
ALLIANCE for
Regenerative Medicine
#SOTI18

2018 CELL & GENE THERAPIES State of the Industry Briefing

JANUARY 8, 2018 | SAN FRANCISCO, CA

8:00am – 8:20am | Introduction & Industry Update

Robert Preti, Chairman, Alliance for Regenerative Medicine; President and CEO; Hitachi Chemical Advanced Therapeutics Solutions; GM, Hitachi Chemical Regenerative Medicine Business Sector

Janet Lynch Lambert, CEO, Alliance for Regenerative Medicine

8:20am – 9:05am | Next Generation CARs & Other Cell-Based Immunotherapies

Moderator: Robert Preti, President and CEO; Hitachi Chemical Advanced Therapeutics Solutions; GM, Hitachi Chemical Regenerative Medicine Business Sector

Featuring: Juno Therapeutics; Mustang Bio; Adaptimmune; Novartis Oncology; Fate Therapeutics

9:05am – 9:50am | Gene Therapy: The Outlook in 2018

Moderator: Martha Rook, Head of Gene Editing and Novel Modalities, MilliporeSigma

Featuring: CRISPR Therapeutics; Sangamo; BioMarin; Adverum, Gladstone Institutes

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Robert Preti
Chairman, Alliance for Regenerative Medicine
President & CEO, Hitachi Chemical Advanced Therapeutics Solutions
GM, Hitachi Chemical Regenerative Medicine Business Sector

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- *2017 marked an inflection point for this sector:*
  - *Recent FDA approvals and increasing clarity around market access*
  - *Bright and robust future pipeline*
- *FDA and the regulatory environment:*
  - *Scott Gottlieb as FDA Commissioner*
  - *Accelerated approvals & RMAT designation*

Clinical Progress: 2017

Anticipated Clinical Data Events: 2018

Sector Financial Performance: 2017

Policy Environment: 2017 & 2018

ARM Mission

The Alliance for Regenerative Medicine (ARM) is the preeminent global advocate for regenerative and advanced therapies. ARM fosters research, development, investment and commercialization of transformational treatments and cures for patients worldwide.

By leveraging the expertise of its membership, ARM empowers multiple stakeholders to promote legislative, regulatory and public understanding of, and support for, this expanding field.

