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
Robert Preti
Chairman, Alliance for Regenerative Medicine
President & CEO, Hitachi Chemical Advanced Therapeutics Solutions
GM, Hitachi Chemical Regenerative Medicine Business Sector
• 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
Cell & Gene Therapies State of the Industry Briefing: 2018

- Clinical Progress: 2017
- Anticipated Clinical Data Events: 2018
- Sector Financial Performance: 2017
- Policy Environment: 2017 & 2018
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
854+
Regenerative Medicine Companies Worldwide, Including Gene and Cell Therapies

Data provided by: informa

Current Global Sector Landscape

- **460**: North America
- **234**: Europe & Israel
- **122**: Asia
- **15**: South America
- **22**: Oceania (Australia, New Zealand, Marshall Islands)
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.
Janet Lynch Lambert
CEO
Alliance for Regenerative Medicine
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 (dilated cardiomyopathy)
946 Total Clinical Trials Worldwide

- **Phase I**: 314 in 2016
  - 271 in 2016
- **Phase II**: 550 in 2016
  - 465 in 2016
- **Phase III**: 82 in 2016
  - 66 in 2016

Data provided by: informa
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
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)
- 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
- Insulet
- Juno Therapeutics
- Kite Pharma
- MaxCyte
- Medigene
- MoiMed
- NexImmune
- Novartis
- OperaX Therapeutics
- Orchard Therapeutics
- Oxford BioMedica
- Poseida Therapeutics/Janssen
- Rocket Pharma
- Takara Bio
- Tocagen
- Unum Therapeutics
- ZIOPHARM Oncology

**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
<table>
<thead>
<tr>
<th>Company</th>
<th>Product</th>
<th>Therapeutic Modality</th>
<th>Indication</th>
<th>Clinical Stage</th>
<th>Expected Reporting Date</th>
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<tbody>
<tr>
<td>Spark Tx</td>
<td>LUXTURNA</td>
<td>AAV-vector gene therapy</td>
<td>Biallelic RPE65-mediated IRD</td>
<td>Administration at select treatment centers</td>
<td>Q1 2018</td>
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<tr>
<td>Kiadis</td>
<td>ATIR101</td>
<td>Allodepleted T-Cell Immunotherapy</td>
<td>AML or ALL</td>
<td>Conditional EU approval</td>
<td>2H 2018; launch 2019</td>
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<td>TriGenix</td>
<td>Cx601</td>
<td>Cell therapy</td>
<td>Crohn’s disease</td>
<td>EU approval</td>
<td>1H 2018</td>
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<tr>
<td>bluebird bio</td>
<td>Lentiglobin</td>
<td>Gene therapy</td>
<td>Transfusion dependent beta-thalassemia</td>
<td>MAA filing</td>
<td>End-year 2018</td>
</tr>
<tr>
<td>Kite (Gilead co)</td>
<td>Yescarta</td>
<td>CD19-directed CAR T cell therapy</td>
<td>Refractory Large B-Cell Lymphoma</td>
<td>Pending MAA</td>
<td>1H 2018</td>
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<tr>
<td>Enzyvant Tx</td>
<td>RVT-802</td>
<td>Tissue-based therapy</td>
<td>Complete DiGeorge Syndrome</td>
<td>BLA submission</td>
<td>2018</td>
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<tr>
<td>Juno</td>
<td>JCAR017</td>
<td>CAR-T cell therapy</td>
<td>Transfusion dependent beta-thalassemia</td>
<td>Ph III – Northstar-2 HGB-207</td>
<td>Mid-year 2018</td>
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<tr>
<td>bluebird bio</td>
<td>Lentiglobin</td>
<td>Gene therapy</td>
<td>Transfusion dependent beta-thalassemia &amp; beta-0/beta-0 genotypes</td>
<td>Ph III – Northstar-3 (HGB-212)</td>
<td>End-year 2018</td>
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<tr>
<td>Histogenics</td>
<td>NeoCart</td>
<td>Tissue-engineering product</td>
<td>Cartilage repair</td>
<td>Ph III (topline data, potential BLA filing)</td>
<td>Q3 2018</td>
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<tr>
<td>Athersys</td>
<td>MultiStem</td>
<td>Allogeneic stem cell (MAPC)</td>
<td>Ischemic Stroke</td>
<td>Ph III (under SPA)</td>
<td>Initiating 1H 2018</td>
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<tr>
<td>Bone Tx</td>
<td>PREOB</td>
<td>Cell therapy (autologous)</td>
<td>Osteonecrosis of the hip</td>
<td>Ph III</td>
<td>2H 2018</td>
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<td>Brainstorm</td>
<td>NurOwn</td>
<td>Mesenchymal Stem Cell Therapy</td>
<td>ALS</td>
<td>Ph III</td>
<td>Day 28 Primary endpoint Q1 2018; Day 100 survival rate Q2 2018</td>
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<tr>
<td>Mesoblast</td>
<td>MSC-100-IV</td>
<td>Mesenchymal Stem Cell Therapy</td>
<td>Acute Graft Versus Host Disease</td>
<td>Ph III</td>
<td>Day 28 Primary endpoint Q1 2018; Day 100 survival rate Q2 2018</td>
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<td>Mesoblast</td>
<td>MPC-150-IM</td>
<td>Mesenchymal Precursor Cell Therapy</td>
<td>Mod to Severe Chronic Heart Failure</td>
<td>Ph III</td>
<td>Complete enrollment 2H 2018</td>
</tr>
<tr>
<td>Mesoblast</td>
<td>MPC-06-ID</td>
<td>Mesenchymal Precursor Cell Therapy</td>
<td>Chronic low back pain due to Disc Degeneration</td>
<td>Ph III</td>
<td>Complete enrollment Q1 2018</td>
</tr>
<tr>
<td>Abeona</td>
<td>EB-101</td>
<td>Gene therapy</td>
<td>Epidermolysis Bullosa</td>
<td>Commence Ph III</td>
<td>Early 2018</td>
</tr>
</tbody>
</table>
$7.5 Billion Total Amount Raised in 2017

