum Pharma** BioBridge Global **BioCardia** **BioLife Solutions** **BioMarin** **BioStage** Biotech Mountains Blood Centers of America **bluebird bio** BlueRock Tx **Bone Tx** **BrainStorm Cell Tx** Brainxell Brammer Bio C3i **Cabaletta Bio** **Caladrius Bio** **Capricor Tx** **Cardinal Health** Caribou Bio Carisma Carpenter Consulting Cartherics Celavie Bio **Celgene (BMS)** CEO Council for Growth CGT Catapult Cell Medica Cellatoz CellCAN **Collect Bio** CellGenix Cello Health **CBMG** Cellular Technology Limited Celonic Celsense Center for the Advancement of Science in Space CCRM Century Tx Cevac Chemelot CIRM City of Hope Cleveland Clinic Cleveland Cord Blood Center ClinicalMind Coalition for Clinical Trials Awareness Cobra Bio Cognate Bio **CombiGene** Cook Myosite Cornell University Covance **CRISPR Tx** **Cryoport Systems** **CSL** CTI Clinical Trial and Consulting Services CureDuchenne **Cynata Tx** Dark Horse Consulting DiscGenics EB Research Partnership **Editas Medicine** Elevate Bio Emerging Therapy Solutions Encoded Tx Enzyvant Tx ERA Consulting ESGCT EVERSANA EveryLife Foundation for Rare Diseases Evidera ExCellThera Exogrades Falcon Tx FARA **Fate Tx** **Fibrocell Science** Fight Colorectal Cancer **Flexion Tx** Fondazione Telethon Foundation for Biomedical Research and Innovation Fraunhofer Institute for Cell Therapy and Immunology Fred Hutchinson Cancer Research Center Frequency Tx **Fresenius Kabi** **FUJIFILM Cellular Dynamics** G-CON Manufacturing GalbraithWight **Gamida Cell** GammaDelta Tx **GE Healthcare** GE2P2 Global Foundation Gemini BioProducts Generation Bio GENETHON **Genprex** **GenSight Biologics** Gift of Life Marrow Registry **Gilead / Kite** Giner **GlaxoSmithKline** Global Genes GPB Scientific Gyroscope Tx Halloran Consulting **Healios K.K.** Histogen **Hitachi Chemical Advanced Tx Solutions** Hogan Lovells **Homology Medicines** Humanscape Huron Consulting Hybrid Concepts International ICON Immusoft InRegen InsightRX **Intellia Tx** Invetech Invitria Invitrx **Iovance** **IQVIA** ISCT ISSCR **IVERIC Bio** Johns Hopkins **Johnson & Johnson** Key Biologics **Kiadis Pharma** Kimera Labs Kytopen L7 Informatics LabConnect Lake Street Capital Markets Latham BioPharma LatticePoint Consulting Legend Biotech Locate Bio LogicBio **Lonza Biologics** Lovelace Biomedical Ludwig Boltzmann Institute **Lysogene** **Magenta Tx** MaSTherCell **MaxCyte** MEDIPOST America **Medpace** **MeiraGTx** MSK Cancer Center **Mesoblast Limited** **MilliporeSigma** **MiMedx** Minerva Bio Miromatrix Medical Missouri Cures **MolMed** Musculoskeletal Transplant Foundation **Mustang Bio** National Disease Research Interchange National Multiple Sclerosis Society National Stem Cell Foundation Nebraska Coalition for Lifesaving Cures Neural Stem Cell Institute Neurogene New Jersey Innovation Institute New York Stem Cell Foundation NexImmune NIIMBL Nkarta Northwestern University Comprehensive Transplant Center Novadip Bio **Novartis / Avexis** Novitas Capital **Novo Nordisk** NYBC Obsidian Odylia Tx Oisin Bio OncoSenX Opsis Tx **Orchard Tx** Organabio **Orgenesis** Orig3n **Oxford BioMedica** panCELLa Parent Project Muscular Dystrophy PDC\*line Pharma SA **Pfizer** **Pluristem Tx** **PolarityTE** Polyplus-transfection **Poseida Tx** Precigen **Precision Bio** **Prevail Tx** Prevent Cancer Foundation Project 8p Promethera Bio **PTC Tx** Recardio Recombinetics Regenerative Patch Technologies ReGenesys **Regeneus** REGENXBIO REMEDI ReNeuron RepliCel Life Sciences Rescue Hearing Rexgenero Rigenrand **Rocket Pharma** RoosterBio Roslin CT Rousselot RxGen **SanBio** Sanford Health Sanford Stem Cell Clinical Center @ UCSD **Sangamo Tx** **Sanofi** **Sarepta** Sartorius Stedim North America SCM LifeScience Scottish National Blood Transfusion Service Semma Tx Seneca Bio Senti Biosciences Sentien Bio Seraxis Sigilon Sirion Biotech Skyland Analytics SmartPharm Tx **Solid Bio** **Spark Tx** StafaCT Starfish Innovations STEL Technologies StemBioSys StemCyte StemExpress Stempeutics Stop ALD Foundation Student Society for Stem Cell Research Synpromics T-Knife **Takeda** Talaris Tx Tenaya TERMIS-Americas Terumo BCT Tessa Tx Texas Heart Institute The Michael J. Fox Foundation Theradaptive **Thermo Fisher Scientific** **ThermoGenesis** TikoMed Tmunity Tx TrakCel TreeFrog Tx Tremont Tx LLC Trizell Tulane University UCSD Stem Cell Program **Ultragenyx** UMass Medical School Unicyte **uniQure** Unite 2 Fight Paralysis United Spinal Association of VA Universidad de los Andes University of Colorado University of Pennsylvania **Unum Tx** VERIGRAFT ViaCyte VidaCel Videregen Vigene VINETI ViveBiotech Vivet Tx Voisin Consulting **Voyager Tx** WiCell WindMIL Tx World Courier **Wuxi Xintela** Xyphos Bio Yposkesi Zelluna **Ziopharm Oncology**