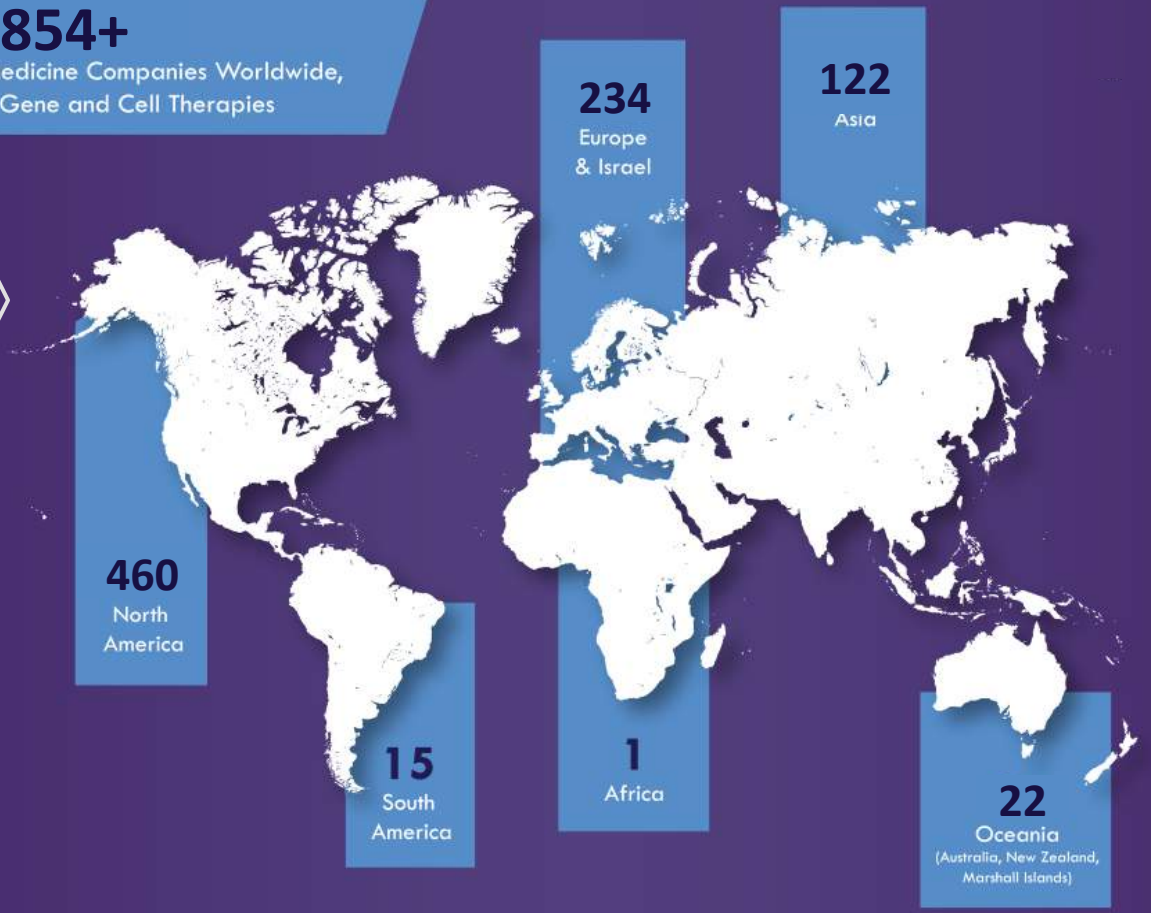
ARM Strategic Priorities

- *Advocate for clear, predictable and harmonized regulatory and review pathways*
- *Enable market access and value-based, favorable reimbursement policies*
- *Address industrialization and manufacturing hurdles*
- *Conduct key stakeholder outreach, communication and education*
- *Facilitate sustainable access to capital and identify sources of potential public funding*

Data provided by: informa

Current Global Sector Landscape

854+
Regenerative Medicine Companies Worldwide, Including Gene and Cell Therapies



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Major Therapeutic Platforms & Enabling Technologies

- ***Advanced cells:*** *Modified T-cells; Hematopoietic stem cells; iPSCs; MSCs; adult progenitor cells (neural, liver, cardiac); etc.*
- ***Cell-based immunotherapies:*** *T-cells; CAR-T; TCR; NK cells; TILs; MILs; GammaDelta, Dendritic vaccines; etc.*
- ***Novel and synthetic gene delivery vehicles:*** *AAV; LV; RV; AD; etc.*
- ***Genome editing:*** *CRISPR/Cas, next-gen CRISPR tech; TALENs; ZFNs; Homologous Recombination; etc.*
- ***Next-gen expression constructs:*** *novel capsids; innovative regulatory elements, including synthetic promoters that enable specificity, strength, and improve capacity; inducible elements to regulate gene expression temporally or in response to external stimuli: molecular kill switches to improve safety; etc.*

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Janet Lynch Lambert
CEO
Alliance for Regenerative Medicine

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Select Significant Clinical & Data Events: 2017

Approvals this year:

- **Spark Therapeutics' LUXTURNA gene therapy** for biallelic RPE65-mediated inherited retinal disease – Dec 19
  - MAA submitted to EMA – July 31
- **Gilead / Kite Pharma's Yescarta CAR T-cell therapy** for the treatment of adult patients with relapsed/refractory large B-cell lymphoma after two or more lines of systemic therapy – Oct 18
  - MAA expected Q1 2018
- **Novartis's Kymriah CAR T-cell therapy** for the treatment of children and young adults with relapsed or refractory B-cell acute lymphoblastic leukemia and for adults with r/r diffuse large B-cell – August 30
  - MAA submitted to EMA – Nov 6
- **TiGenix's Cx601 allogeneic cell therapy** for treatment of Crohn's received EMA CHMP endorsement – Dec 15

U.S. FDA RMAT Designations:

- Asterias's AST-OPC1 (spinal cord injury)
- Athersys's MultiStem (ischemic stroke)
- bluebird bio's LentiGlobin (severe sickle cell disease)
- Cellvation's CEVA101 (traumatic brain injury)
- Humacyte's Humacyl (vascular access for hemodialysis)
- Enzyvant's RVT-802 (DiGeorge syndrome)
- jCyte's jCell (retinitis pigmentosa)
- Juno's JCAR017 (r/r aggressive large B cell NHL)
- Kiadis's ATIR101 (leukemia)
- Mallinckrodt's Stratagraft (deep partial-thickness burns)
- Mesoblast's MPC-150-IM (heart failure)
- Vericel's ixmyelocel (dialated cardiomyopathy)

