WELCOME AND STATE OF THE INDUSTRY REMARKS

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CEO, Alliance for Regenerative Medicine
• The Alliance for Regenerative Medicine (ARM) is the only international organization specifically focused on issues facing the regenerative medicine sector, including gene therapy, cell therapy, and tissue engineering.

• ARM’s 290+ global member organizations include small and large therapeutic companies, non-profit research institutions, patient organizations, and tool and technology providers.

• ARM convenes, connects, and advocates for the sector.

• Working with our members and policymakers, we foster investment, research & development, and successful commercialization of safe, effective, and transformational therapies for patients around the world.
ARM Priorities

- Advocate for clear, predictable and harmonized regulatory and review pathways
- Enable market access and value-based 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
Position paper released today, responding to EMA & EC’s Oct 2017 action plan to foster ATMP development via improved regulatory framework

ARM’s recommendations:

- **R&D**: pragmatic approach on innovative manufacturing models or use of Master Files; GMO requirements; regulatory convergence, industry-wide standards
- **Regulatory processes**: ATMP certification for non-SMEs; increased sponsor-agency interaction; guidance on IMPD & MAA structure
- **Hospital exemption**: increased guidance on scope and requirements; increased transparency; educational activities
- **Funding, investment & market access**: increase available risk capital; address market access barriers to ATMP adoption by enhanced dialogue with HTA and payers to seek pragmatic solutions
Accomplishments: 2017

**Regulatory**
- Position paper on Hospital Exemption
- Drove publication of multi-EU organization position paper on GMO requirements for clinical trials with ATMPs
- Contributed to the review of the Blood and Cells & Tissues Directives and recommended potential improvements

**Reimbursement**
- Educated Members on latest developments in P&R environment that could impact ATMPs
- Advanced position and messaging on key issues
- Demonstrated thought leadership and engaged key stakeholders on P&R

Looking ahead: 2018 priorities

**Regulatory**
- Contribute to development and finalization of key ATMP guidelines, e.g. guideline on comparability for ATMPs
- Promote pan-EU convergence of requirements & implementation for HE, GMO, GMP, Blood/Tissues & Cells Directives

**Reimbursement**
- Develop principles of ARM-endorsed global value framework
- Identify key market access enablers for ATMPs and engage with HTA and payers in major EU markets to seek their adoption
European Sector Overview: 2017

Sector Clinical Overview: 2017

Sector Financial Performance: 2017
• **Sector-specific statistics and trends** from 850+ regenerative medicine companies worldwide.

• **Data includes** industry financings (overall, by tech type, and by financing type), partnerships and other deals, clinical milestones, clinical trial figures (by phase and tech type), and more.

• **Global & Europe-specific** information available.
• **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; Gamma Delta cells, 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.
Current European Sector Landscape

234+
ATMP companies based in Europe/Israel

Not shown on map, included in Europe totals:

Israel: 24

Data provided by: informa
200 Total Clinical Trials Based in Europe & Israel

- Phase I: 39 trials
- Phase II: 124 trials
- Phase III: 37 trials

Data provided by: informa
European- & Israeli-Based Clinical Trials by Therapeutic Category

Of 200 total current clinical trials in Europe & Israel:

- Nearly half (48%) are in oncology
- Nearly 10% are in cardiovascular disorders

Data provided by: informa

*As of end 2017
## Major companies and research institutions in this space in Europe & Israel:

<table>
<thead>
<tr>
<th>CAR-T</th>
<th>TCRs and Modified T Cells</th>
<th>NK cells</th>
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<tr>
<td>Autolous Ltd. (U.K.)</td>
<td>AmBTU (Netherlands)</td>
<td>Celyad (Belgium)</td>
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<td>Celllectis (France)</td>
<td>Adaptimmune (U.K.)</td>
<td>Gamida Cell Ltd. (Israel)</td>
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<td>Celyad (Belgium)</td>
<td>Immatics (Germany)</td>
<td>Glycostem (Netherlands)</td>
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<td>Immatics (Germany)</td>
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<td>Orbsen Therapeutics (Ireland)</td>
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<td>MediGene (Germany)</td>
<td>Kiadis Pharma (Netherlands)</td>
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<tr>
<td>Novartis / UPenn / Oxford BioMedica</td>
<td>PDC*Line (France)</td>
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<tr>
<td>University College London (U.K.)</td>
<td>Zelluna Immunotherapy (Norway)</td>
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**Gamma Delta Cells**
- Gamma Delta Therapeutics (U.K.)
- TC BioPharm (U.K.)