# Phacilitate Leaders World 2020

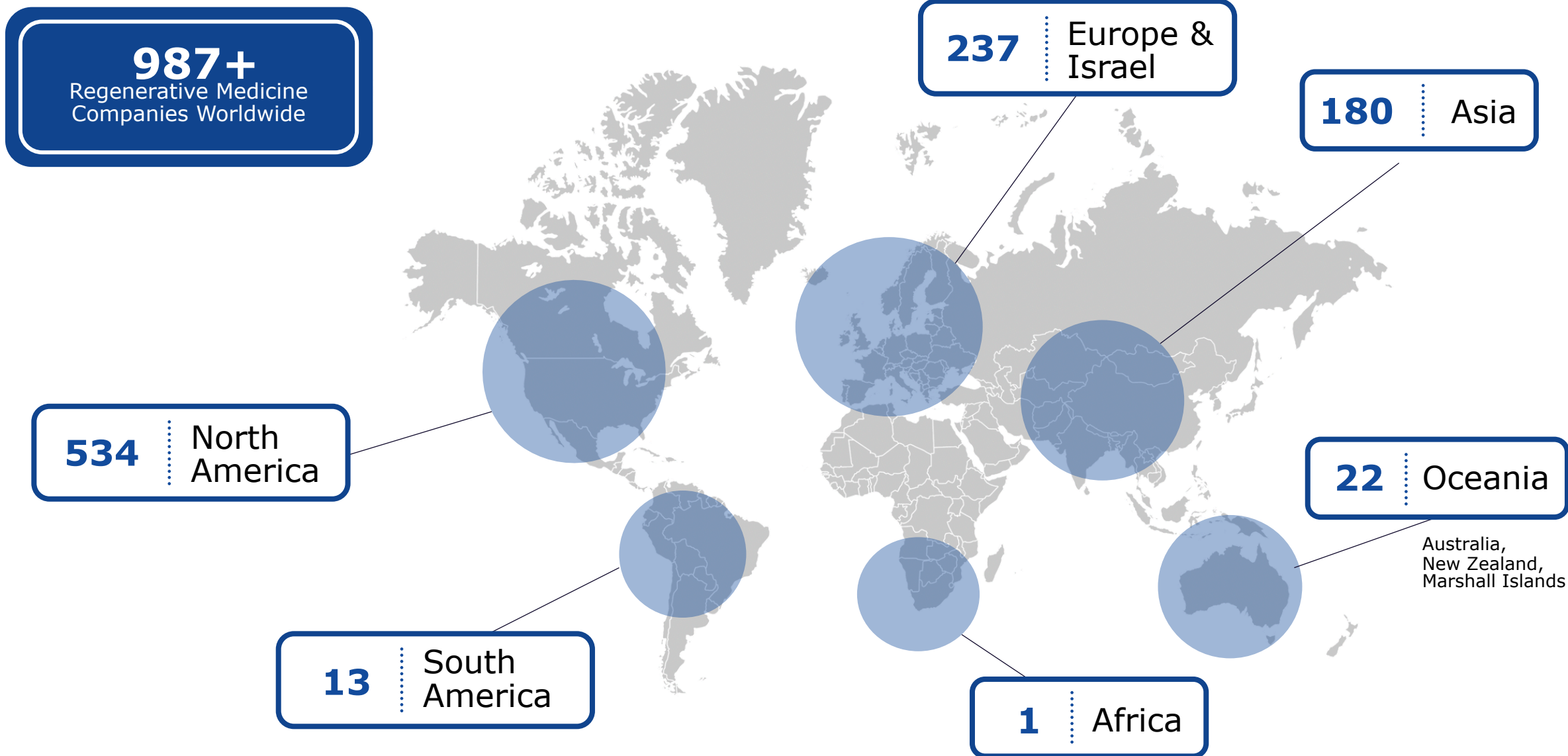
*Access to the Slides:*

**[www.alliancerm.org](http://www.alliancerm.org)**

**Twitter:  @alliancerm**



# Current Global Sector Landscape





**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 has been a significant year of growth for the  
regenerative medicine sector***

# Patient Impact

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- ✓ *Dramatic impact of early products*
- ✓ *Thousands benefiting from trials and commercial products*
- ✓ *Robust pipeline, with several more products poised to come to market*

# Patient Impact of Recently Approved Products

Therapy Name	Product Developer	Response
<b>Zynteglo</b>	bluebird bio	<ul style="list-style-type: none"> <li><b>75%</b> of patients with TDT without <math>\beta 0/\beta 0</math> genotype treated achieved transfusion independence</li> </ul>
<b>Zolgensma</b>	AveXis, a Novartis company	<ul style="list-style-type: none"> <li><b>93%</b> of SMA Type 1 patients treated were alive without permanent ventilation at 24 months post-treatment</li> </ul>
<b>LUXTURN A</b>	Spark Therapeutics	<ul style="list-style-type: none"> <li><b>93%</b> of patients treated showed an improvement of at least 1 light level from baseline</li> </ul>
<b>Yescarta</b>	Kite Pharma, a Gilead company	<ul style="list-style-type: none"> <li><b>58%</b> of patients with R/R B-Cell NHL treated experienced a complete response</li> </ul>
<b>Kymriah</b>	Novartis	<ul style="list-style-type: none"> <li><b>40%</b> of patients with R/R DLBCL treated experienced a complete response</li> <li><b>82%</b> of patients with R/R B-Cell ALL treated experienced complete remission or complete remission with incomplete hematologic recovery</li> </ul>



- 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\*



# Select Anticipated Approvals in 2020



## Gene Therapy

### **Zolgensma** (AveXis / Novartis)

- Spinal muscular atrophy type 1
- Filed for approval in EU and Japan mid-2019

### **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



## Cell-Based Immuno-Oncology

### **liso-cel** (Bristol-Myers Squibb)

- Relapsed or refractory large B cell lymphoma
- Filed for approval in the US in December 2019

### **KTE-X19** (Kite Pharma / Gilead)

- Relapsed or refractory mantle cell lymphoma
- Filed for approval in the US in December 2019



## Cell Therapy

### **Remestemcel-L** (Mesoblast)

- Acute graft versus host disease
- Initiated rolling BLA in US in May 2019

### **TEMCELL** (Mesoblast / JCR Pharma)

- Epidermolysis bullosa
- Filed for market approval for additional indication in Japan in March 2019



## Tissue Engineering

### **RVT-802** (Enzyvant Therapeutics)

- Pediatric Congenital Athymia
- US filing accepted for review in June 2019

### **Expecting to file in 2020:**

- Atara Bio – *tab-cel*
- Audentes Tx – *AT132*
- bluebird bio / BMS – *ide-cel*
- bluebird bio – *Zynteglo*
- GenSight Bio – *GS010*
- Humacyte – *Human Acellular Vessel*
- Iovance – *LN-145, lifileucel*
- Mallinkrodt – *Stratagraft*
- Orchard – *OTL-101, OTL-200 (US)*
- PTC Tx – *GT-AADC*
- Poseida – *P-BMCA-101*

# Scientific & Clinical Advances

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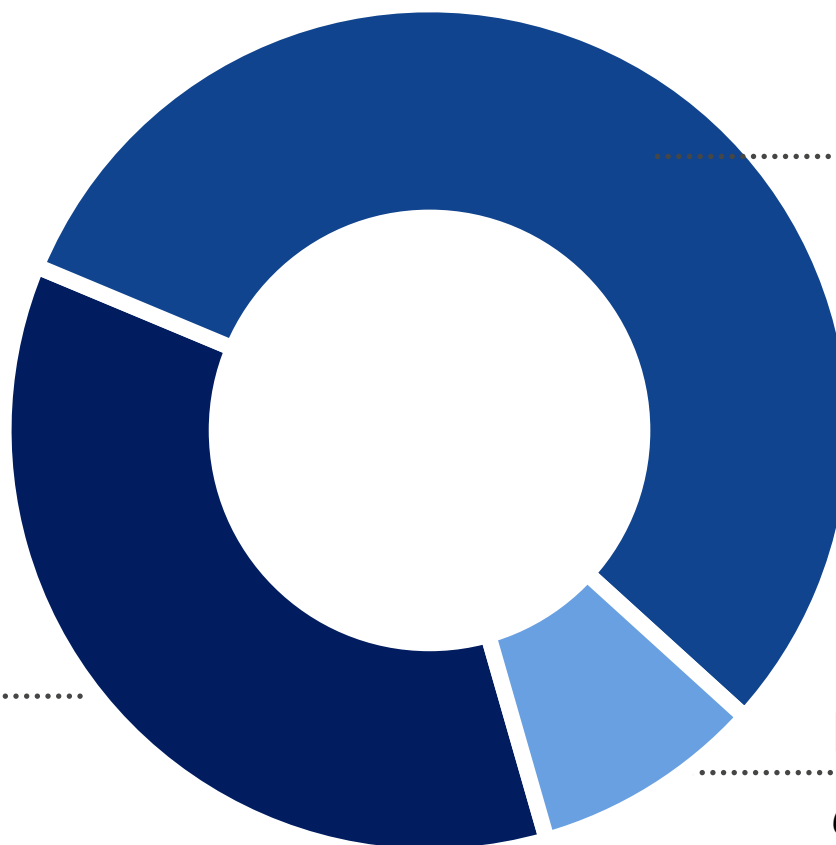
- ✓ *Substantial late stage clinical activity*
- ✓ *Explosion of gene-modified cell therapies, including allogeneic GMCTs and GMCT trials in immunology*
- ✓ *Increasing clinical activity in diverse and more prevalent indications*
- ✓ *Advances in somatic cell gene editing*
- ✓ *Advances in viral and non-viral gene delivery methods for gene therapies*

