ALLIANCE for Regenerative Medicine

8th Annual

ADVANCED THERAPIES SUMMIT

March 14, 2018 | Amsterdam, The Netherlands

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MARCH 14, 2018

WELCOME AND STATE OF THE INDUSTRY REMARKS

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CEO, Alliance for Regenerative Medicine

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.*

- *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

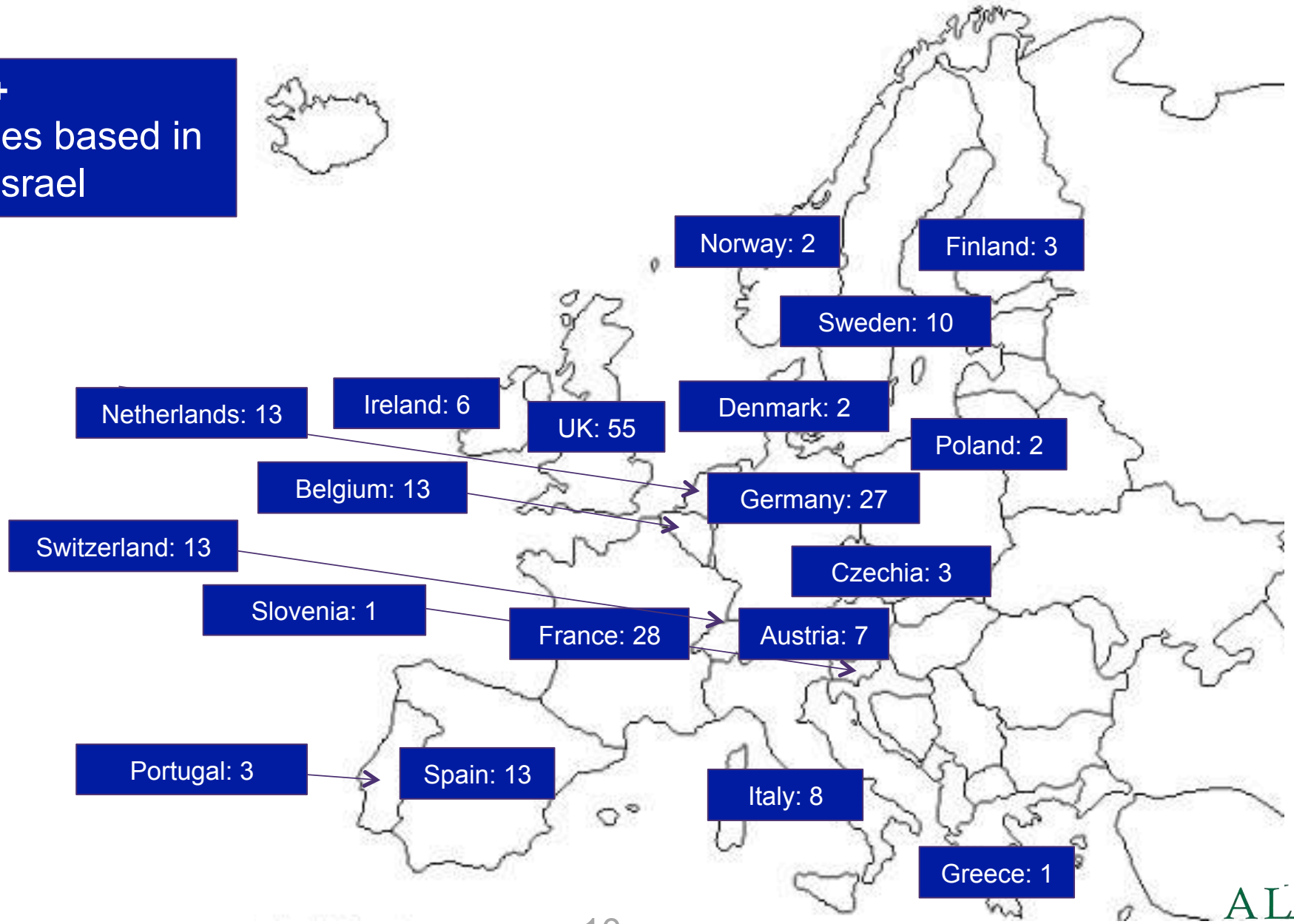
Sector Clinical Overview: 2017

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.*

234+
ATMP companies based in Europe/Israel



Not shown on map, included in Europe totals:

Israel: 24

200 Total Clinical Trials Based in Europe & Israel

Data provided by: informa

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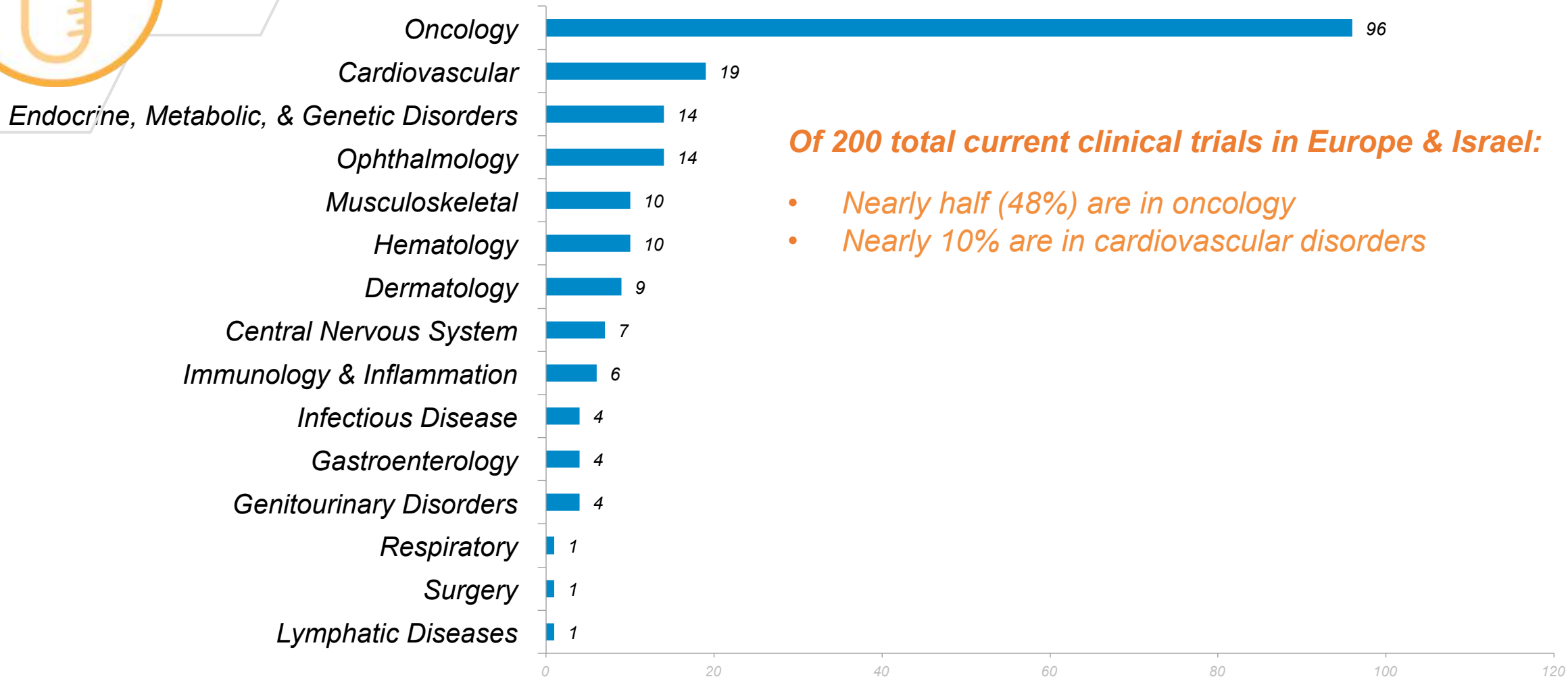
European- & Israeli-Based Clinical Trials by Therapeutic Category



Of 200 total current clinical trials in Europe & Israel:

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

**As of end 2017*
Data provided by: informa

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Major companies and research institutions in this space in Europe & Israel:

CAR-T

- Autolous Ltd. (U.K.)
- Cellectis (France)
- Celyad (Belgium)
- Immatics (Germany)
- Juno Therapeutics (Germany)
- MediGene (Germany)
- Novartis / UPenn / Oxford BioMedica
- University College London (U.K.)

