



STATE *of the* INDUSTRY BRIEFING

#SOTI20

Janet Lambert, CEO
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
 - Compile sector data, **educate** media and other stakeholders

350+ ARM Members

***Members in bold are publicly traded companies*



4BIO Capital 4D Molecular Tx AAB **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**

State of the Industry Briefing

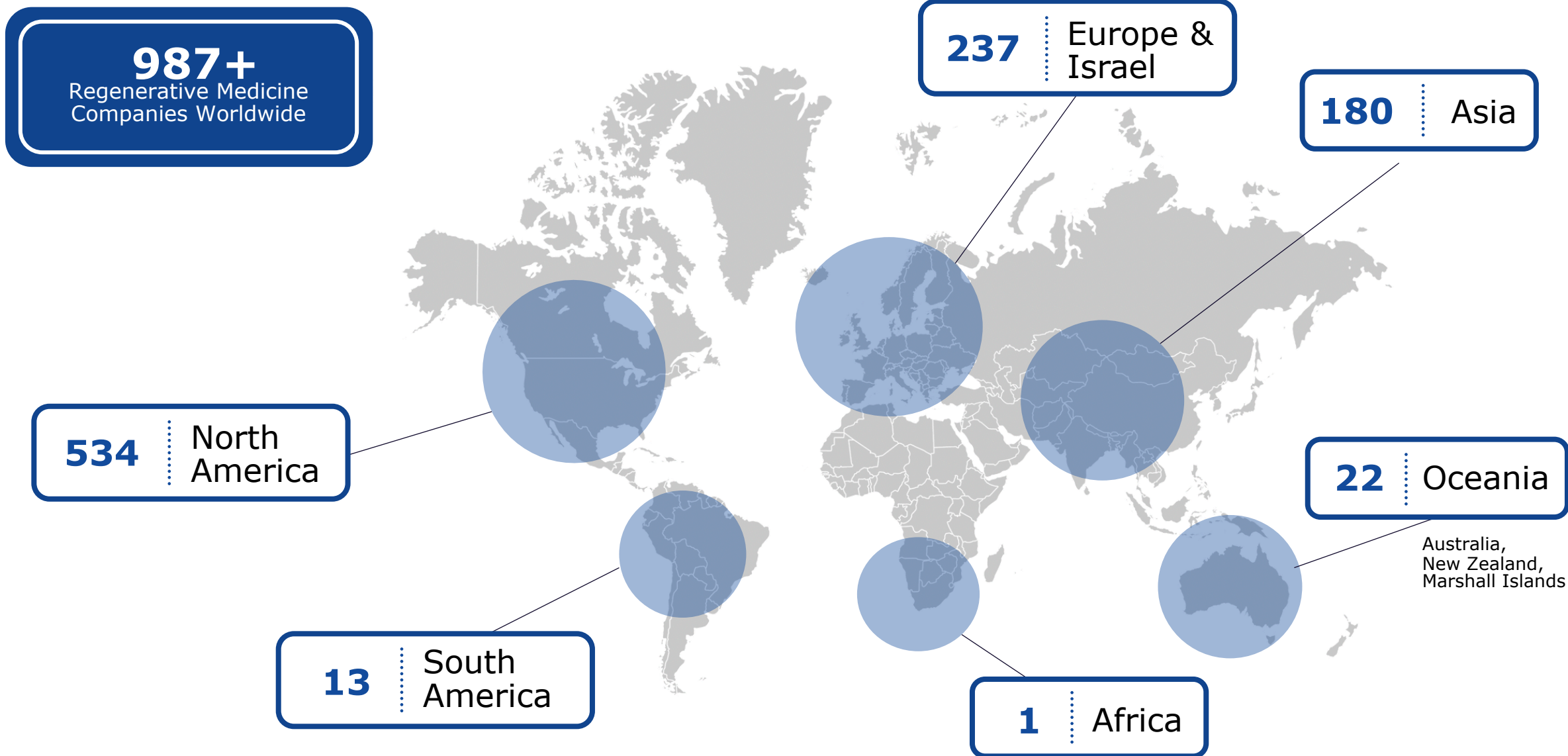
Access to the Slides:

www.alliancerm.org

Twitter:  @alliancerm



Current Global Sector Landscape



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

- ✓ *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
Zynteglo	bluebird bio	<ul style="list-style-type: none"> 75% of patients with TDT without $\beta 0/\beta 0$ genotype treated achieved transfusion independence
Zolgensma	AveXis, a Novartis company	<ul style="list-style-type: none"> 93% of SMA Type 1 patients treated were alive without permanent ventilation at 24 months post-treatment
LUXTURN A	Spark Therapeutics	<ul style="list-style-type: none"> 93% of patients treated showed an improvement of at least 1 light level from baseline
Yescarta	Kite Pharma, a Gilead company	<ul style="list-style-type: none"> 58% of patients with R/R B-Cell NHL treated experienced a complete response
Kymriah	Novartis	<ul style="list-style-type: none"> 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*

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:

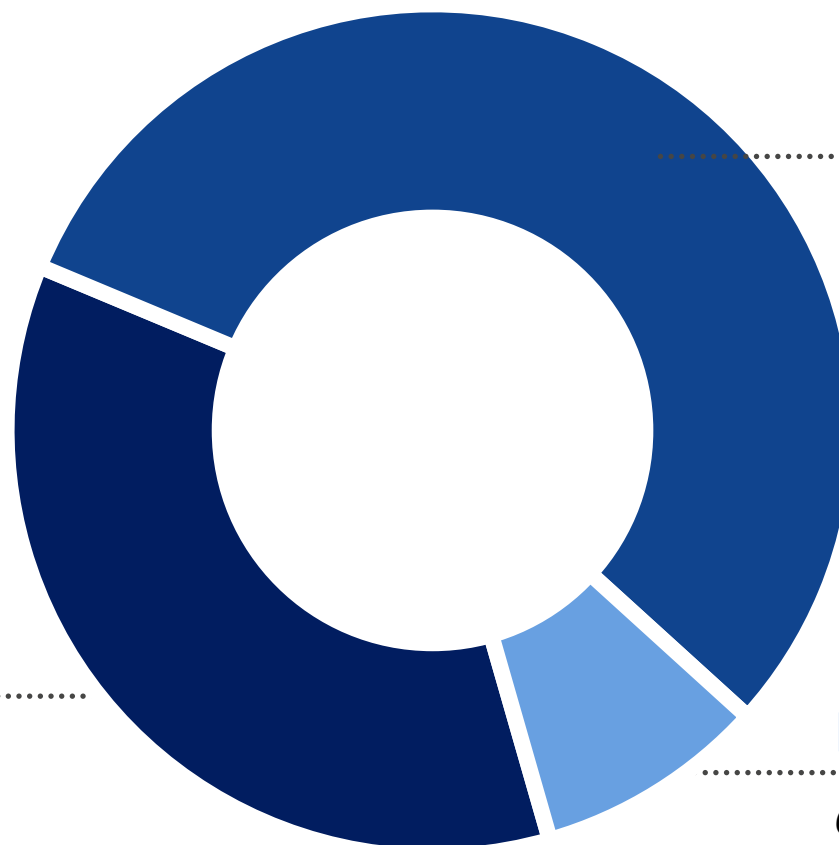
- Atara Bio – *tab-cel*
- Audentes Tx – *AT132*
- bluebird bio / BMS – *ide-cel*
- bluebird bio – *Zynteglo*
- GenSight Bio – *GS010*
- Humacyte – *Human Acellular Vessel*
- Iovance – *LN-145, lifileucel*
- Mallinkrodt – *Stratagraft*
- Orchard – *OTL-101, OTL-200 (US)*
- PTC Tx – *GT-AADC*
- Poseida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

Scientific & Clinical Advances

- ✓ *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

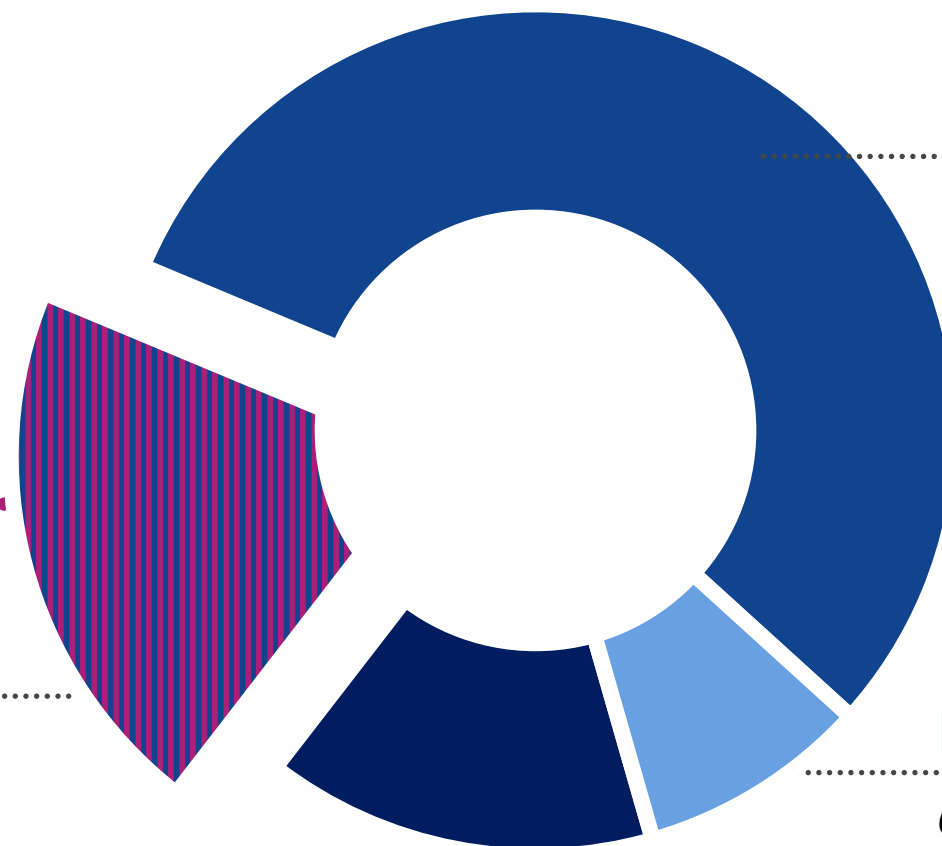
The Clinical Landscape for Regenerative Medicine