# The Clinical Landscape for Regenerative Medicine

**1,066**  
Ongoing Regen  
Med Clinical Trials

## Phase 1: 381

*Gene Therapy: 111*  
*Gene-Modified Cell Therapy: 222*  
*Cell Therapy: 42*  
*Tissue Engineering: 6*



## Phase 2: 591

*Gene Therapy: 209*  
*Gene-Modified Cell Therapy: 215*  
*Cell Therapy: 144*  
*Tissue Engineering: 23*

## Phase 3: 94

*Gene Therapy: 32*  
*Gene-Modified Cell Therapy: 15*  
*Cell Therapy: 30*  
*Tissue Engineering: 17*

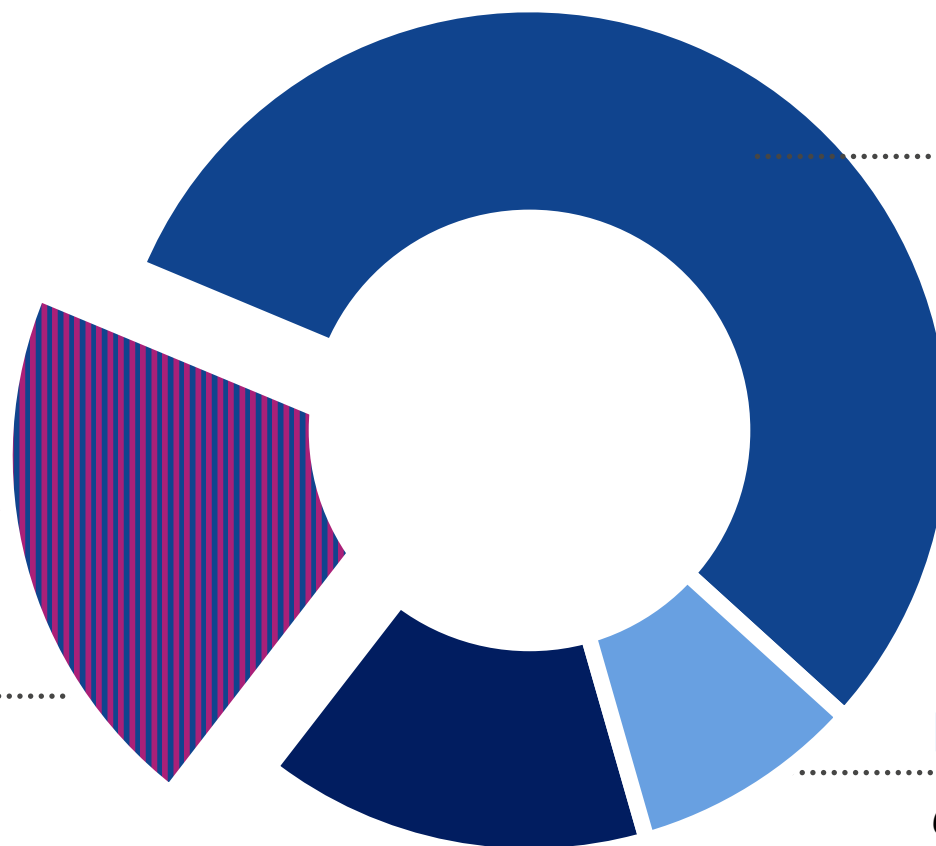
# The Clinical Landscape for Regenerative Medicine

**58%**

of Phase 1 Trials are  
in gene-modified cell  
therapies

## Phase 1: 381

*Gene Therapy: 111*  
*Gene-Modified Cell Therapy: 222*  
*Cell Therapy: 42*  
*Tissue Engineering: 6*



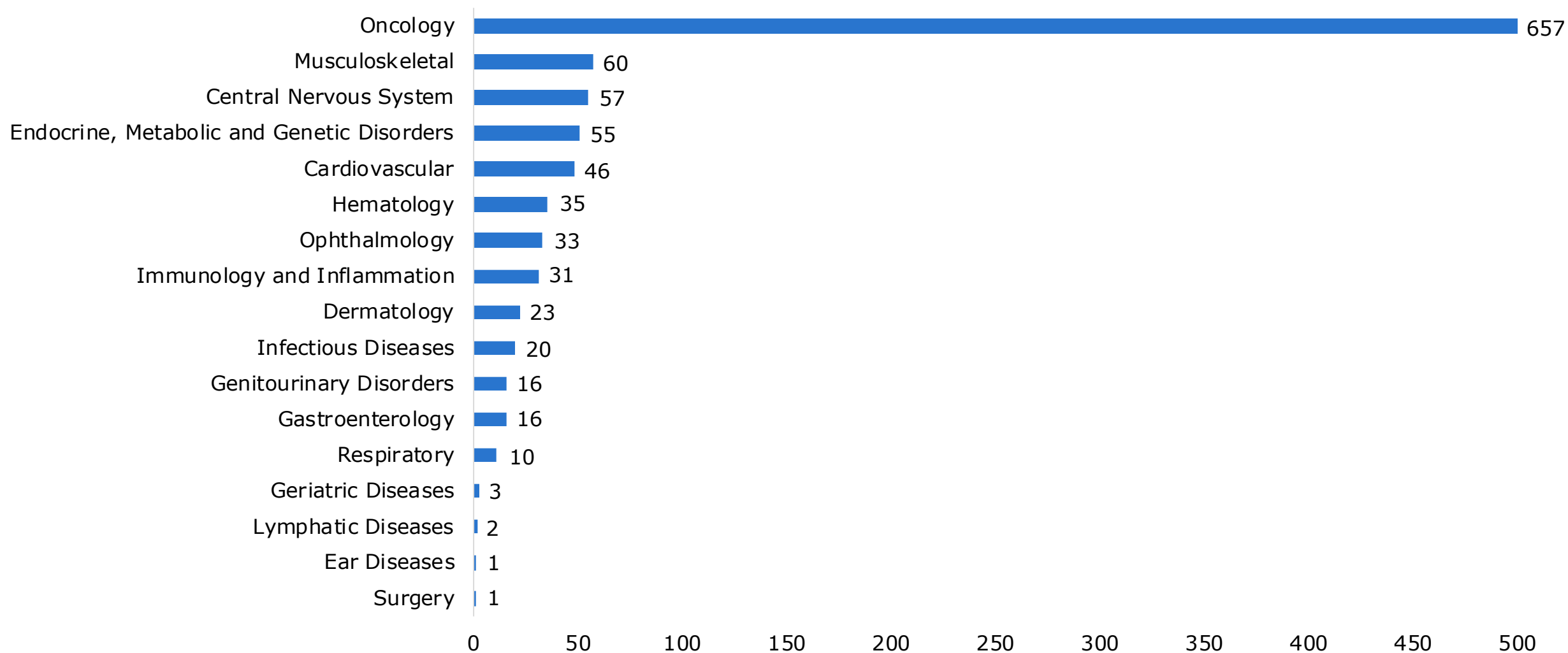
## Phase 2: 591

*Gene Therapy: 209*  
*Gene-Modified Cell Therapy: 215*  
*Cell Therapy: 144*  
*Tissue Engineering: 23*

