2017 ALLIANCE for Regenerative Medicine

Annual Data Report

ALLIANCE for
Regenerative Medicine

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.

www.alliancerm.org

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Letter from ARM's CEO

I joined the Alliance for Regenerative Medicine (ARM) as the organization's first CEO in July 2017. Over the next few months, this sector experienced a number of exciting, long-awaited, and hard fought milestones, including the approval of three new products: the first two commercially available CAR T-cell therapy products, Novartis's Kymriah and Kite/Gilead's Yescarta; and the first AAV gene therapy approved in the U.S. (and also the first gene therapy for a genetic disease), Spark Therapeutics' LUXTURNA. All three are now on the market in the U.S.

Janet Lynch Lambert
CEO
Alliance for Regenerative Medicine

These groundbreaking product approvals and continued clinical momentum in 2017 fostered growing investor and overall public interest regarding the truly transformative potential of these therapies. This increased attention and anticipation has heightened the importance of ARM's role as the leading advocate for legislative, regulatory, and financial support for the development of regenerative medicine therapies.

In 2017, ARM:

- Drove the rapid and successful implementation of the regenerative medicine provisions contained in the 21st Century Cures Act, creating an enhanced regulatory approval pathway for regenerative medicine products, including gene therapy and genome editing products.
- Developed and published in-depth analyses of the U.S. reimbursement landscape for regenerative medicine and advanced therapy products, and launched an enhanced advocacy effort to adapt the reimbursement environment for these products in Medicare and Medicaid.
- Helped shape the European Commission/European Medicine Agency's ATMP action plan for ATMP and advocated for multiple changes to improve the European environment.
- Published and presented unique and important sector data analyses, highlighting the clinical and financial progress and milestones of 850+ therapeutic developers worldwide.
- Successfully launched the Standards Coordinating Body, to enhance the focus and coordination of RM/AT standards efforts and to create an effective forum for stakeholder input.
- Successfully initiated the ARM Foundation, focused on gene medicine and cell therapy education, and the study of their economic impact.

In 2018, ARM will continue to lead the conversation and activities around market access and the immense value of regenerative medicine and advanced therapy products. We are recognized by regulators as the primary sector expert, and will continue to drive improvements in the regulatory landscape. We will serve as a reliable data source for life science and mainstream media eager to learn more about these products and sector direction. Finally, we will play a leadership role in addressing the manufacturing and infrastructure requirements that come with expanded adoption of these therapies. As always, ARM will work closely with our patient advocate, research institution, and non-profit members to convey our message of the whole sector.

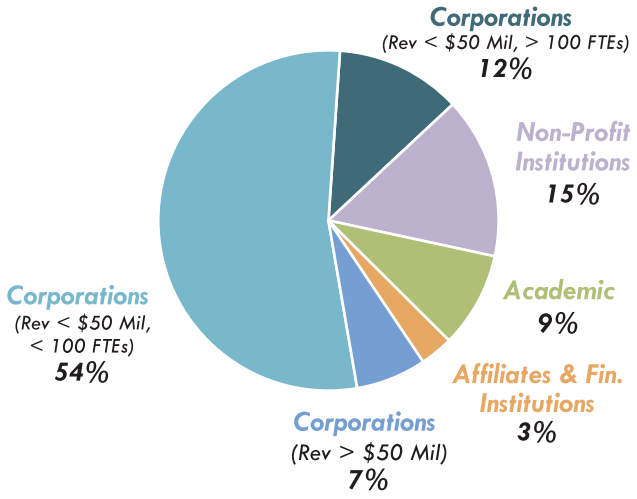
There's no shortage of hard work and opportunity ahead and I'm thrilled and honored to serve as CEO to this vital and dynamic organization. Thank you for your support for our sector; I look forward to working together in 2018.