946 Total Clinical Trials Worldwide

314
Phase I

271 in 2016

550
Phase II

465 in 2016

82
Phase III

66 in 2016

Data provided by: informa

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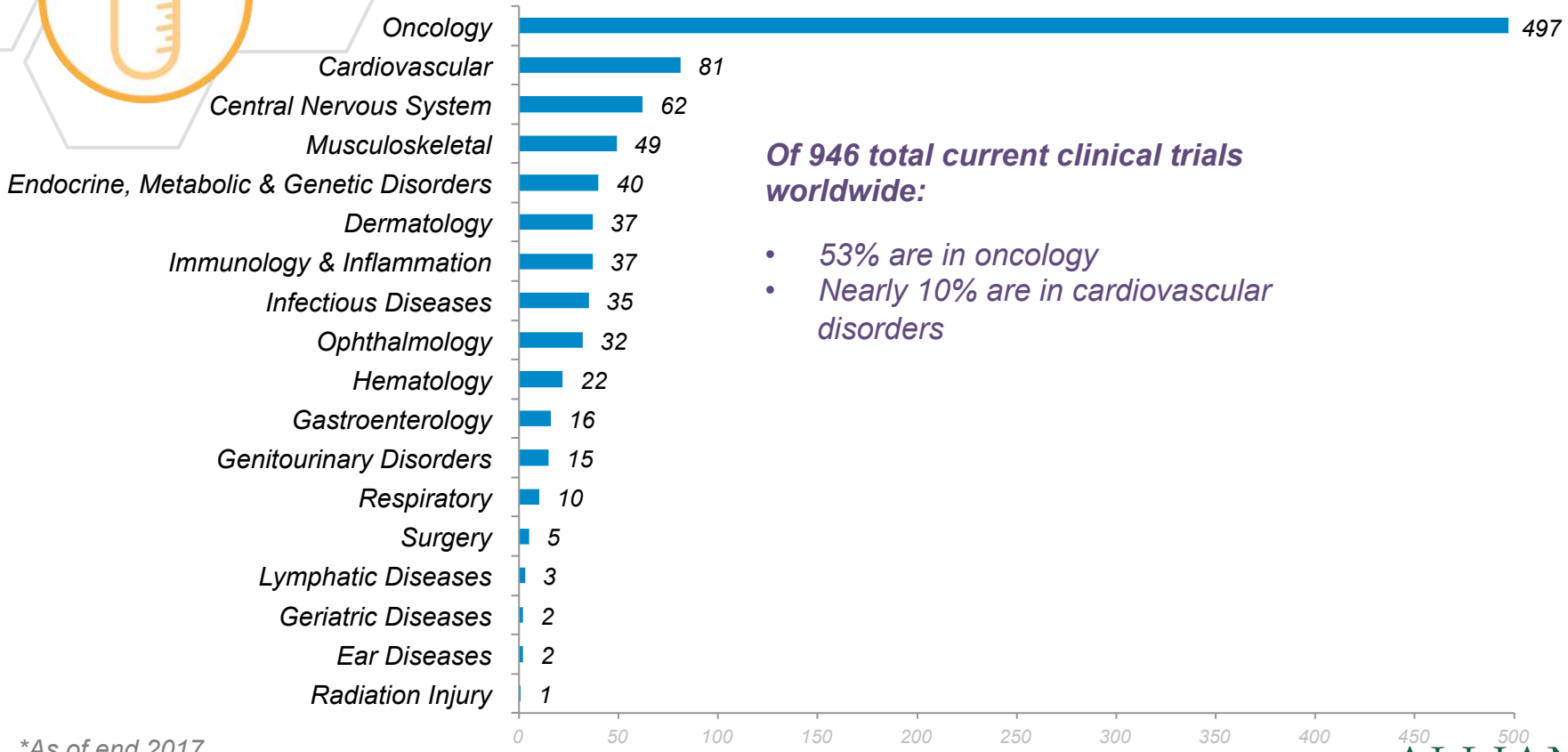
Clinical Trials by Therapeutic Category



Of 946 total current clinical trials worldwide:

- *53% are in oncology*
- *Nearly 10% are in cardiovascular disorders*

**As of end 2017*

Data provided by: **informa**

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Cell-Based Immuno-Oncology Clinical Overview

Major companies and research institutions in this space:

CAR-T

- *Bellicum Pharmaceuticals*
- *bluebird bio / Celgene / Baylor College of Medicine – Center for Cell & Gene Therapy*
- *Cellectis*
- *Cellular Biomedicine Group*
- *Celyad*
- *Editas Medicine (via Juno collaboration)*
- *Janssen Global / Legend Biotech*
- *Juno Therapeutics*
- *Gilead / Kite Pharma*
- *MaxCyte*
- *MediGene*
- *Memorial Sloan Kettering Cancer Center*
- *MustangBio*
- *Novartis / UPenn / Oxford BioMedica / GE Life Sciences / Intellia Therapeutics*
- *Opexa Therapeutics*
- *Pfizer (via Cellectis collaboration)*
- *Poseida/Janssen*
- *University College London*
- *Unum Therapeutics / Seattle Genetics*
- *ZIOPHARM/Intrexon/ UT Texas MD Anderson Cancer Center*