## Phase 3: 94

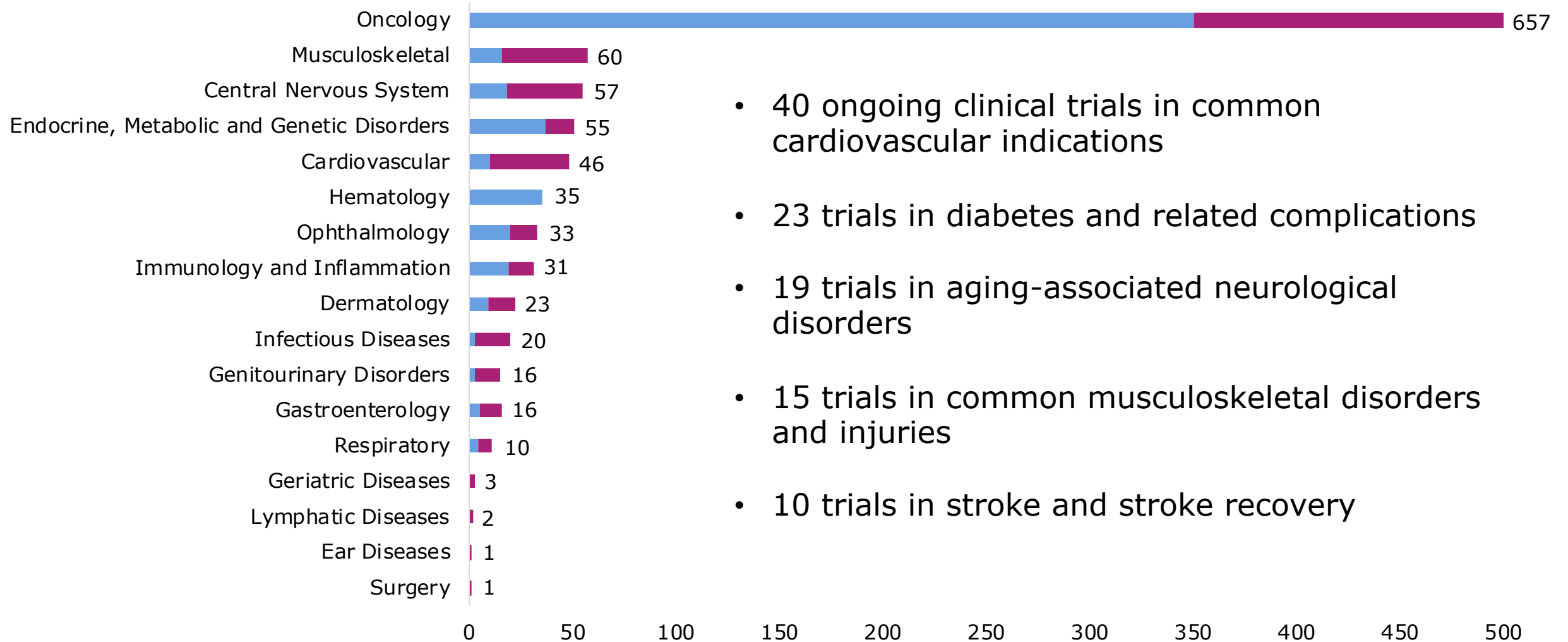
*Gene Therapy: 32*  
*Gene-Modified Cell Therapy: 15*  
*Cell Therapy: 30*  
*Tissue Engineering: 17*

# Clinical Trials Across Diverse Indications



# Increasing Clinical Activity in Larger Indications

*More prevalent indications indicated in purple*



- 40 ongoing clinical trials in common cardiovascular indications
- 23 trials in diabetes and related complications
- 19 trials in aging-associated neurological disorders
- 15 trials in common musculoskeletal disorders and injuries
- 10 trials in stroke and stroke recovery



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

## 31 ongoing Phase 1 gene editing trials worldwide

- 20 in oncology, 8 in inherited disorders, 3 in HIV
- CRISPR joined ZFNs and TALENs in the clinic
  - First patients treated in trials to treat beta thalassemia, sickle cell (**Vertex/CRISPR**)
  - First patient treated in trial of CRISPR-edited TCR for sarcoma (**Tmunity/PICI/Penn Medicine**)
  - Evidence of successful *in vivo* editing in Phase 1/ 2 Study (**Sangamo**)
  - First *in vivo* CRISPR patient to be treated early this year (**Editas**)
- **Allogene**, **Collectis**, and **Precision** entered the clinic in 2019 with gene-edited allogeneic CAR-Ts

# Advances in Gene Therapy Delivery

## Researchers drove progress in gene therapy delivery methods:



BU researchers create new protocol to improve gene therapy tool production



**A new gene therapy strategy, courtesy of Mother Nature**  
*Scientists turn a natural cellular process into a drug-delivery system*



NIH researchers create new viral vector for improved gene therapy in sickle cell disease



**NEWS**

Tiny capsules packed with gene-editing tools offer alternative to viral delivery of gene therapy



Johns Hopkins Researchers Advance Search For Safer, Easier Way to Deliver Vision-Saving Gene Therapy to The Retina



*Scripps Research team finds that a nontoxic molecule can overcome barriers to delivering gene therapy into stem cells.*

## Non-viral delivery advancements:

- Japan approved Colletagene, a non-viral gene therapy to treat critical limb ischemia
- There are currently 57 ongoing gene therapy trials utilizing non-viral delivery methods

## Companies are partnering to overcome challenges in gene therapy & gene-modified cell therapy manufacturing:

- Ziopharm Oncology and MD Anderson announced a new R&D agreement to expand TCR-T program
- SQZ Biotech and AskBio announced collaboration to overcome AAV immunogenicity