All the best,

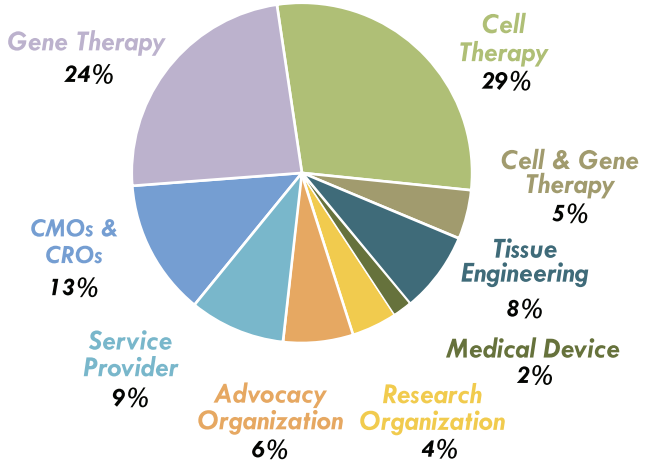
Janet Lynch Lambert
CEO
Alliance for Regenerative Medicine

ARM's Multi-Stakeholder Membership

Diversity of Organizations



Diversity of Technology Focus



ARM's Strategic Focus Areas

Regulatory

- Promote clear, predictable, and efficient regulatory framework.
- Assess all FDA, EMA, and related guidance relevant to cell and gene therapy, including guidance related to manufacturing, CMC, and related issues.
- Promote international convergence of key regulation and guidance to promote global product development by identifying specific areas of regulatory inconsistency among jurisdictions and developing proposals for adoption by regulatory agencies.

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 U.S. and in key EU countries.
- Secure favorable access and reimbursement for RM / AT products.

Industrialization and Manufacturing

- Reduce standards, technical, and regulatory barriers to scale up of RM / AT therapies.

Global Landscape

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

460
North America

15
South America

234
Europe & Israel

1
Africa

122
Asia

22
Oceania
(Australia, New Zealand, Marshall Islands)

Industry Overview

It was a banner year for regenerative and advanced therapies. The historic FDA approvals of CAR T-cell therapies Kymriah (Novartis) and Yescarta (Kite/Gilead), AAV-mediated gene therapy Luxturna (Spark Therapeutics) as well as the South Korean approval of *ex vivo* allogeneic cell therapy Invossa (Kolon Life Sciences) triggered great excitement across the sector. We have moved decisively into a new era in medicine, bringing significant benefits to the patients who have waited for these transformative and potentially curative therapies.

Keeping the momentum going in the wake of these seismic events will require even more collaboration and coordination among many stakeholders across the healthcare spectrum. Safe administration of these technologies will necessitate establishing additional and widespread treatment centers. Therapeutic developers also face challenges such as scaling up, establishing safe and reproducible manufacturing and reliable supply chains, not to mention addressing issues related to pricing and reimbursement. In order to properly clear these hurdles, developers will need to make strategic deals across the board with experts from concept to delivery.

Partnerships over the past year saw several instances of large pharma continuing to partner and collaborate with companies developing novel approaches in rare diseases. Examples include Amgen and Immatics; Pfizer and Sangamo Therapeutics; Biomarin and Spark Therapeutics; Janssen and Legend Biotech (USA and Ireland); and Allergan and Editas Medicine.

Several eye-opening acquisitions in 2017 included Gilead's $11.9 billion acquisition of Kite Pharma, followed by Gilead buying out Cell Design Labs for $567 million. CSL Behring took over Calimmune for $416 million and Ultragenyx acquired Dimension for $151 million after outbidding REGENXBIO with a superior deal. The aggressive M&A trend has appeared to continue in 2018, with several mega deals already on the books: Celgene's to acquire Juno for $9 billion and Sanofi to buy Bioverativ for $11.5 billion.

Rapid-fire regulatory approvals of cell and gene therapies and other regenerative medicines will continue to push pricing and reimbursement issues to the forefront. One-time treatments with six-figure price tags have spurred debates on alternative payment models, weighing the viability of one-time payments compared to annuity-based model with payments over time. As more regenerative medicine products are approved, these discussions will hold increased urgency, as patient access hangs in the balance.