Gamma Delta Cells

- Gamma Delta Therapeutics (U.K.)
- TC BioPharm (U.K.)

TCRs and Modified T Cells

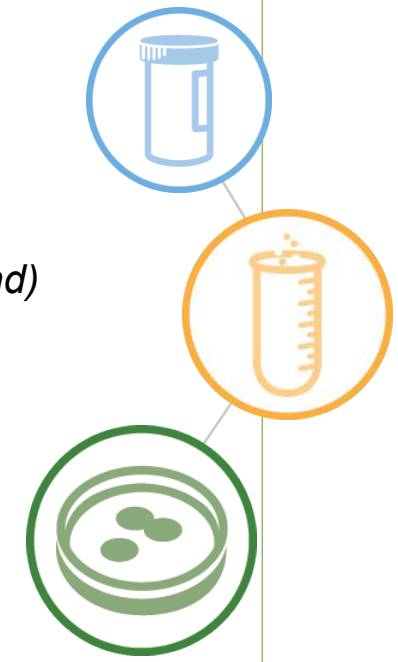
- AmBTU (Netherlands)
- Adaptimmune (U.K.)
- Immatics (Germany)
- Immunocore (U.K.)
- Juno Therapeutics (Germany)
- Kiadis Pharma (Netherlands)
- PDC*Line (France)
- Zelluna Immunotherapy (Norway)

TILs and MILs

- AmBTU (Netherlands)
- Tilt Biotherapeutics (Finland)

NK cells

- Celyad (Belgium)
- Gamida Cell Ltd. (Israel)
- Glycostem (Netherlands)
- Lokon Pharma (Sweden)
- Orbsen Therapeutics (Ireland)



Major companies in this space in Europe & Israel:

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

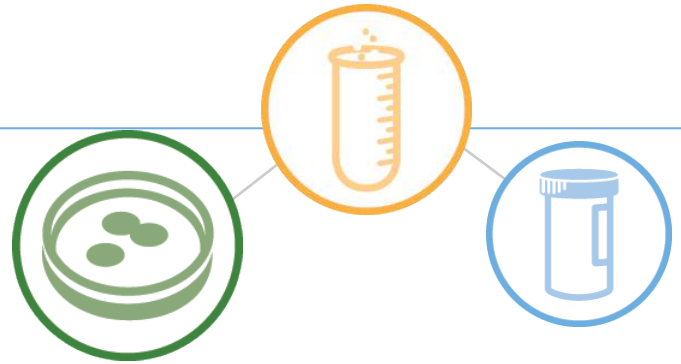
- *Cellectis (France)*
- *CRISPR Therapeutics (Switzerland)*
- *Hphar (Belgium)*
- *LogicBio (Israel)*

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

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 Europe/Israeli Financings: 2017