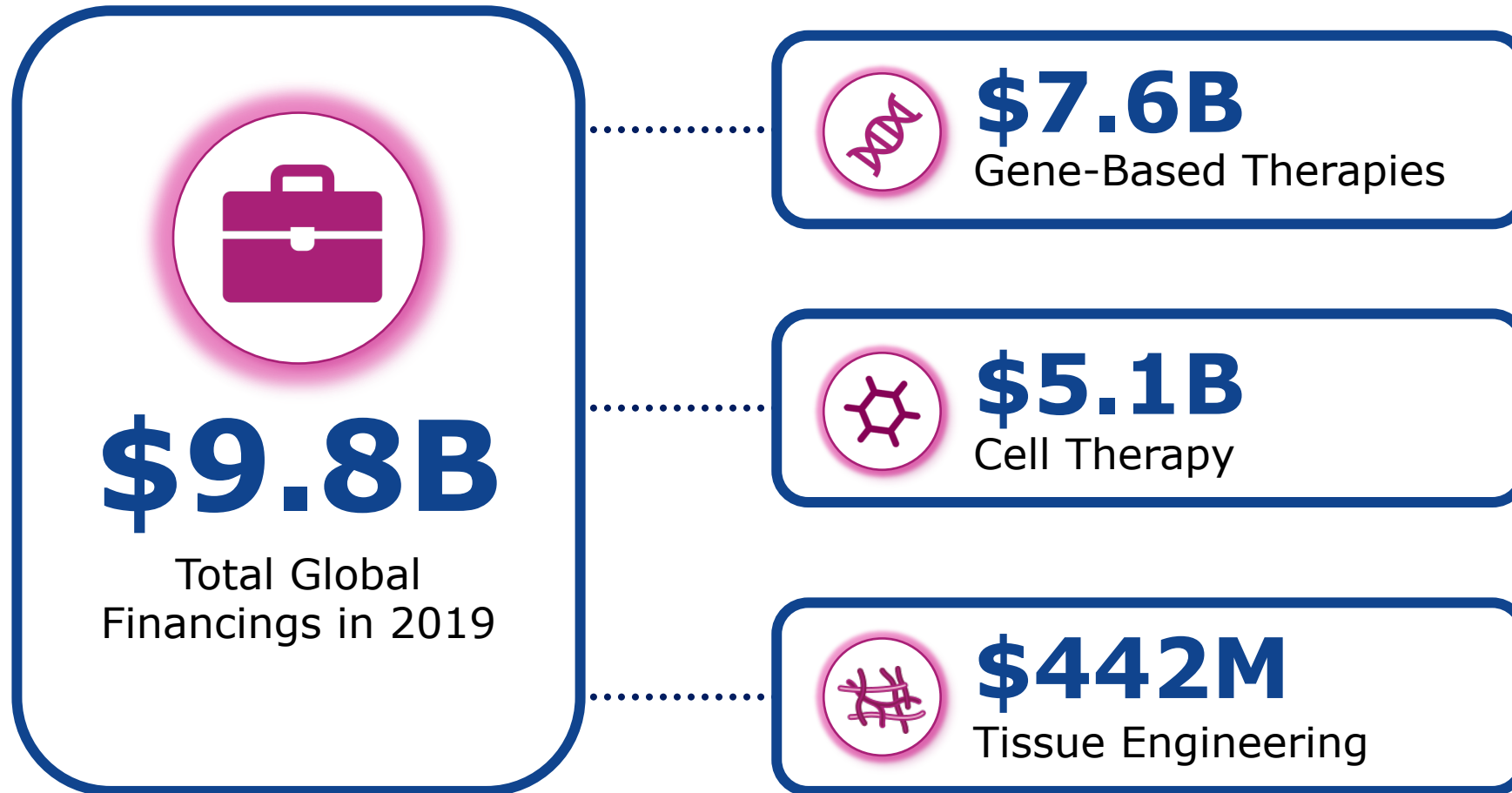


# Financing Trends

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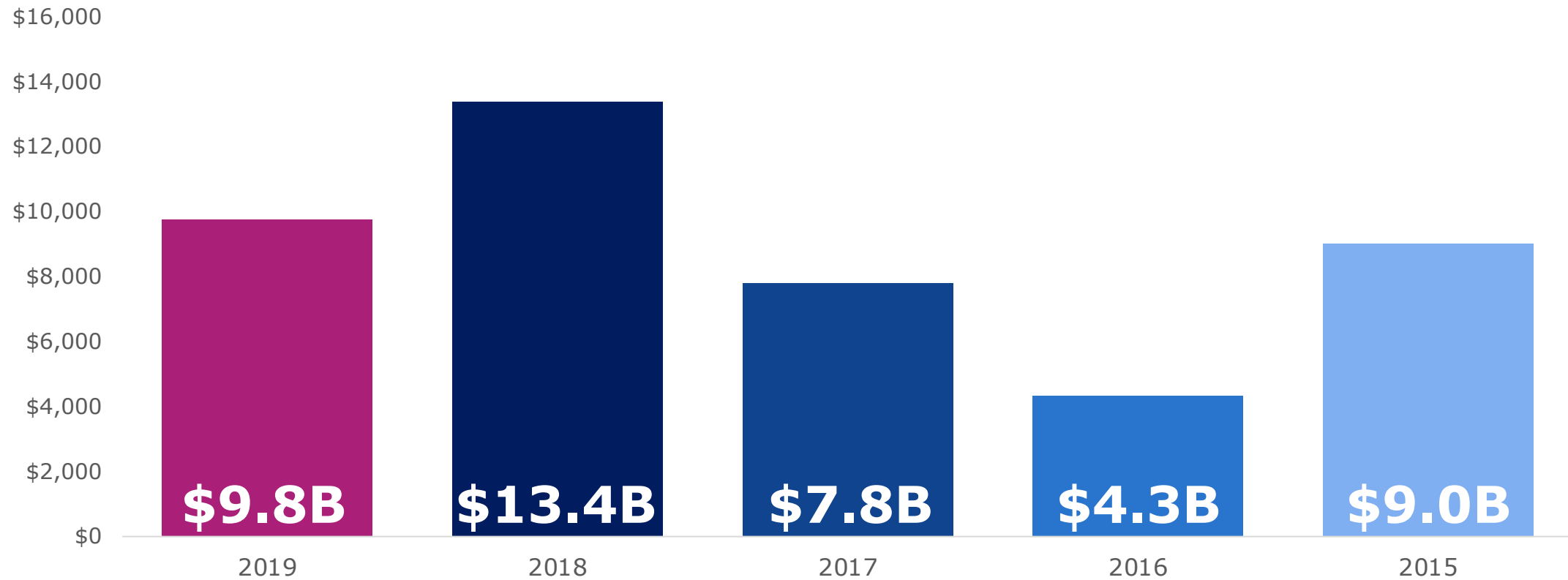
- ✓ *Total global financings in 2019 second highest ever for the sector*
- ✓ *Strong year for venture financing and corporate partnerships*
- ✓ *Large- and mid-cap pharma company M&A interest in cell & gene therapy*
- ✓ *European companies had a strong year for financings, on par with 2018*

# Total Global Financings 2019



*\*both Gene-Based Therapies & Cell Therapy categories include financings from companies active in developing gene-modified cell therapies – therefore, total financings does not equal the sum of each technology category*

# Total Global Financings by Year



***2019 surpassed 2015 in total global financings, making it the second highest year for financings ever***

# Select Corporate Partnerships & Financings 2019

## 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
- Mesoblast signs **\$150M** upfront agreement with Grünenthal – September 10
- Turnstone Biologics signs **\$120M** upfront agreement with Takeda – December 19
- Neurocrine Bio and Voyager Tx sign **\$115M** upfront agreement – January 29
- Janssen signs **\$100M** upfront agreement with MeiraGTx – January 31