$4.2 Billion raised in 2016

$446.1 Million Tissue Engineering

$425.4 Million raised in 2016

$4.5 Billion Gene & Gene-Modified Cell Therapy

$1.7 Billion 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
Total Financings by Type, by Year

- **Follow-Ons**
  - 2017: $1,653
  - 2016: $1,832
  - 2015: $2,244
  - Up 348% YoY

- **Venture Capital**
  - 2017: $963
  - 2016: $837
  - 2015: $1,194
  - Up 11% YoY

- **Corporate Partnership Upfront**
  - 2017: $588
  - 2016: $647
  - 2015: $1,086
  - Up 68% YoY

- **PIPS**
  - 2017: $889
  - 2016: $1,194
  - 2015: $1,328

- **Private Equity**
  - 2017: $6
  - 2016: $246
  - 2015: $143

- **IPO**
  - 2017: $230
  - 2016: $588
  - 2015: $1,653

*Data provided by: informa*

*in millions USD*
Total M&A Transaction Values: By Year

M&A Upfront

2017
2016
2015

$1,761
$1,053
$0

(includes $11.9B Gilead / Kite acquisition)

*in millions USD

Data provided by: informa
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

- RM/AT Average
- Cell-based Immuno-oncology Therapy Average
- Gene Therapy Average
- Nasdaq Biotech Index %
- Nasdaq Index %
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
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
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
GENE THERAPY: THE OUTLOOK IN 2018

MODERATOR:
MARTHA ROOK
HEAD OF GENE EDITING AND NOVEL MODALITIES, MILLIPORESIGMA

PANELISTS:
BILL LUNDBERG
CSO, CRISPR THERAPEUTICS
SANDY MACRAE
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