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



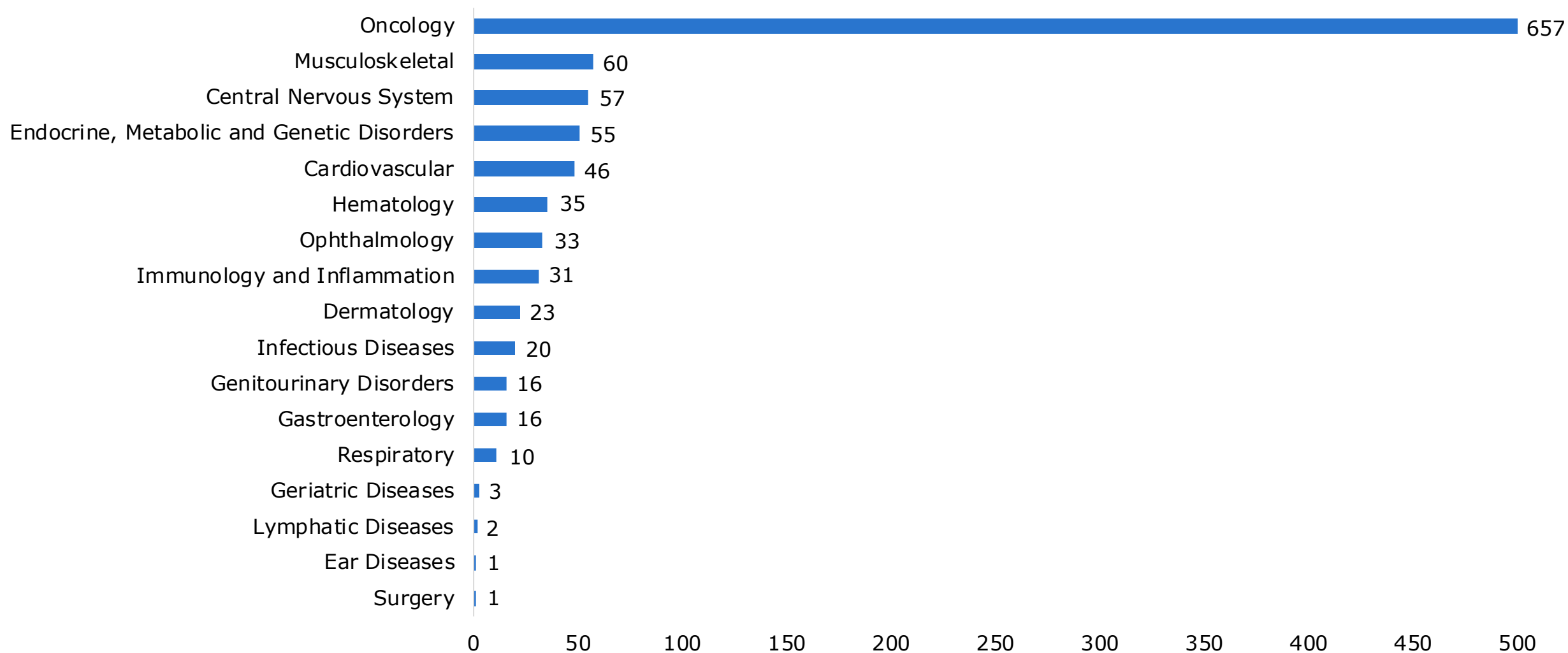
Phase 2: 591

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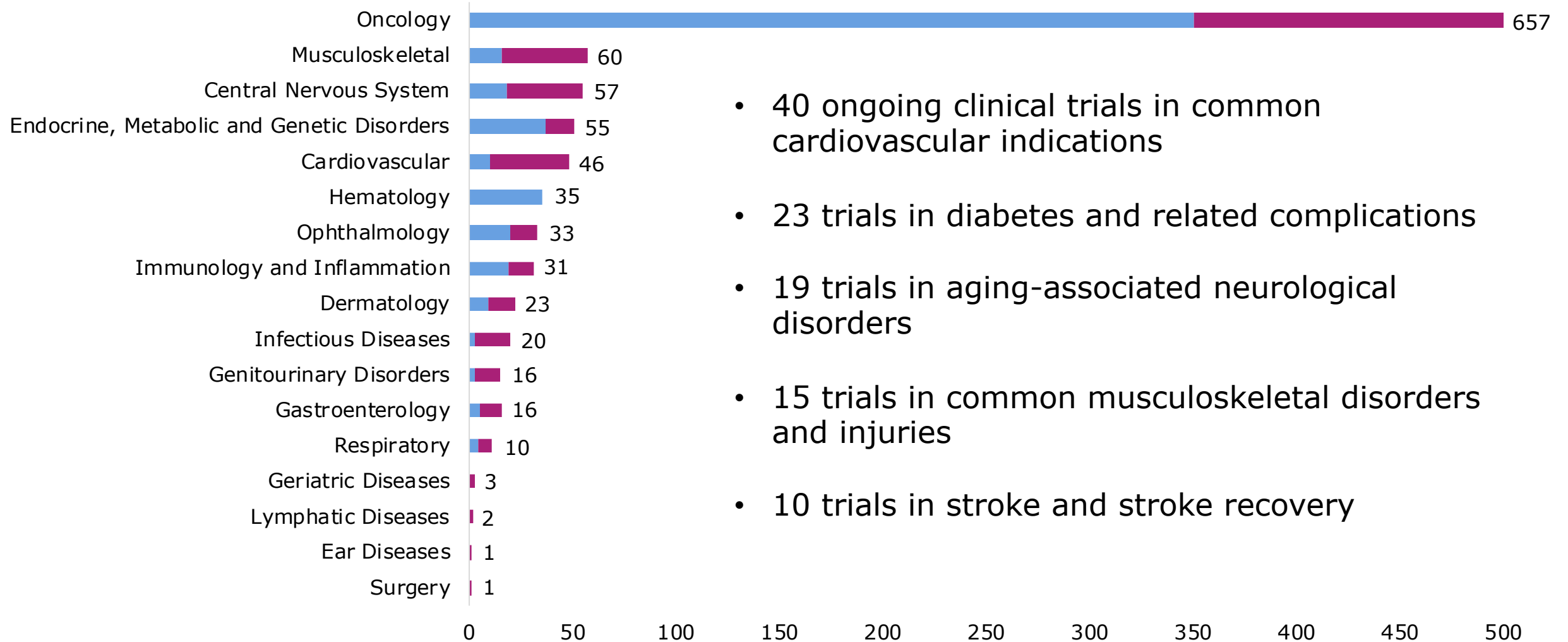
Gene Therapy: 32
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Clinical Trials Across Diverse Indications



Increasing Clinical Activity in Larger Indications

More prevalent indications indicated in purple





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**, **Cellctis**, 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

Focus on Manufacturing

- ✓ *In-house manufacturing capabilities often a strategic priority*
- ✓ *Companies invested in manufacturing earlier in the development process*
- ✓ *CMOs were attractive acquisition targets*