Among the many developments to look for in 2018: the FDA's Center for Biologics Evaluation and Research (CBER) plans to update a suite of disease-specific guidance documents related to gene therapy manufacturing and safety. The first guidance will focus on gene therapy approaches to treat hemophilia. In addition, we expect additional clarity around several tenets of the FDA's Comprehensive Policy Framework for Regenerative Medicine, issued last November.

There is every reason to be optimistic about what 2018 will bring for this dynamic sector.

–Patricia Reilly
Vice President, Intelligence Alliances and Unification
Pharma Intelligence

–Nancy Dvorin
Managing Editor, IN VIVO, Start-Up and Medtech Insight

Informa Business Intelligence, Pharma and Healthcare

Total 2017 Global Financings

TOTAL 2017 GLOBAL FINANCINGS

$7.5 Billion raised in 2017

78.5% increase from 2016

GENE & GENE-MODIFIED CELL THERAPY

$4.5 Billion raised in 2017

164% increase from 2016

CELL THERAPY

$4.0 Billion raised in 2017

122% increase from 2016

TISSUE ENGINEERING

$446.1 Million raised in 2017

5% increase from 2016

**Total amount raised represents sector-wide figures; please note that some companies utilize technology from more than one technology group. As a result, the total financings amount does not equal the sum of the raises of the individual technology groups.*

*** Figures do not include M&A transaction totals.*

Select Corporate Partnerships, Financings, M&A: 2017

Corporate Partnerships/ Collaborations:

- Sangamo Therapeutics signs $545M hemophilia A gene therapy collaboration with Pfizer, including $70M upfront – May 10, 2017
- Janssen Biotech signs $350M agreement with Legend Biotech USA & Legend Biotech Ireland – Dec 21, 2017
- Kite Pharma signs $250M agreement with Daiichi Sankyo, including $50M upfront – January 9, 2017
- Oxford BioMedica signs $100M agreement with Novartis, including $10M upfront – July 6, 2017
- Takeda signs $100M agreement with GammaDelta Therapeutics – May 9, 2017
- Histogenics signs $97M agreement with MEDINET for NeoCart, including $10M upfront – December 21, 2017

Follow-on Financings:

- bluebird bio $460M – July 30, 2017
- Kite Pharma $409.7M – March 8, 2017
- Spark Therapeutics $402.5M – August 9, 2017
- AveXis $287.8M – June 26, 2017
- Juno Therapeutics $287.6M – September 26, 2017
- Intellia Therapeutics $150M – November 6, 2017