TCRs and Modified T Cells

- *Adaptimmune / Caladrius*
- *Bellicum Pharmaceuticals*
- *Cellular Biomedicine Group*
- *Editas (via Juno collaboration)*
- *Fate Therapeutics*
- *GSK via Adaptimmune*
- *Immatics*
- *Immunocore*
- *Juno Therapeutics*
- *Kite Pharma*
- *NexImmune*
- *PDC*Line*
- *Takara Bio*
- *Tessa Therapeutics*
- *TCR2*
- *Unum Therapeutics*

Gamma Delta Cells

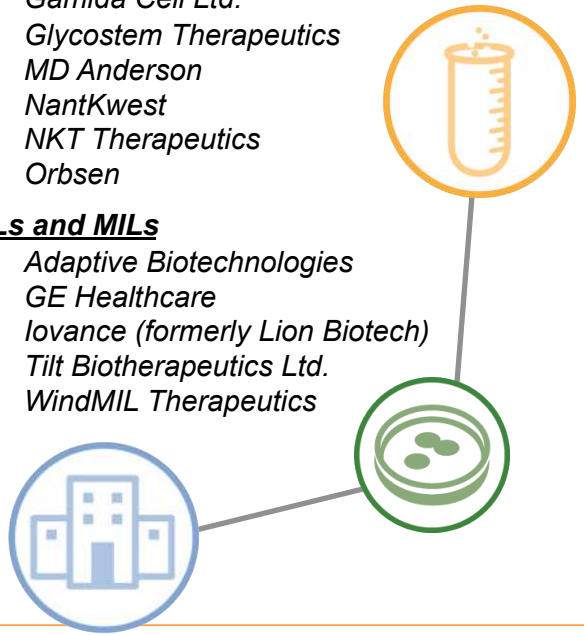
- *Gamma Delta Therapeutics*
- *MD Anderson*
- *American Gene Technologies*
- *TC BioPharm*

NK cells

- *Celyad*
- *DragonFly*
- *Fate Therapeutics*
- *Gamida Cell Ltd.*
- *Glycostem Therapeutics*
- *MD Anderson*
- *NantKwest*
- *NKT Therapeutics*
- *Orbsen*

TILs and MILs

- *Adaptive Biotechnologies*
- *GE Healthcare*
- *Iovance (formerly Lion Biotech)*
- *Tilt Biotherapeutics Ltd.*
- *WindMIL Therapeutics*



Gene Therapy & Genome Editing

Major companies in this space:

AAV Vectors
- 4D Molecular Therapeutics
- Abeona Therapeutics
- Acucela
- Adverum Biotechnologies
- Agilis Biotherapeutics
- AGTC
- Allergan (Retrosense Tx acquisition)
- Audentes Therapeutics
- AveXis
- Biogen
- BioMarin
- CombiGene
- Dimension Therapeutics
- Esteve
- Freeline Therapeutics
- Genethon
- Gensight Biologics
- Global BioTherapeutics
- Homology Medicines
- HORAMA
- Lysogene
- Milo Biotechnology
- NightstaRx
- Pfizer (Bamboo Tx acquisition)
- REGENXBIO
- Shire
- Solid Biosciences
- Spark Therapeutics
- Theragene Pharmaceuticals
- uniQure
- Voyager Therapeutics

Lenti/Retroviral Vectors
- Adaptimmune
- AVROBIO
- Bellicum Pharmaceuticals
- bluebird bio
- Calimmune
- Celgene
- Cellular Biomedicine Group
- Cellectis/Pfizer
- Celyad
- Editas Medicine
- EMD Serono
- Errant Gene Therapeutics
- Fate Therapeutics
- Fibrocell Science
- GE Healthcare Life Sciences
- Genenta Science
- GSK
- Immunocore
- Insulete
- Juno Therapeutics
- Kite Pharma
- MaxCyte
- Medigene
- MolMed
- NexImmune
- Novartis
- Opexa Therapeutics
- Orchard Therapeutics
- Oxford BioMedica
- Poseida Therapeutics/Janssen
- Rocket Pharma
- Takara Bio
- Tocagen
- Unum Therapeutics
- ZIOPHARM Oncology

Adenoviral Vectors
- Angionetics (Taxus Cardium Pharmaceuticals)
- Cell Medica
- GenVec
- Global Biotherapeutics
- Aevi Genomic Medicine
- PeriphaGen
- Renova Therapeutics

Genome Editing
- Biogen
- bluebird bio
- Caribou Biosciences
- Cellectis
- CRISPR Therapeutics
- Casebia Therapeutics (Bayer/CRISPR)
- Editas Medicine
- Homology Medicines
- Intellia Therapeutics
- LogicBio
- Poseida Therapeutics
- Precision BioSciences
- Sangamo Therapeutics
- Universal Cells