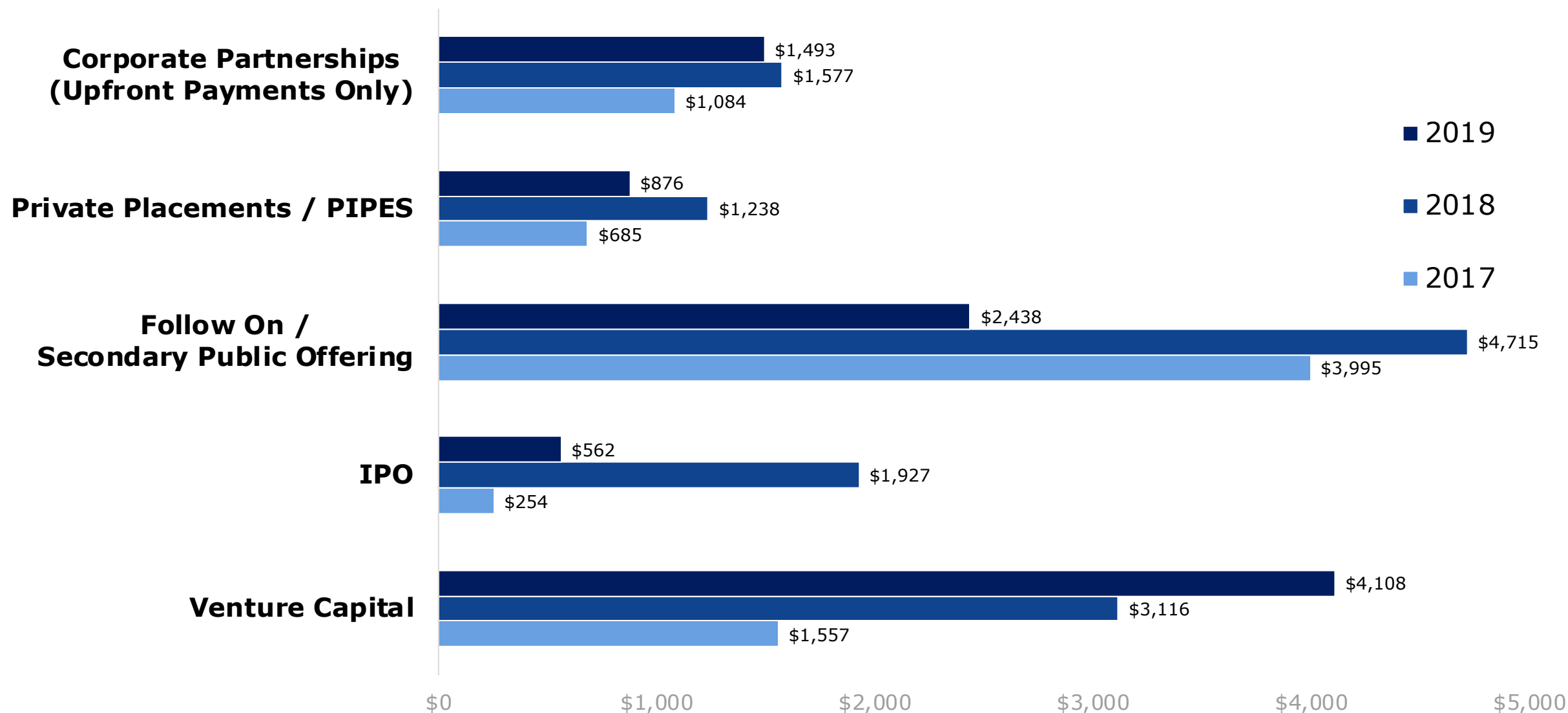
## Venture Financings & Private Placements:

- 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 A – March 6
- Inscripta raises **\$125M** in Series D – December 10
- Achilles Tx raises **\$121M** in Series B – September 3
- AlloVir raises **\$120M** in Series B – May 22
- Passage Bio raises **\$115.5M** in Series A – February 15
- Nkarta raises **\$114M** in Series B – September 4
- Passage Bio raises **\$110M** in Series B – September 4
- Healios raises **\$107M** in private placements – July 10
- Talaris Tx raises **\$100M** in Series A – April 18
- Juvenescence raises **\$100M** in Series B – August 19
- eGenesis raises **\$100M** in Series B – November 7

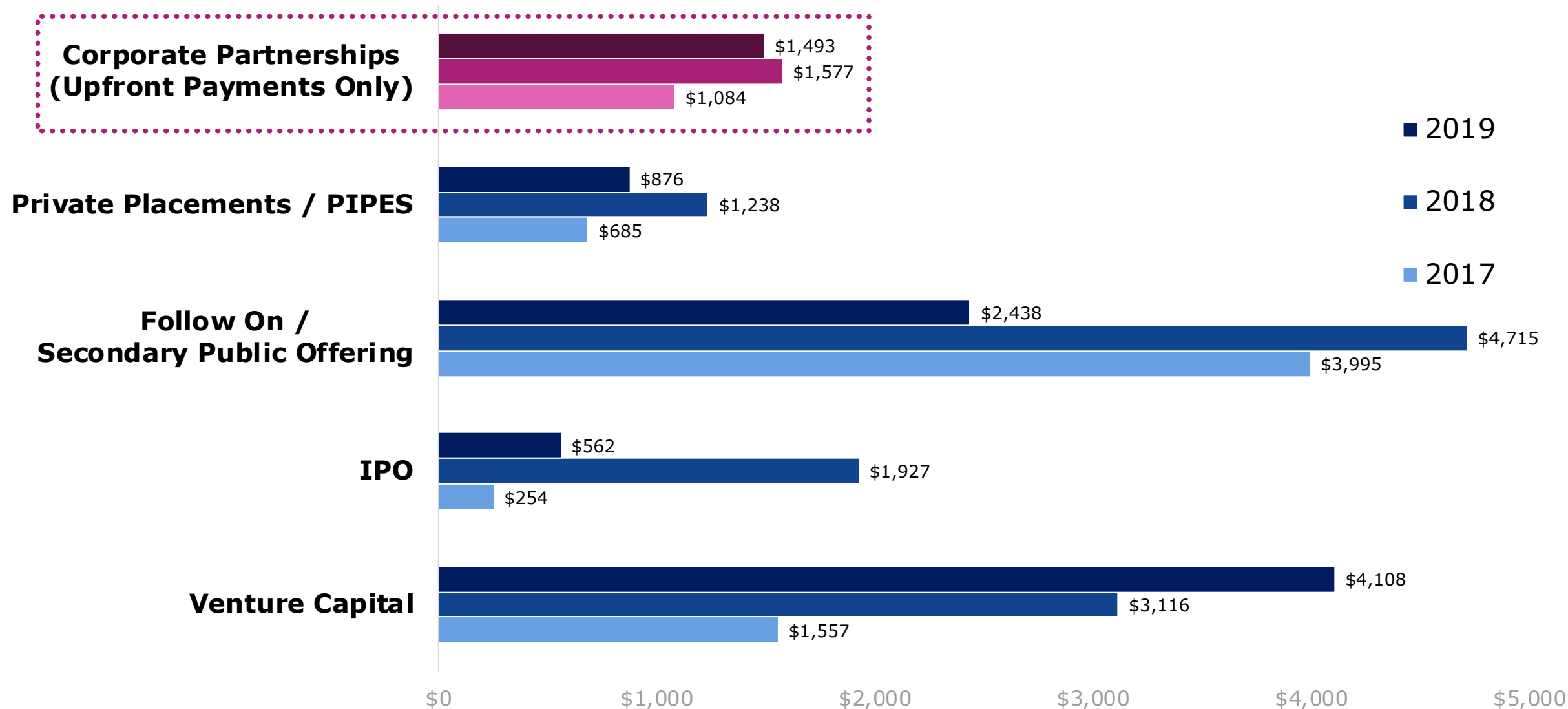
## Public Offerings: (IPOs & Follow-Ons)