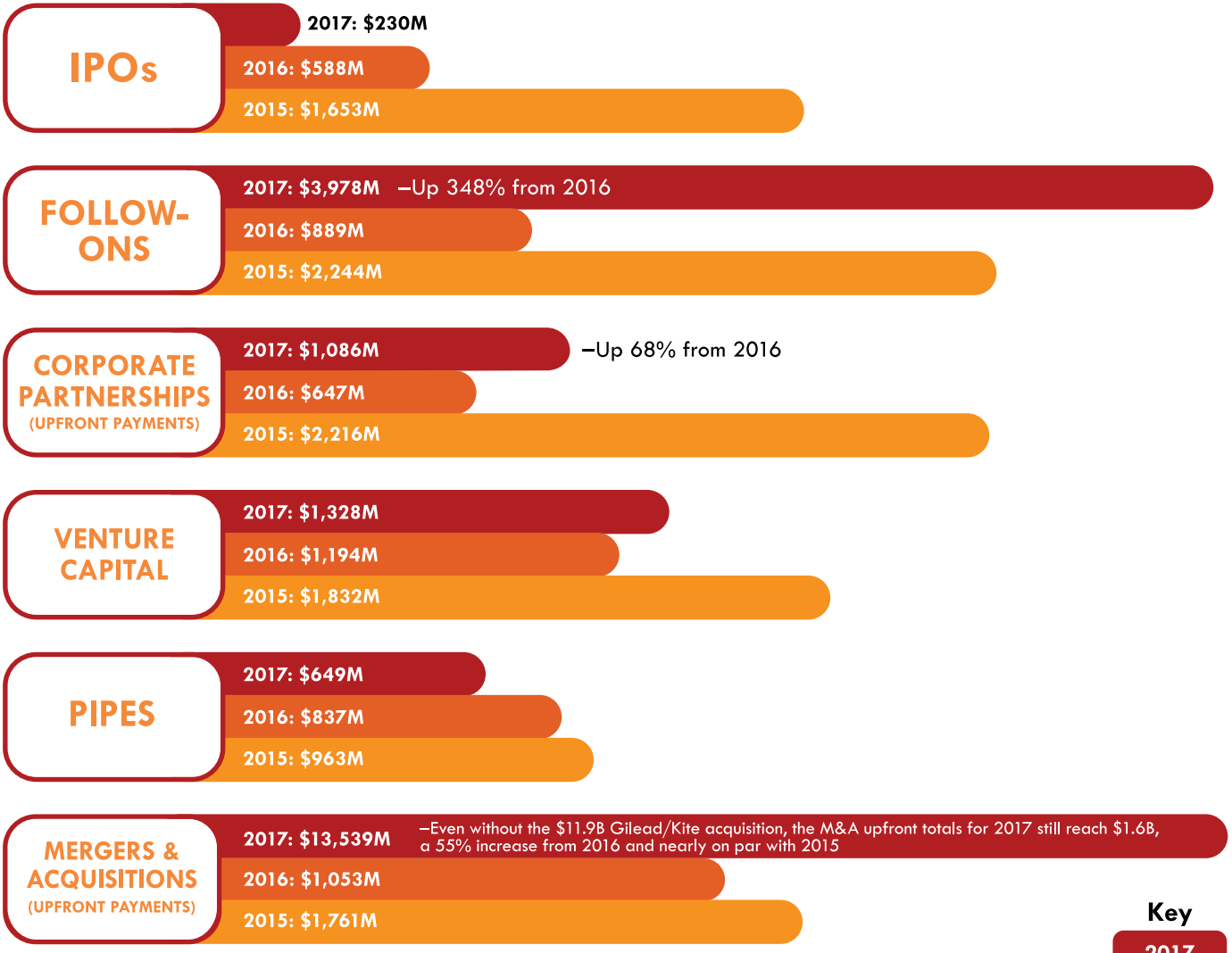
Venture Financings:

- Rubius Therapeutics $120M – June 21, 2017
- Semma Therapeutics $114M – November 30, 2017
- Orchard Therapeutics $110M – December 20, 2017
- Homology Medicines $83.5M – August 1, 2017
- Tessa Therapeutics $80M – December 20, 2017

Mergers & Acquisitions:

- Gilead's $11.9B acquisition of Kite Pharma – October 3, 2017
- Sanpower Group completes Dendreon acquisition from Valeant for $819.9M – June 29, 2017
- Gilead acquires Cell Design Labs for $567M, including $175M upfront – December 7, 2017
- CSL Behring acquires Calimmune for $416M, including $91M upfront – August 28, 2017
- Ultragenyx acquires Dimension Therapeutics for $152.3M – November 7, 2017