Enabling Platforms
- Aldevron
- Brammer Bio
- Cell Design Labs
- Cognate BioServices
- EMD Millipore
- Hitachi Chemical Advanced Therapeutics
- Intrexon
- Lonza
- Novasep
- PharmaCell
- Synpromics
- ThermoFisher Scientific
- WuXi AppTec

Select Anticipated Late-Stage Clinical Data Events

Company	*Product*	*Therapeutic Modality*	*Indication*	*Clinical Stage*	*Expected Reporting Date*
Spark Tx	LUXTURNA	AAV-vector gene therapy	Biallelic RPE65-mediated IRD	Administration at select treatment centers	Q1 2018
Kiadis	ATIR101	Allodepleted T-Cell Immunotherapy	AML or ALL	Conditional EU approval	2H 2018; launch 2019
TiGenix	Cx601	Cell therapy	Crohn's disease	EU approval	1H 2018
bluebird bio	Lentiglobin	Gene therapy	Transfusion dependent beta-thalassemia	MAA filing	End-year 2018
Kite (Gilead co)	Yescarta	CD19-directed CAR T cell therapy	Refractory Large B-Cell Lymphoma	Pending MAA	1H 2018
Enzyvant Tx	RVT-802	Tissue-based therapy	Complete DiGeorge Syndrome	BLA submission	2018
Juno	JCAR017	CAR-T cell therapy	NHL	BLA submission	2H 2018
bluebird bio	Lentiglobin	Gene therapy	Transfusion dependent beta-thalassemia	Ph III – Northstar-2 HGB-207	Mid-year 2018
bluebird bio	Lentiglobin	Gene therapy	Transfusion dependent beta-thalassemia & beta-0/beta-0 genotypes	Ph III – Northstar-3 (HGB-212)	End-year 2018
Histogenics	NeoCart	Tissue-engineering product	Cartilage repair	Ph III (topline data, potential BLA filing)	Q3 2018
Athersys	MultiStem	Allogeneic stem cell (MAPC)	Ischemic Stroke	Ph III (under SPA)	Initiating 1H 2018
Bone Tx	PREOB	Cell therapy (autologous)	Osteonecrosis of the hip	Ph III	2H 2018
Brainstorm	NurOwn	Mesenchymal Stem Cell Therapy	ALS	Ph III	Interim safety data June 2018; top-line data 2019
Mesoblast	MSC-100-IV	Mesenchymal Stem Cell Therapy	Acute Graft Versus Host Disease	Ph III	Day 28 Primary endpoint Q1 2018; Day 100 survival rate Q2 2018
Mesoblast	MPC-150-IM	Mesenchymal Precursor Cell Therapy	Mod to Severe Chronic Heart Failure	Ph III	Complete enrollment 2H 2018
Mesoblast	MPC-06-ID	Mesenchymal Precursor Cell Therapy	Chronic low back pain due to Disc Degeneration	Ph III	Complete enrollment Q1 2018
Abeona	EB-101	Gene therapy	Epidermolysis Bullosa	Commence Ph III	Early 2018

Total Global Financings: 2017

$7.5 Billion
Total Amount Raised in 2017

$4.2 Billion raised in 2016

$4.5 Billion
Gene & Gene-Modified Cell Therapy

$1.7 Billion raised in 2016

$446.1 Million
Tissue Engineering

$425.4 Million raised in 2016

$4.0 Billion
Cell Therapy

$1.8 Billion raised in 2016

*in USD
Data provided by: informa

** Please note: total amount raised represents sector-wide figures; some companies are active in more than one technology group.
*** Data does not include M&A transactions