Expanding Manufacturing Capabilities

Numerous companies invested in in-house manufacturing capabilities:



⋮ Pfizer, Novartis lead \$2 billion spending spree on gene therapy production

Bloomberg

⋮ **Kite Announces Plans for New State-of-the-Art Facility to Expand Cell Therapy Production Capabilities**



BRIEF

⋮ **Thermo Fisher opens \$90M viral vector manufacturing plant in Massachusetts**

Expanding Manufacturing Capabilities

Pre-market companies invested in manufacturing early:

AUDENTES 

Audentes announced addition of cGMP plasmid manufacturing to existing large scale AAV operations



REGENXBIO announced new manufacturing facility, to be operational in 2021

elevatebio 

ElevateBio launched with \$150M to provide centralized R&D and manufacturing capabilities to suite of CGT developers



Precision BioSciences opened first in-house cGMP manufacturing facility dedicated to genome-edited allogeneic CAR-Ts in the US

Expanding Manufacturing Capabilities

CMOs were attractive acquisition targets in 2019:



Novartis acquires CellforCure to boost CAR-T manufacturing

FiercePharma

Hitachi gets EU cell manufacturing facilities with deal to buy Apceth Biopharma



Thermo Fisher to Acquire Brammer Bio for \$1.7B

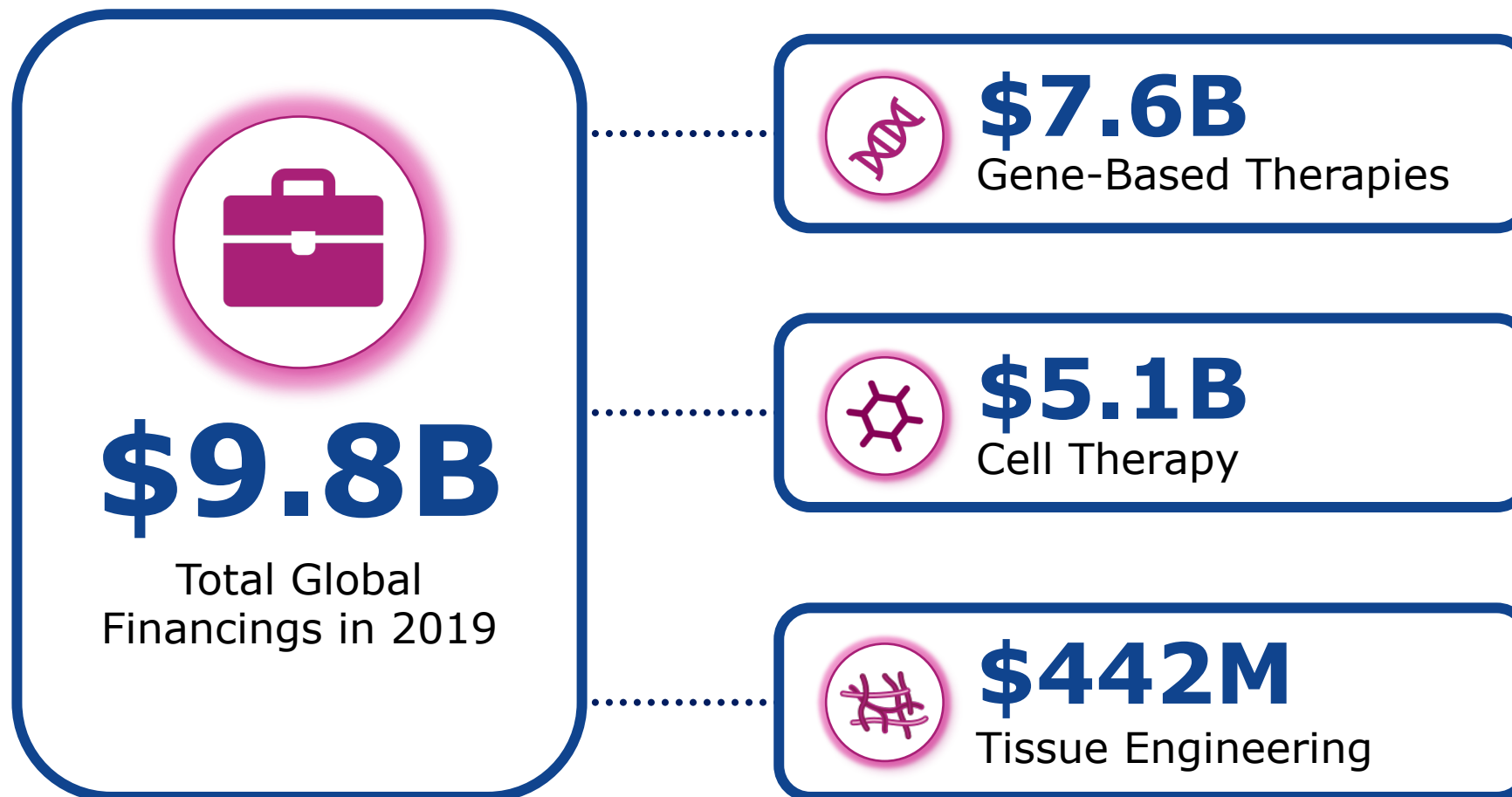


Catalent acquires gene therapy specialist Paragon for \$1.2bn

Financing Trends

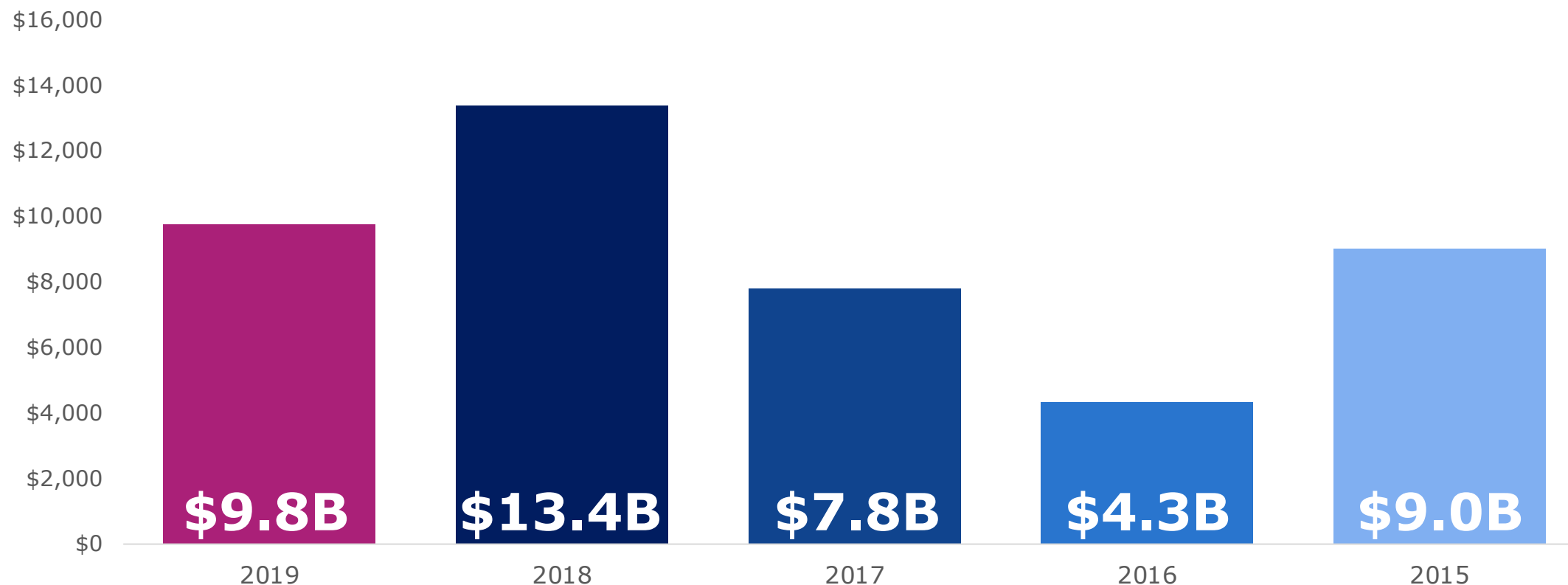
- ✓ *Total global financings in 2019 second highest ever for the sector*
- ✓ *Strong year for venture financing and corporate partnerships*
- ✓ *Large- and mid-cap pharma company M&A interest in cell & gene therapy*
- ✓ *European companies had a strong year for financings, on par with 2018*

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

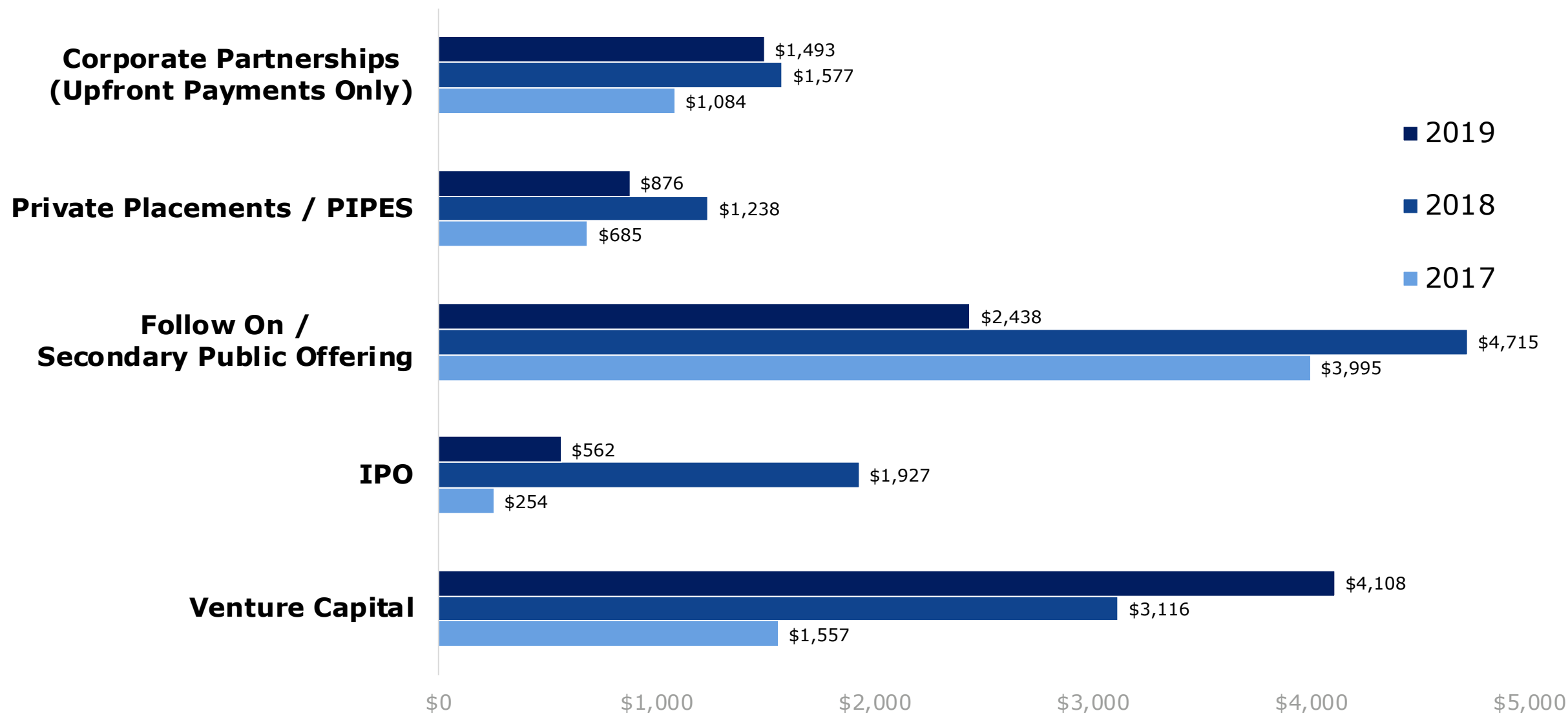
Venture Financings:

- 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 placement – 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

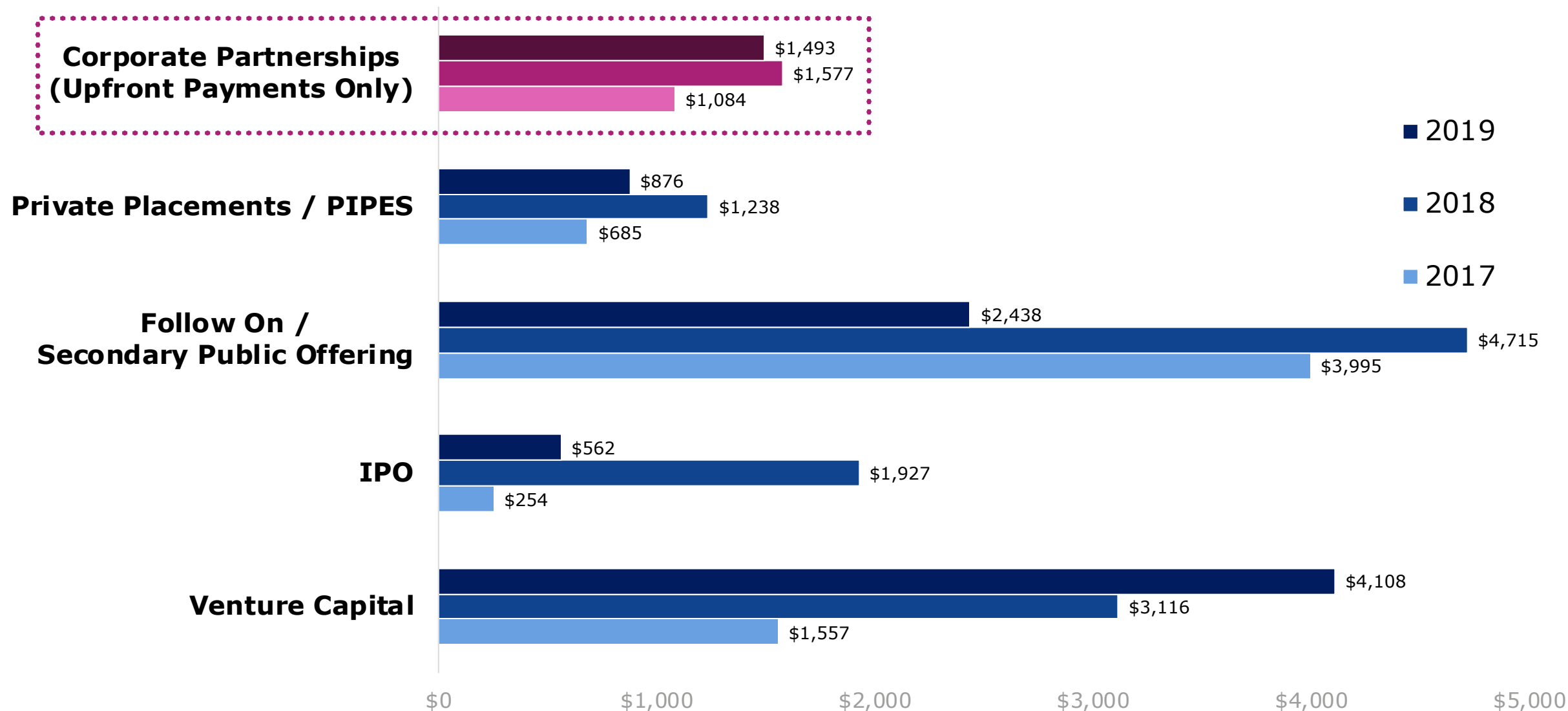
Public Offerings: (IPOs & Follow-Ons)