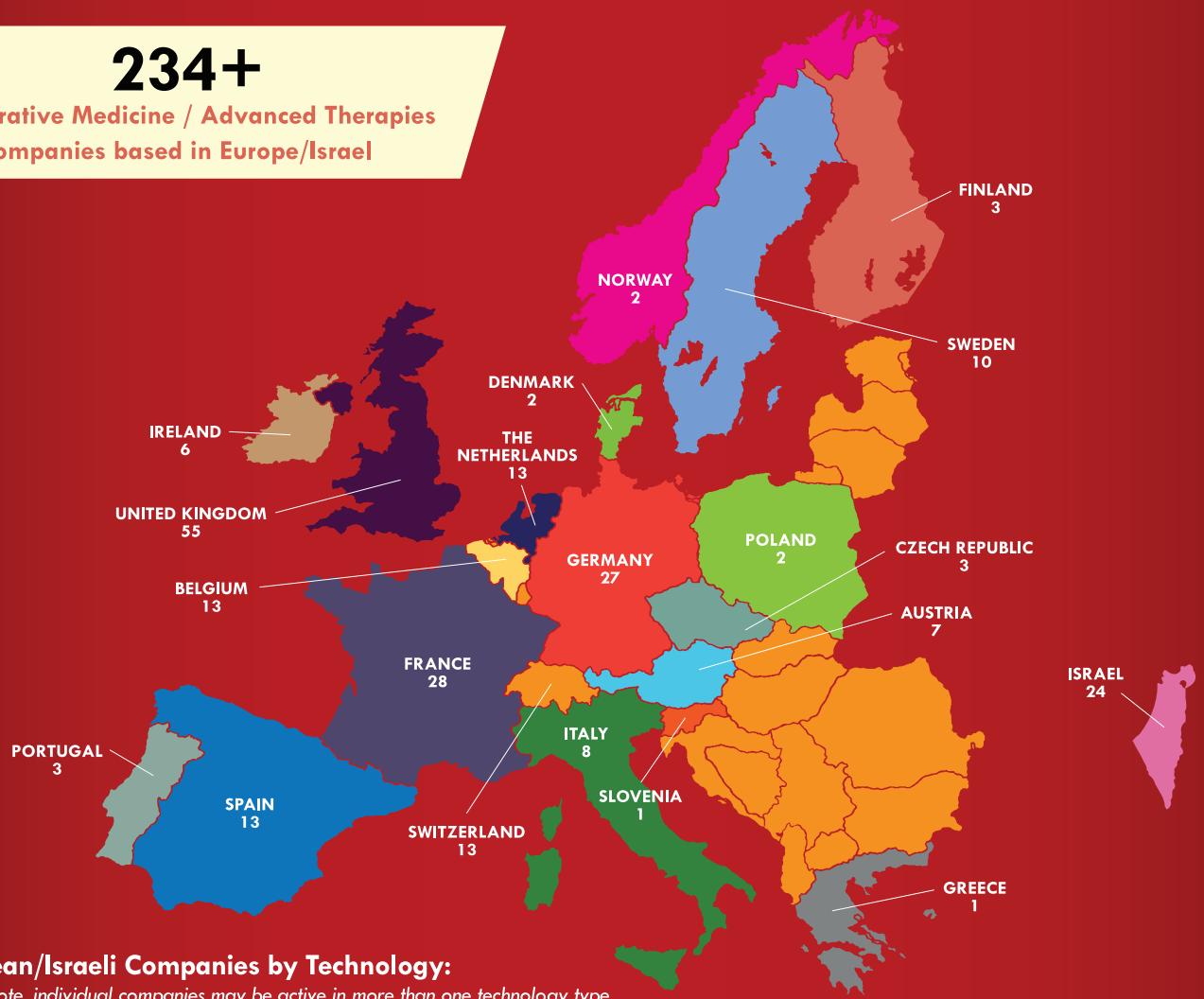
Total Global Financings by Type, by Year



European Sector Overview

234+

Regenerative Medicine / Advanced Therapies Companies based in Europe/Israel



European/Israeli Companies by Technology:

**please note, individual companies may be active in more than one technology type*

GENE THERAPY: 95

CELL THERAPY: 144

TISSUE ENGINEERING / BIOMATERIALS : 39

European Sector Overview

TOTAL 2017 EUROPEAN/ISRAELI FINANCINGS

$1.5 Billion (appx €1.22 Billion) raised in 2017 across all technology types

46% increase from 2016

GENE & GENE-MODIFIED CELL THERAPY

$901 Million (appx €730 Million) raised in 2017

126% increase from 2016

CELL THERAPY

$799 Million (appx €648 Million) raised in 2017

40% increase from 2016

TISSUE ENGINEERING

$106 Million (appx €86 Million) raised in 2017

49% decrease from 2016

**Total amount raised represents sector-wide figures; please note that some companies utilize technology from more than one technology group. As a result, the total financings amount does not equal the sum of the raises of the individual technology groups.*