**TCRs and Modified T Cells**
- AmBTU (Netherlands)
- Adaptimmune (U.K.)
- Immatics (Germany)
- Immunocore (U.K.)
- Juno Therapeutics (Germany)
- Kiadis Pharma (Netherlands)
- PDC*Line (France)
- Zelluna Immunotherapy (Norway)

**TILs and MILs**
- AmBTU (Netherlands)
- Tilt Biotherapeutics (Finland)
### AAV Vectors
- Allergan (Ireland)
- Arthrogen (Netherlands)
- CEVEC (Germany)
- CombiGene (Sweden)
- Esteve (Spain)
- Genethon (France)
- Gensight Biologics (France)
- HORAMA (France)
- Lysogene (France)
- NightstaRx (U.K.)
- Quethera (U.K.)
- Shire (Ireland)
- Spark Therapeutics Ireland (Ireland)
- Treeway (Netherlands)
- uniQure (Netherlands)
- Viralgen (Spain)
- Vivet Therapeutics (France)

### Lenti/Retroviral Vectors
- Adaptimmune (U.K.)
- Cellectis (France)
- Celyad (Belgium)
- CEVEC (Germany)
- EMD Serono (Germany)
- Finvector (U.K.)
- Genenta Science (Italy)
- GSK (U.K.)
- Immunocore (U.K.)
- Juno Therapeutics (Germany)
- Medigene (Germany)
- MolMed (Italy)
- Novartis (Switzerland)
- Orchard Therapeutics (U.K.)
- Oxford BioMedica (U.K.)
- VIVEbioTECH (Spain)

### Adenoviral Vectors
- Cell Medica (U.K.)
- CEVEC (Germany)
- Finvector (U.K.)

### Genome Editing
- Cellectis (France)
- CRISPR Therapeutics (Switzerland)
- Hphar (Belgium)
- LogicBio (Israel)

### Enabling Platforms
- Novasep (France)
- PharmaCell (Netherlands)
- Synpromics (U.K.)
Near term:

- **bluebird bio Lentiglobin gene therapy** MAA filing expected by EOY 2018
- **Gilead / Kite Pharma’s Yescarta CAR T-cell therapy** approved in U.S. 18 Oct; MAA expected early 2018
- **Kiadis ATIR101 T-cell immunotherapy** conditional EU approval expected mid-2018; EU launch 2019
- **MolMed's Zalmoxis**, currently reimbursable in Germany and as of 1 March, in Italy
- **Novartis’s Kymriah CAR T-cell therapy** approved in U.S. 30 Aug; MAA submitted to EMA 6 Nov
- **Spark Therapeutics’ LUXTURNA gene therapy** approved in U.S. 19 Dec; MAA submitted to EMA 31 July
- **TiGenix Cx601 allogeneic cell therapy** EMA CHMP endorsement 15 Dec; pending approval early 2018
€6.1 Billion
Total Amount Raised in 2017
€3.4 Billion raised in 2016

€3.7 Billion
Gene & Gene-Modified Cell Therapy
€1.4 Billion raised in 2016

€362.5 Million
Tissue Engineering
€345.6 Million raised in 2016

€3.3 Billion
Cell Therapy
€1.5 Billion raised in 2016

** 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 Europe/Israeli Financings: 2017

- €1.2 Billion Total Amount Raised in 2017, 46% increase from 2016
- €86.1 Million Tissue Engineering, 49% decrease from 2016
- €731.8 Million Gene & Gene-Modified Cell Therapy, 126% increase from 2016
- €648.9 Million Cell Therapy, 40% increase from 2016

** 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 European/Israeli Financings by Type, by Year

- **Follow-Ons**
  - Up 1,179% YoY

- **Venture Capital**
  - Up 18% YoY

- **Corporate Partnership Upfront**
  - Up 135% YoY

- **PIPEC**
  - 2017: €114.50, 2016: €125.90, 2015: €168.00

- **IPO**
  - 2017: €121.80, 2016: €125.90, 2015: €471.10

*in millions EUR

Data provided by: informa
Follow-On Financings

- uniQure €74.2M – 27 Oct
- Adapimmune €53.5M – 27 March
- VBL Therapeutics €15.3M – 16 Nov
- Pluristem €14.1M – 25 Jan
- Pluristem €12.2M – 31 Oct

Corporate Partnerships / Collaborations

- Lonza & Sanofi form €270M joint venture, all upfront – 27 Feb
- NanoCarrier €93.4M agreement with VBL Therapeutics, €9.9M upfront – 6 Nov
- Oxford BioMedica €81.2M agreement with Novartis, €6.5M upfront – 6 July
- Celyad €78M agreement with Novartis – 2 May

PIPS/Private Placements:

- Adapimmune €34.1M – 10 April
- GenSight €20M – 23 June
- Kiadis Pharma €18M – 10 Oct
- Co.don €14.9M – 19 Oct

IPOs:

- NightStar €70.1M – 2 Oct

Venture & Private Equity Financings:

- Orchard Therapeutics €89.3M Series B – 20 Dec
- CellMedica €59.4M Series C – 16 March
- Xeltis €42.9M Series C – 15 Nov
- Nouscom €39.6M Series B – 6 Nov
- LogicBio €36.6M Series B – 28 June
- NightStar €36.6M – 29 June
- Gamida Cell €32.5M – 16 June
We are experiencing a turning point for the sector:

- Significant product approvals; with potentially many more to follow near-term
- Growing public awareness and anticipation
- Financial maturity, broad and sustained investor interest

Brings heightened emphasis on readiness in key areas:

- Reimbursement, market access
- Regulatory convergence and sector-supportive initiatives
- Industrialization and manufacturing