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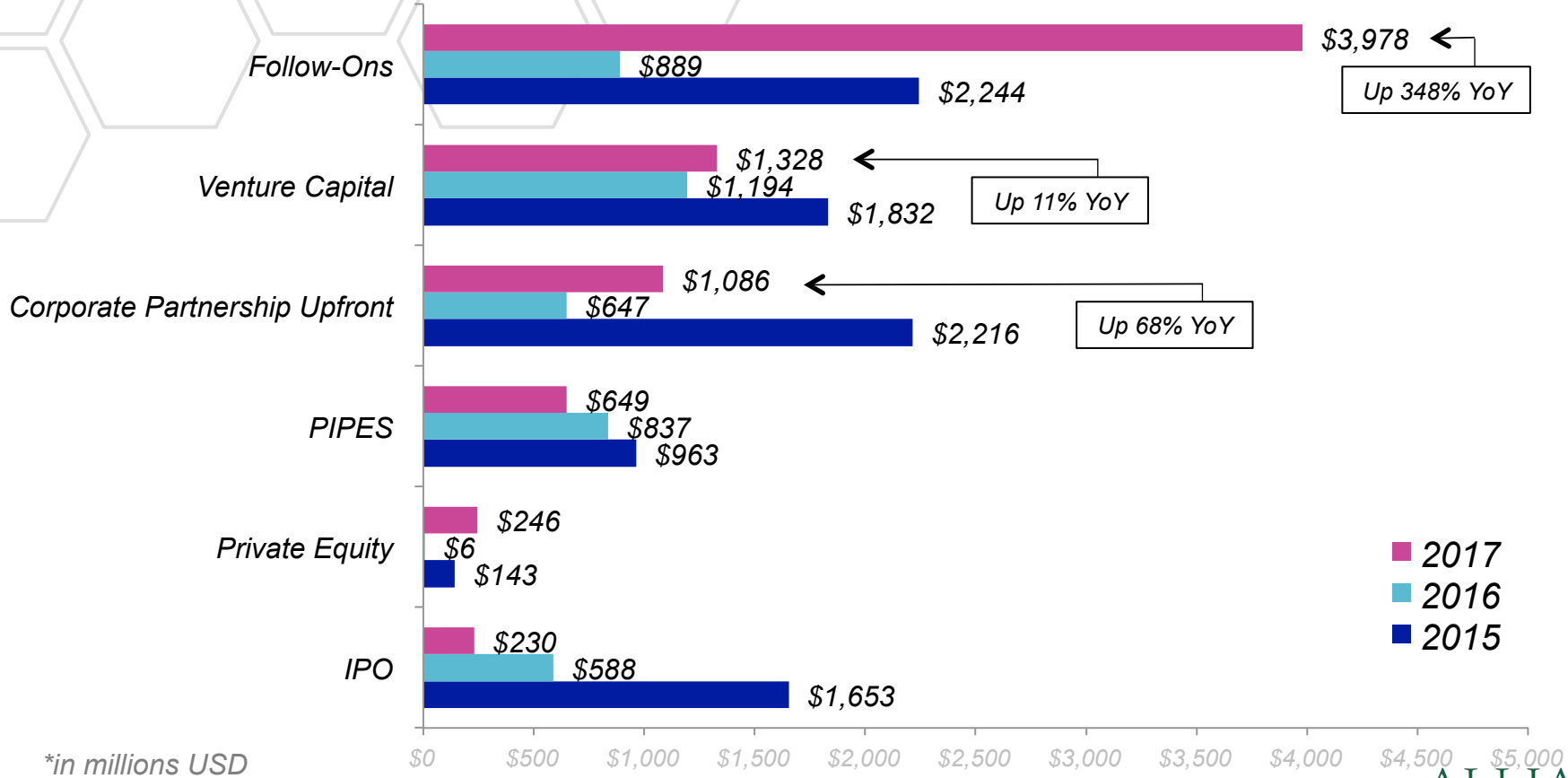
Total Financings by Type, by Year



*in millions USD

Data provided by: informa

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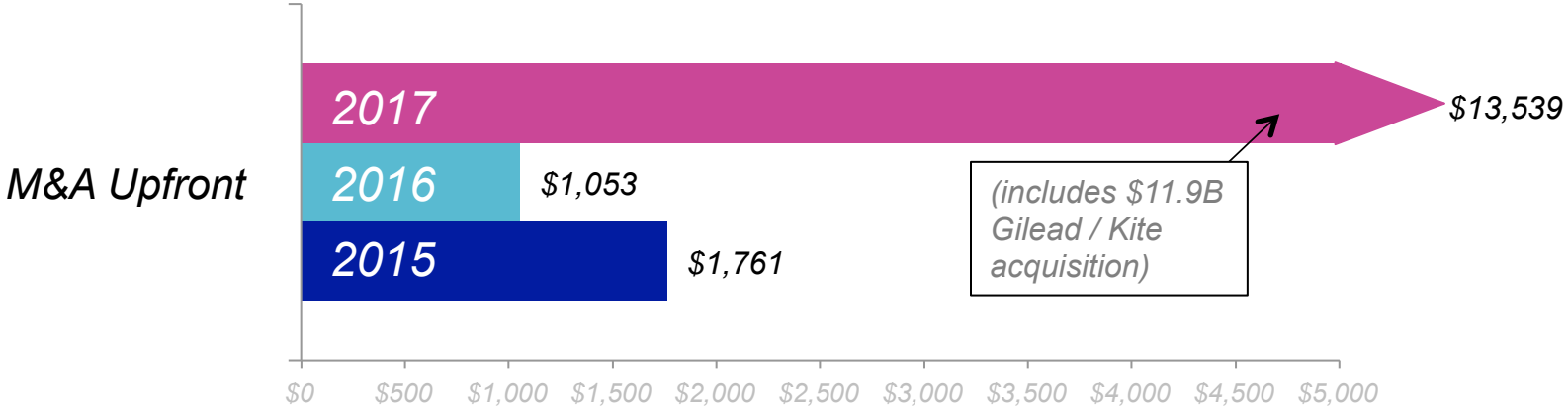
Total M&A Transaction Values: By Year