*** Deals counted involve at least one European or Israeli company and include industry-funded deals only.*

Clinical Trials Sponsored by a European or Israeli Therapeutic Developer:

200

Clinical trials underway by end of 2017

Ph. I: 39

Ph. II: 124

Ph. III: 37

- Nearly half (48%) of all European or Israeli clinical trials are in oncology, including leukemia, lymphoma, glioblastoma, melanoma, myeloma, and cancers of the head, neck, bladder, breast, pancreas, prostate, and colon, among others.
- Nearly 10% focus on cardiovascular diseases and disorders, including congestive heart failure, critical limb ischemia, myocardial infarction, peripheral vascular disease, and others.

Sector Commentary: FDA & Regenerative Medicine

Dr. Scott Gottlieb
U.S. FDA Commissioner

Dr. Scott Gottlieb, U.S. FDA Commissioner since May 11, 2017, has demonstrated great interest and public support of the regenerative medicine and advanced therapy sector throughout 2017:

"One of the most promising new fields of science and medicine is the area of cell therapies and their use in regenerative medicine. These new technologies, most of which are in early stages of development, hold significant promise for transformative and potentially curative treatments for some of humanity's most troubling and intractable maladies.

The FDA will continue to work closely with industry to find other ways to aid in the effort to bring novel therapies to patients as quickly, and as safely, as possible. One of these will include our continued commitment to fully implement the Regenerative Medicine Advanced Therapy (RMAT) designation. This pathway enables regenerative cell therapies to access the FDA's existing expedited programs to help foster the development and approval of these novel products. Among other things, we plan to include certain gene therapy products that permanently alter tissue and produce a sustained therapeutic benefit as part of the products that will meet the definition of being eligible to come under the pathway enabled by RMAT. This is part of our broader commitment to pursue efforts that will advance innovation in this space."

- Statement on the FDA's new policy steps and enforcement efforts to ensure proper oversight of stem cell therapies and regenerative medicine, August 28, 2017

"These concepts are no longer the stuff of science fiction, but rather real-life science where cells and tissues can be engineered to grow healthy, functional organs to replace diseased ones; where new genes can be introduced into the body to combat disease; and where adult stem cells can generate replacements for cells that are lost to injury or illness. The promise of this technology is why the FDA is so committed to encouraging and supporting innovation in this field."

- Statement on FDA's comprehensive new policy approach to facilitating the development of innovative regenerative medicine products to improve human health, November 16, 2017

"I believe we're at a similar turning point when it comes to gene therapy. Over the next several years, we'll see this approach become a mainstay of treating, and probably curing, a lot of our most devastating and intractable illness. At FDA, we're focused right now on establishing the right policy framework to capitalize on this scientific opening."

- Testimony before the U.S. Senate HELP Committee on the agency's implementation of the 21st Century Cures Act, December 7, 2017

"We're at an inflection point in medicine and health. We're witnessing the advent of brand new technology platforms that have the potential to improve health, and cure disease, in fundamentally novel ways. Applications like gene therapy and regenerative medicine may cure inherited disorders and rejuvenate damaged cells and organs.

We're taking steps to extend the opportunities offered by gene therapy innovation. We recently announced our comprehensive policy framework for regenerative medicine, including a draft guidance that describes the expedited programs that may be available to sponsors of these therapies."

- Remarks on FDA's Role in Advancing a Modern Framework for Gene Therapy, December 19, 2017

Sector Commentary: FDA & Regenerative Medicine

The 21st Century Cures Act, passed December 2016, included several regenerative medicine / advanced therapies provisions, including *Accelerated Approval for Regenerative Advanced Therapies*, which the FDA began implementing this shortly after the bill's passage, creating the Regenerative Medicine Advanced Therapies (RMAT) Designation.