- CRISPR Tx raises **\$274M** in follow-on offering – November 19
- uniQure raises **\$225M** in follow-on offering – September 4
- Fate Tx raises **\$173M** in follow-on offering – September 18
- 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 **\$116M** in follow-on offering – April 15
- Krystal Bio raises **\$115M** in follow-on offering – June 24
- Abeona raises **\$103M** in follow-on offering – December 24

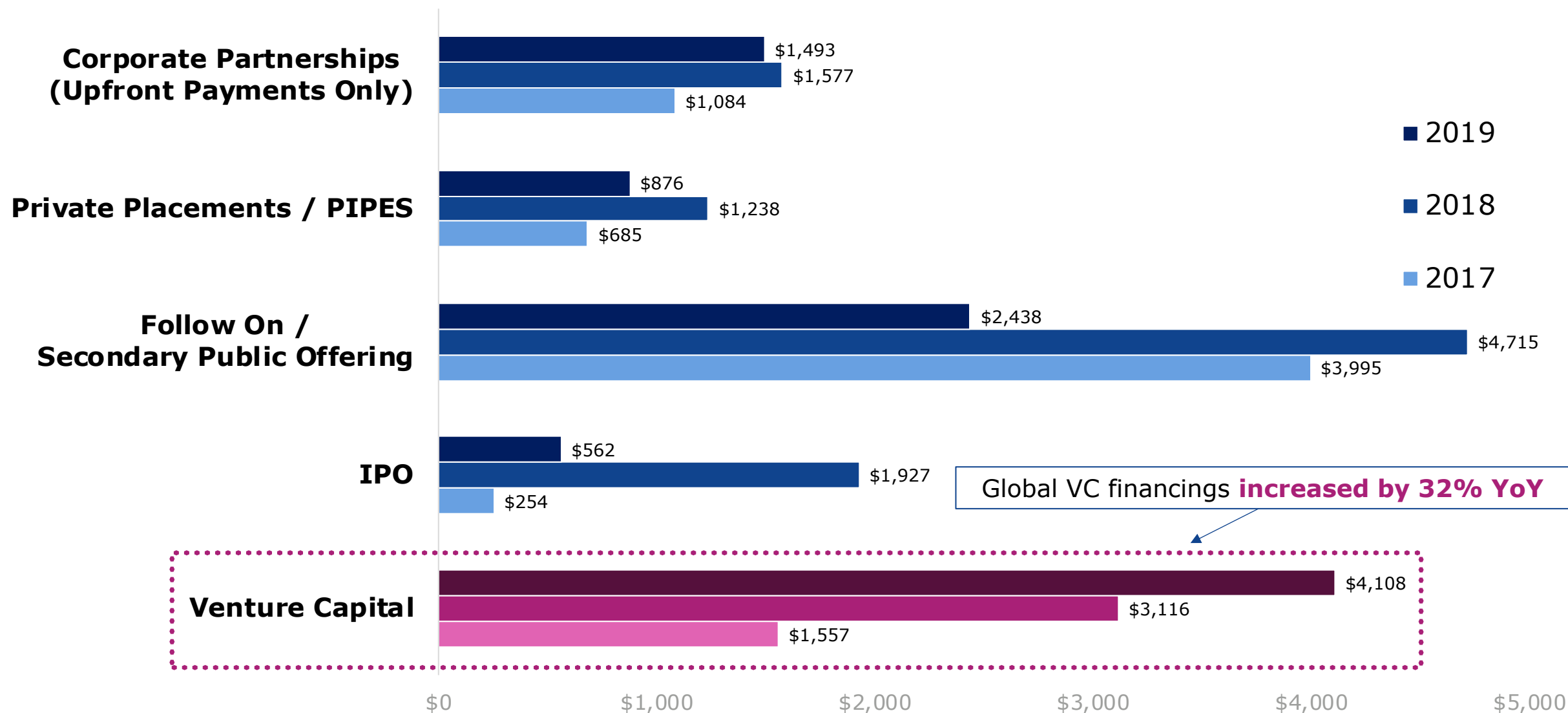
# Global Financings by Type & Year



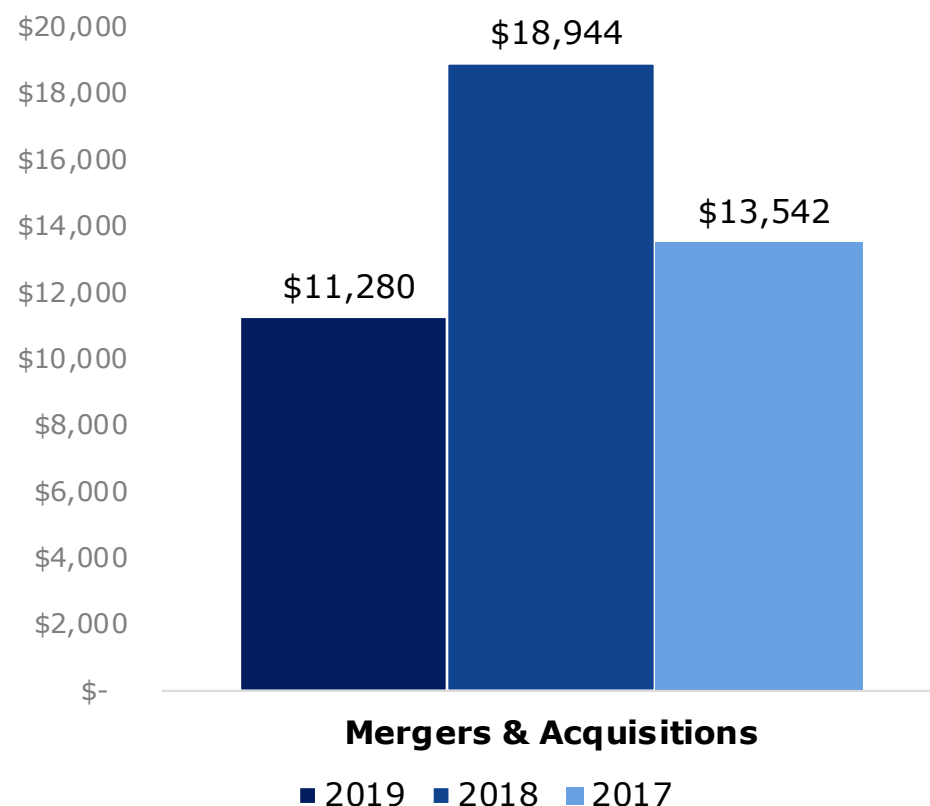
# Global Financings by Type & Year



# Global Financings by Type & Year



# M&A Activity Reflects Growing Interest in Cell & Gene Therapy



## Large and mid-cap pharma/bio acquisitions in the sector:

- Astellas acquires Audentes Tx for \$3B\*
- Roche acquires Spark Tx for \$4.8B
- Vertex acquires Semma for \$950M
- Biogen acquires Nightstar Tx for \$877M
- Bayer acquires remaining stake in BlueRock Tx for \$240M