*in millions USD

Data provided by: informa

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Select Corporate Partnerships / Collaborations & Public Financings: 2017

Corporate Partnerships / Collaborations

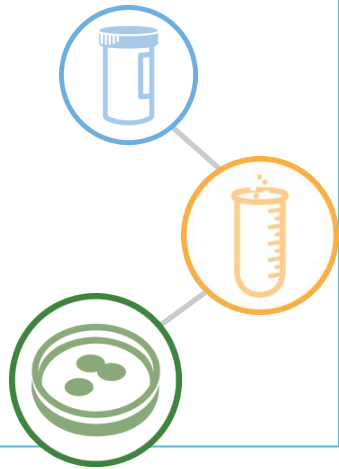
- *Sangamo signs $545M hemophilia A gene therapy collaboration with Pfizer, incl $70M upfront – May 10*
- *Janssen Biotech signs $350M agreement with Legend Biotech USA & Legend Biotech Ireland – Dec 21*
- *Kite Pharma signs $250M agreement with Daiichi Sankyo, incl $50M upfront – Jan 9*
- *Oxford BioMedica signs $100M agreement with Novartis, incl $10M upfront – July 6*
- *Takeda signs $100M agreement with GammaDelta Therapeutics – May 9*
- *Histogenics signs $97M agreement with MEDINET for NeoCart, incl $10M upfront – Dec 21*

Follow-On Financings

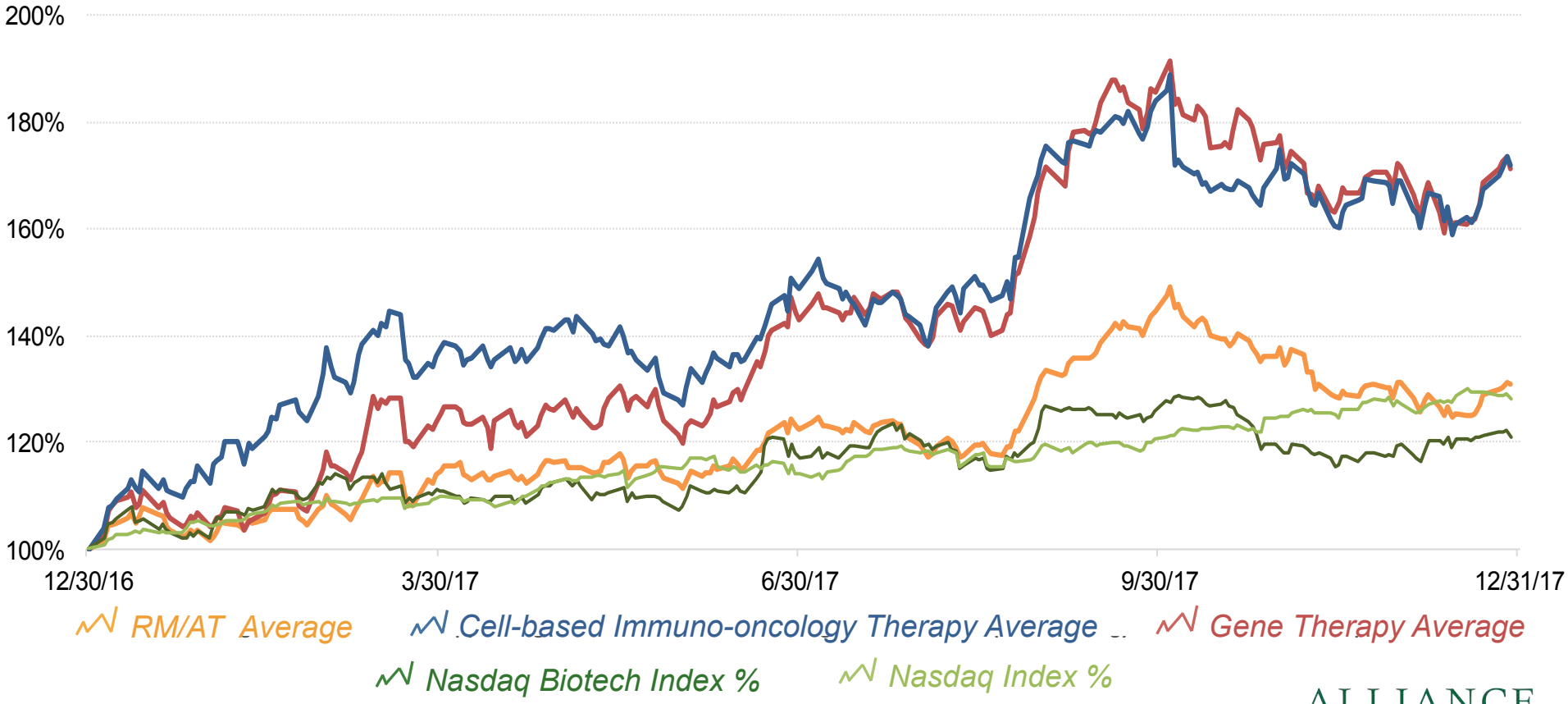
- *Bluebird bio $460M – July 30*
- *Kite Pharma $409.7M – March 8*
- *Spark Therapeutics $402.5M – August 9*
- *AveXis $287.8M – June 26*
- *Juno Therapeutics $287.6M – Sept 26*
- *Intellia Therapeutics $150M – Nov 6*