The Regenerative Medicine Advanced Therapy (RMAT) Designation:

- Creates an optimized, accelerated approval program for RM / AT-specific products
- Protects patients by maintaining FDA's high approval standards for product safety and efficacy
- Provides product developers a clear regulatory pathway to market

A product is eligible for RMAT Designation if:

- The drug is a regenerative medicine therapy, defined as a cell therapy, gene therapies (including genetically modified cells, that lead to a durable modification of cells or tissues), therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations;
- The drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and
- Preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition

Product Sponsor Benefits:

- Guaranteed interactions with the FDA
- Eligibility for priority review and accelerated approval
- Flexibility in the number of clinical sites used and the possibility to use patient registry data and other sources of "real-world" evidence for post-approval studies (pending FDA approval)

946

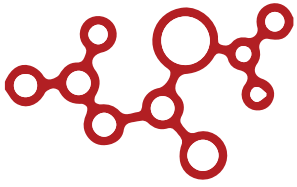
Clinical trials underway worldwide by end of 2017

Ph. I: 314
Ph. II: 550
Ph. III: 82

Number of Clinical Trials Utilizing Specific RM/AT Technology: 2017

GENE THERAPY

Total: 313
Ph. I: 113
Ph. II: 170
Ph. III: 30

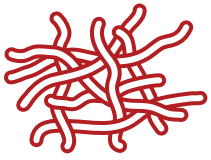


GENE-MODIFIED CELL THERAPY

Total: 259
Ph. I: 106
Ph. II: 144
Ph. III: 9

CELL THERAPY

Total: 353
Ph. I: 90
Ph. II: 225
Ph. III: 38



TISSUE ENGINEERING

Total: 21
Ph. I: 5
Ph. II: 11
Ph. III: 5

Clinical Trials by Indication: 2017

Of 946 total current clinical trials worldwide:

- 53% of all current clinical trials are in oncology, including leukemia, lymphoma, and cancers of the brain, breast, bladder, cervix, colon, esophagus, ovaries, pancreas, and others.

- Nearly 10% are in cardiovascular disorders, including congestive heart failure, myocardial infarction, critical limb ischemia, heart disease, and others.

Select Significant Clinical & Key Data Events

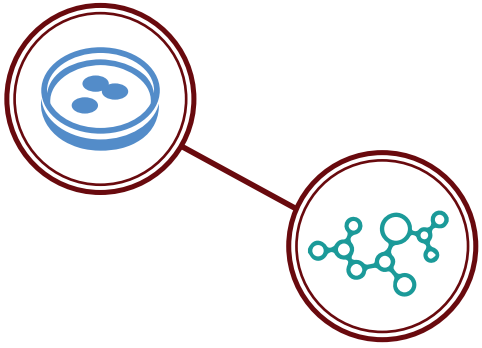
Approvals in 2017:

- Spark Therapeutics' LUXTURNA gene therapy for biallelic RPE65-mediated inherited retinal disease – December 19, 2017
    - MAA submitted to EMA – July 31, 2017

- 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 – October 18, 2017
    - 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, 2017
    - MAA submitted to EMA – November 6, 2017

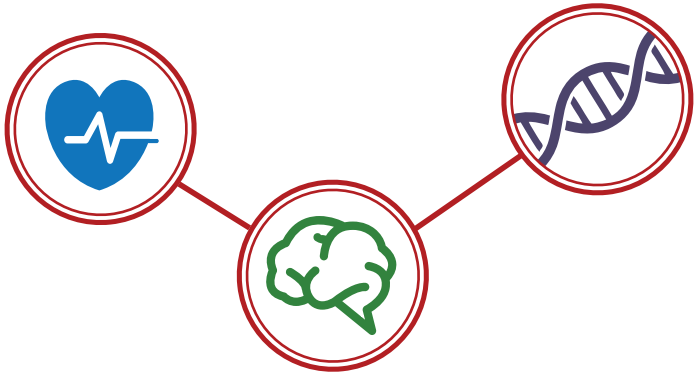
- TissueGene's exclusive Asia licensee Kolon Life Science receives marketing approval for Invossa-K Inj. for degenerative arthritis from the Korean Ministry of Food and Drug Safety – July 12, 2017



U.S. FDA RMAT Designations:

** includes only those that had been publicly announced as of December 31, 2017*

- 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)



ARM Board, Officers & Staff

ARM Officers:

- Robert Preti, ARM Officer: Chairman
  President and CEO, Hitachi Chemical Advanced Therapeutics Solutions;
  GM, Hitachi Chemical Regenerative Medicine Business Sector
- Matt Patterson, ARM Officer: Vice Chairman
  President & CEO, Audentes Therapeutics
- Martha Rook, ARM Officer: Secretary
  Head of Gene Editing and Novel Modalities, MilliporeSigma / EMD Millipore
- Rahul Aras, ARM Officer: Treasurer
  Co-Founder, President & CEO, Juventas Therapeutics

ARM Board of Directors:

- Zami Aberman, Chief Executive Officer, Pluristem Therapeutics
- Rahul Aras, (also ARM Officer: Treasurer), Co-Founder, President and Chief Executive Officer, Juventas Therapeutics
- Usman Azam, President & CEO, Tmunity Therapeutics
- Bob Azelby, Executive Vice President & Chief Commercial Officer, Juno Therapeutics
- Ron Bartek, President, Director & Co-Founder, Friedreich's Ataxia Research Alliance
- Nessan Bermingham, CEO, President & Founder, Intellia Therapeutics
- Eduardo Bravo, Chief Executive Officer, TiGenix
- Samuele Butera, Global Cell & Gene Therapies Business Leader, Novartis Oncology
- Amy Butler, Vice President and General Manager Cell Biology, Thermo Fisher Scientific
- Sarah Creviston, Vice President & Global Head for Patient Advocacy & Public Affairs, Shire
- Deborah Dean, Executive Vice President & Chief Compliance Officer, MiMedx
- Flagg Flanagan, Chairman & Chief Executive Director, DiscGenics
- Michael Hunt, Chief Financial Officer, ReNeuron
- Dena Ladd, Executive Director, Missouri Cures
- Paul Laikind, President & CEO, ViaCyte
- Bruce Levine, Professor, Cancer Gene Therapy, Abramson Cancer Center, University of Pennsylvania
- Bill Lundberg, Senior Adviser, CRISPR Therapeutics
- Michael May, President & Chief Executive Officer, Centre for Commercialization of Regenerative Medicine (CCRM)
- Emile Nuwaysir, President & CEO, BlueRock Therapeutics
- Matt Patterson, (also ARM Officer: Vice Chairman), President & CEO, Audentes Therapeutics
- Robert Preti, (also ARM Officer: Chairman), President and CEO, Hitachi Chemical Advanced Therapeutics Solutions;
  GM, Hitachi Chemical Regenerative Medicine Business Sector
- Isabelle Riviere, Director, Cell Therapy and Cell Engineering Facility, Memorial Sloan Kettering Cancer Center
- Martha Rook, (also ARM Officer: Secretary), Head of Gene Editing and Novel Modalities, MilliporeSigma / EMD Millipore
- Sanjaya Singh, Vice President and Global Head, Janssen BioTherapeutics
- Donna Skerrett, Chief Medical Officer, Mesoblast Limited
- Bob Smith, SVP, Global Gene Therapy Business, Pfizer
- Joe Tarnowski, Senior Vice President, Cell & Gene Therapy Platform, GSK
- Keith Thompson, Chief Executive Officer, Cell & Gene Therapy Catapult
- Gil Van Bokkelen, Co-Founder, President & CEO, Athersys
- Phil Vanek, General Manager, Cell Therapy Technologies, GE Healthcare Life Sciences
- Jeffrey Walsh, Chief Financial and Strategy Officer, bluebird bio
- Susan Washer, President & CEO, AGCT
- Jason Wertheim, Assistant Professor of Surgery - Organ Transplantation, Department of Surgery,
  Institute for BioNanotechnology in Medicine, Feinberg School of Medicine and Chemistry of Life Processes Institute,
  Northwestern University
- Claudia Zylberberg, Founder & CEO, Akron Biotech

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ALLIANCE for Regenerative Medicine

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