€1.2 Billion Total Amount Raised in 2017

46% increase from 2016

€731.8 Million Gene & Gene-Modified Cell Therapy

126% increase from 2016

€86.1 Million Tissue Engineering

49% decrease 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

Data provided by: informa

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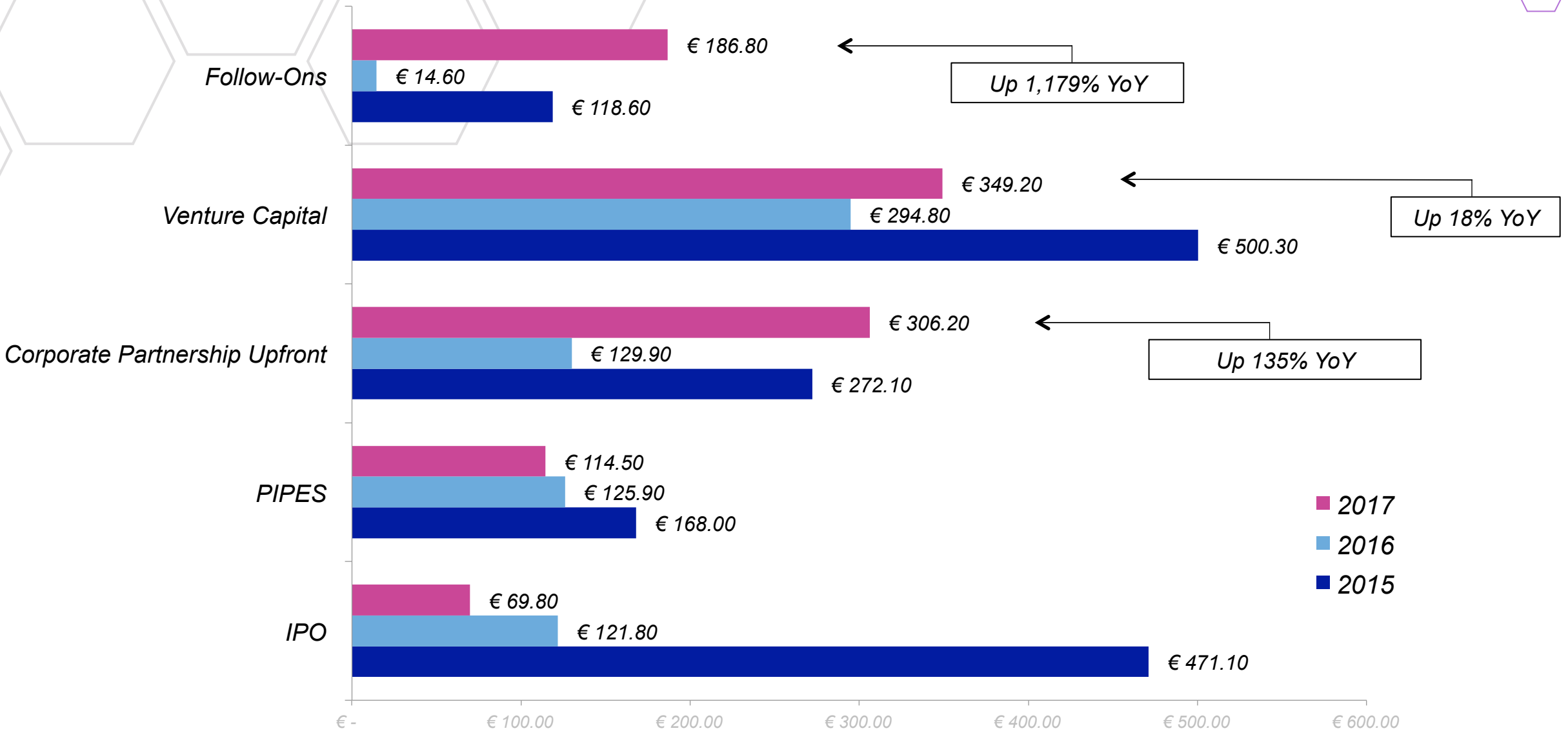
Total European/Israeli Financings by Type, by Year



*in millions EUR

Data provided by: informa

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Follow-On Financings

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

PIPES/Private Placements:

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

IPOs:

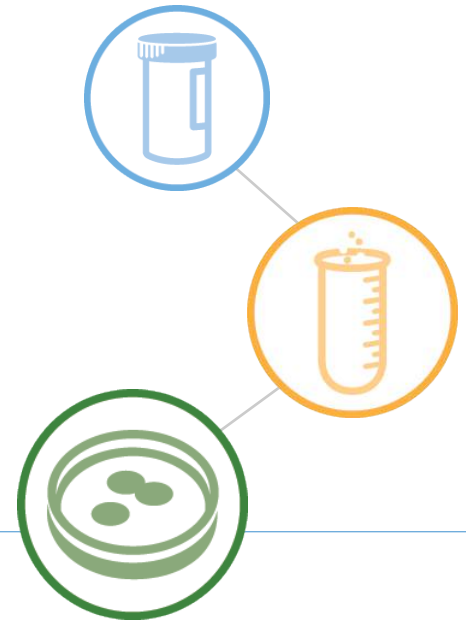
- *NightStar €70.1M – 2 Oct*

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*

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*