Venture Financings:

- *Rubius Therapeutics $120M – June 21*
- *Semma Therapeutics $114M – Nov 30*
- *Orchard Therapeutics $110M – Dec 20*
- *Homology Medicines $83.5M – Aug 1*
- *Tessa Therapeutics $80M – Dec 20*



Advanced Therapies Public Company Performance



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Key Takeaways: 2017

Turning point for the sector

- *Significant product approvals; with potentially many more to follow near-term*
- *Growing public awareness and anticipation*
- *FDA recognition of the unique and transformative nature of the sector*
  - *RMAT designation implementation*
- *Financial maturity, broad and sustained investor interest*

Emphasized need for commercial support and readiness in key areas:

- *Reimbursement, regulatory, industrialization, and manufacturing*

ARM's U.S. & Europe Regulatory & Policy Priorities

Recap: 2017

Regulatory

- *ARM-initiated 21st Century Cures provisions: RMAT, FDA Regulatory Framework & Standards*
- *Secured inclusion of GT in RMAT designation*
- *Legal evaluation of Hospital Exemption in EU*
- *Drove multi-EU org. position paper on GMO requirements for clinical trials with ATMPs*

Reimbursement

- *Promoted value-based payment in Medicare, Medicaid and commercial insurance*
- *Identified barriers and possible solutions to promote alternative financing models; white paper series*

Industrialization & Manufacturing

- *Established Standards Coordinating Body*
- *Defined current sector best practices, incl process analytical technologies, approaches to assess product comparability, reference standards, validation of potency assays*

Looking ahead: 2018 priorities

Regulatory

- *New regulatory framework/RMAT designation*
- *Anticipated FDA disease-specific gene therapy guidances*
- *Updated guidance re CMC, manufacturing*
- *Promote regulatory convergence across EU (incl. HE, GMO, GMP, Blood/Tissues & Cells Directives)*

Reimbursement

- *Develop principles of ARM-endorsed global value framework*
- *Develop strategies to remove or mitigate barriers via regulatory changes or legislation for public and private payers both in the US and in key EU countries*

Industrialization and Manufacturing

- *Reduce technical and regulatory barriers to scale up RM / AT therapies*

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NEXT-GENERATION CARS & OTHER CELL-BASED IMMUNOTHERAPIES

MODERATOR:

ROBERT PRETI

CHAIRMAN, ARM; PRESIDENT & CEO, HITACHI CHEMICAL ADVANCED THERAPEUTIC SOLUTIONS; GM, HITACHI CHEMICAL REGENERATIVE MEDICINE BUSINESS SECTOR

PANELISTS:

BOB AZELBY

EVP, CHIEF COMMERCIAL OFFICER, JUNO THERAPEUTICS

MANUEL LITCHMAN

PRESIDENT, CEO AND DIRECTOR, MUSTANG BIO

JAMES NOBLE

CEO, ADAPTIMMUNE

PASCAL TOUCHON

SVP AND GLOBAL HEAD, CELL AND GENE, NOVARTIS ONCOLOGY

SCOTT WOLCHKO

PRESIDENT AND CEO, FATE THERAPEUTICS

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GENE THERAPY: THE OUTLOOK IN 2018

MODERATOR:

MARTHA ROOK

HEAD OF GENE EDITING AND NOVEL MODALITIES, MILLIPORESIGMA

PANELISTS:

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PRESIDENT AND CEO, SANGAMO THERAPEUTICS

GEOFF NICHOL

SVP, GLOBAL CLINICAL DEVELOPMENT AND CMO; BIOMARIN PHARMACEUTICAL

AMBER SALZMAN

PRESIDENT AND CEO, ADVERUM BIOTECHNOLOGIES

DEEPAK SRIVASTAVA

PRESIDENT, GLADSTONE INSTITUTES

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