- 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

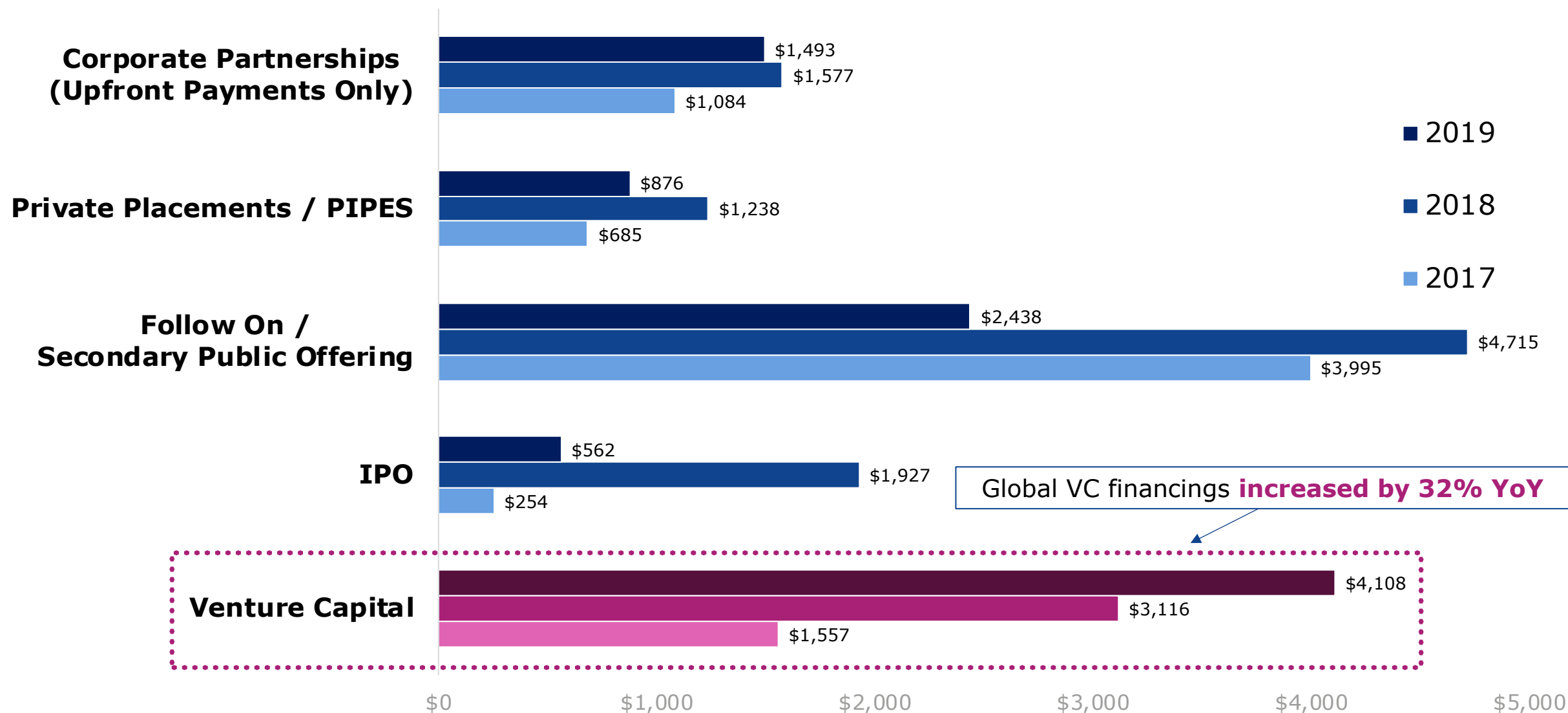
Global Financings by Type & Year



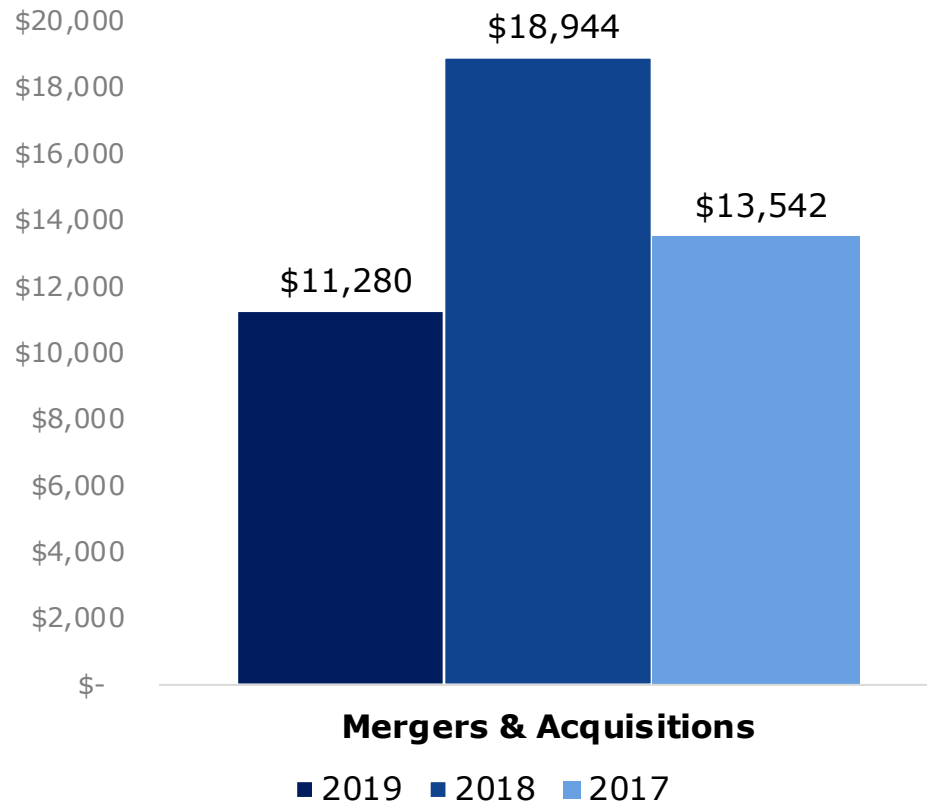
Global Financings by Type & Year



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

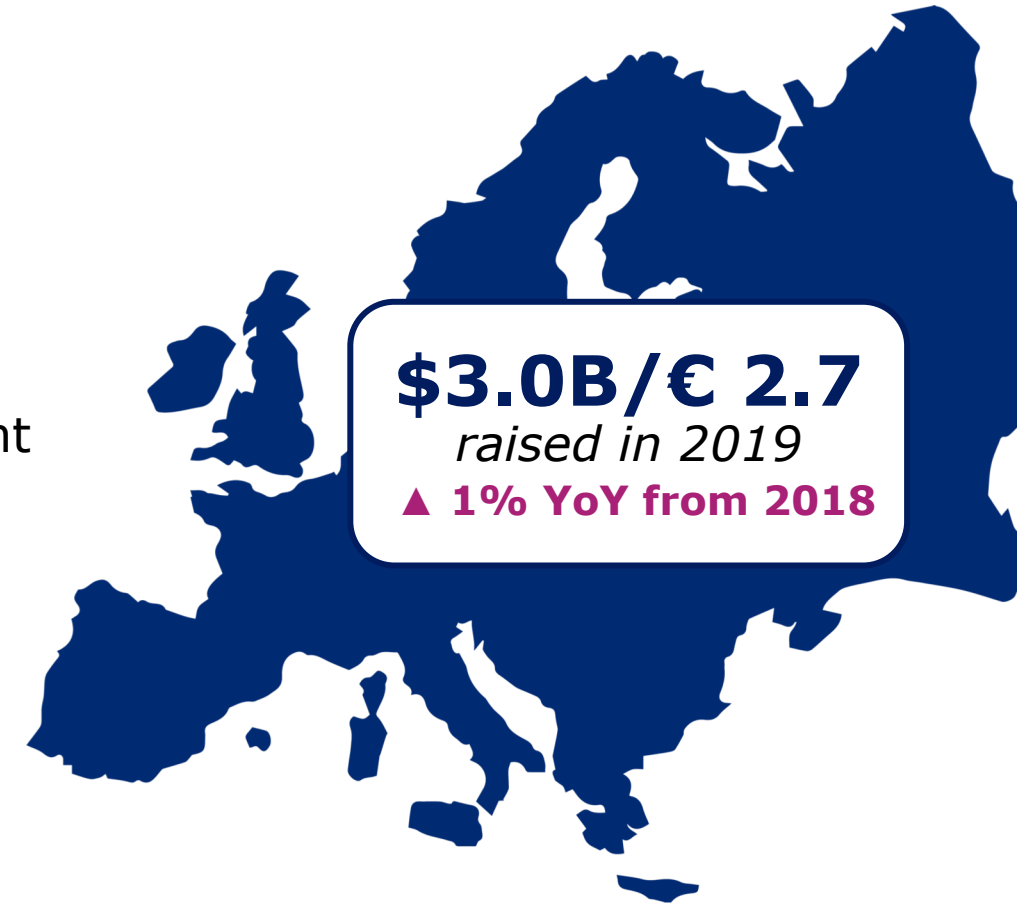
**Not included in 2019 figure; deal expected to close Q1 2020*

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+

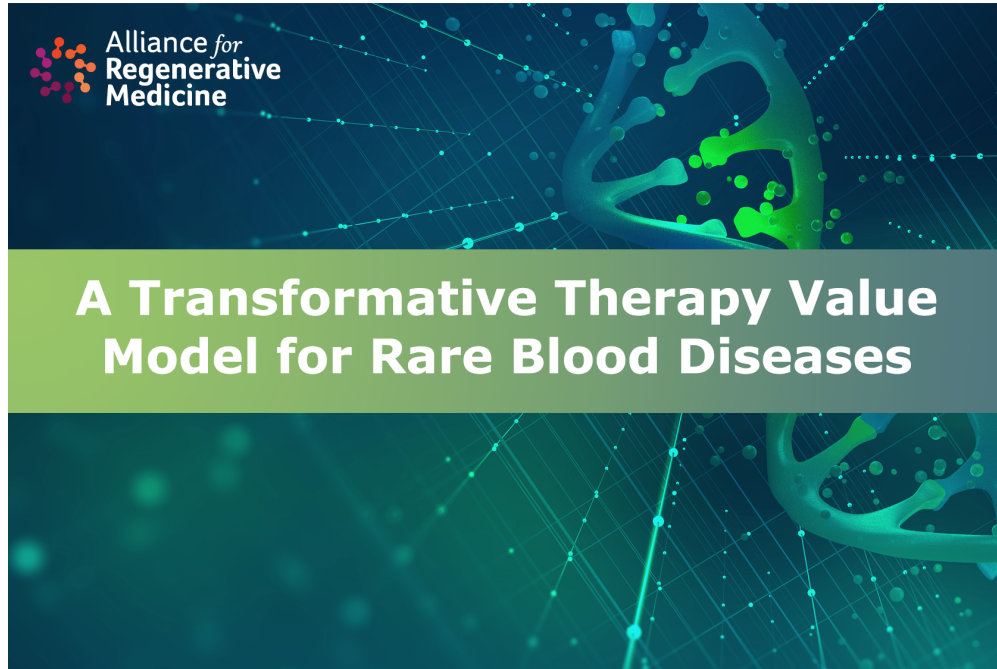
Patient Access to Regenerative Medicines Is Increasing Rapidly

Positive reimbursement decisions for select regenerative medicine products

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

The Outlook for 2020



Clinical Data Readouts

Numerous high-profile data readouts expected in 2020



Hospital Exemption

Additional focus on safety & efficacy for point-of-care administration



Product Approvals

Several anticipated product approvals; gene therapies likely to double within 1-2 years



Stem Cell Clinics

Additional enforcement actions to be taken against 'rogue' stem cell clinics



Sector Financing

Strong demand for financing; IPO market constrained by US elections; indications generally strong



Drug Pricing

Moderate solution with increased emphasis on value in the RM sector



Gene Therapy Advances

Continued improvements in gene therapy delivery & manufacturing



Regulatory Environment

Continued support for the sector, with additional RMAT / PRIME designations expected

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
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

EMERGING CELL THERAPIES FOR CANCER

SESSION CHAIR

Usman “Oz” Azam, President & CEO, Tmunity Therapeutics

PANELISTS

Claudia Mitchell, Senior VP, Product & Portfolio Strategy, Astellas Pharma

Samarth Kulkarni, CEO, CRISPR

Pascal Touchon, CEO, Atara Biotherapeutics

Matthew Kane, Co-Founder & CEO, Precision BioSciences

NEXT GENERATION GENE AND CELL TECHNOLOGIES

SESSION CHAIR

Timothy Miller, President & CEO, Gene Therapy Newco

PANELISTS

Laurence Cooper, CEO, Ziopharm Oncology

Emile Nuwaysir, President & CEO, BlueRock Therapeutics

Tim Lu, Co-Founder & CEO, Senti Bio

Shelia Mikhail, CEO, AskBio

Thank You!

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