*\*Not included in 2019 figure; deal expected to close Q1 2020*

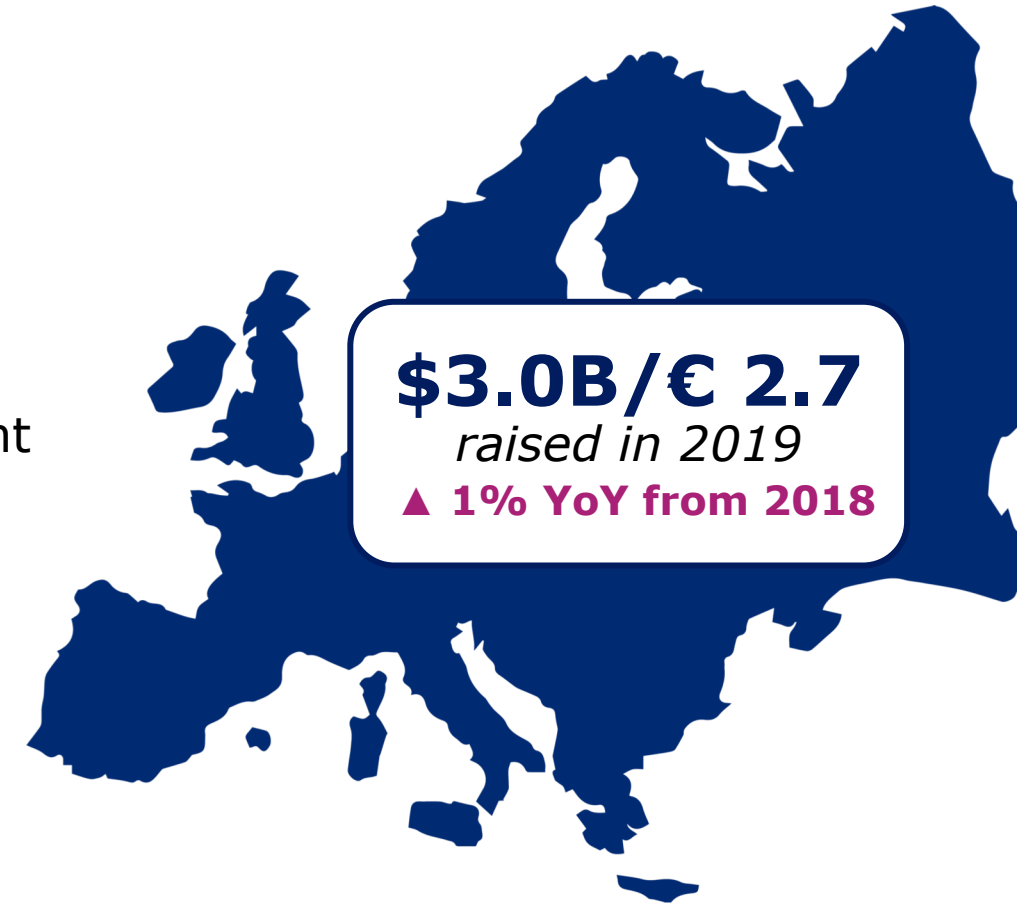


## Comparatively Strong Year in Europe

Despite YoY decreases in global financings, financings from regenerative medicine companies headquartered in Europe were on par with 2018.

### Significant financings include:

- Adaptive Bio & Genentech sign **\$300M** upfront agreement
- uniQure raises **\$225M** in follow-on financing
- Orchard Tx raises **\$128M** in follow-on financing
- Achilles Tx raises **\$121M** in Series B financing
- Autolus Tx raises **\$116M** in follow-on financing


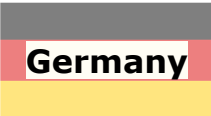









# Looking Forward: 2020+

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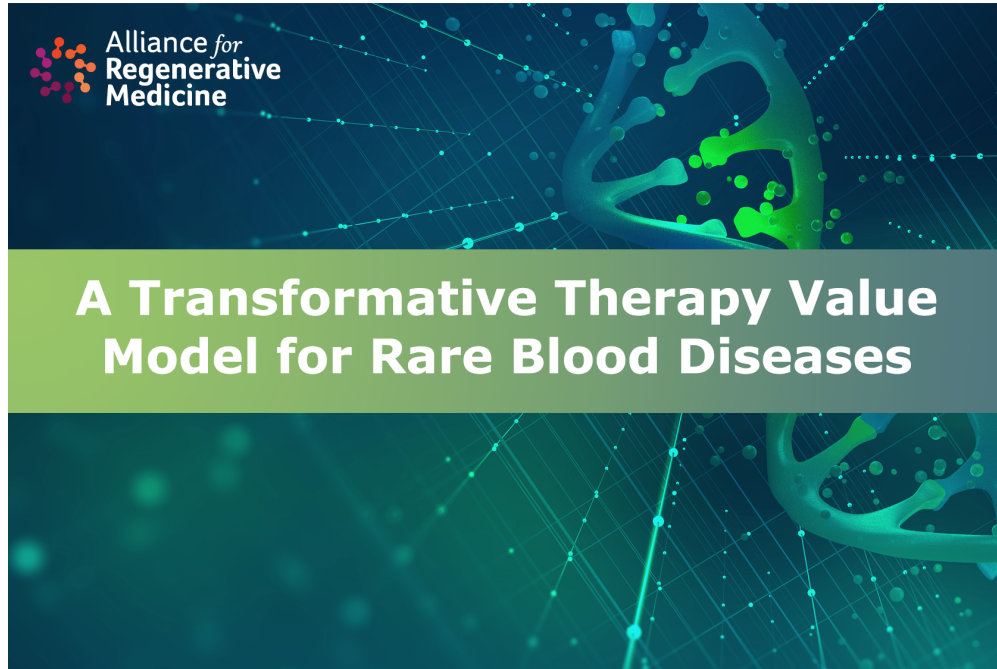
# Patient Access to Regenerative Medicines Is Increasing Rapidly

## Positive reimbursement decisions for select regenerative medicine products

	 France	 Germany	 UK	 Italy	 Spain	 US	 Canada	 Australia	 Japan
<b>Imlygic</b> <i>Melanoma</i>			✓	✓		✓			
<b>Holoclax</b> <i>Corneal Injury</i>			✓	✓					
<b>Strimvelis</b> <i>ADA-SCID</i>			✓	✓					
<b>Alofisel</b> <i>Crohn's</i>		✓			✓				
<b>Kymriah</b> <i>Blood cancers</i>	✓	✓	✓	✓	✓	✓	✓	✓	✓
<b>Yescarta</b> <i>Blood cancers</i>	✓	✓	✓	✓	✓	✓	✓		
<b>Luxturna</b> <i>IRD</i>		✓	✓			✓			
<b>Zolgensma</b> <i>SMA</i>						✓			

- = Product approved, but not currently reimbursed
- = Positive reimbursement
- = Product not currently approved

# New Analysis of 10 Year Cost Impact of Cell & Gene Therapy



- A Transformative Therapy Value Model (TVM): a refined model developed to evaluate long-term value of regenerative medicines
- Employs 10-year timeframe used by US Congressional Budget Office
- Sickle cell disease, hemophilia A, and multiple myeloma are case studies
- Conclusion: **cell and gene therapies could provide cost savings of 18-30% over a 10-year period** in these indications

*Released January 10, 2019 and available at [www.alliancerm.org](http://www.alliancerm.org)*

## In Summary

- 2019 a year of significant growth in the regenerative medicine sector; we enter 2020 poised for continued expansion
- Many patients are already benefitting from regenerative medicines, and the clinical results are dramatic
- The pipeline is robust, with several next-gen technologies entering the clinic and an increase in clinical trials for indications with large patient populations
- Considerable effort and progress in addressing various manufacturing challenges
- While financing dipped in 2019 vs. 2018, financing remains strong across venture capital and partnerships, with M&A activity showcasing large and middle cap pharma's interest in the cell & gene therapy space

# 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