# Q3

ALLIANCE for Regenerative Medicine

2017

# Quarterly Data Report

*on gene and cellular therapies and the regenerative medicine sector*

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.*

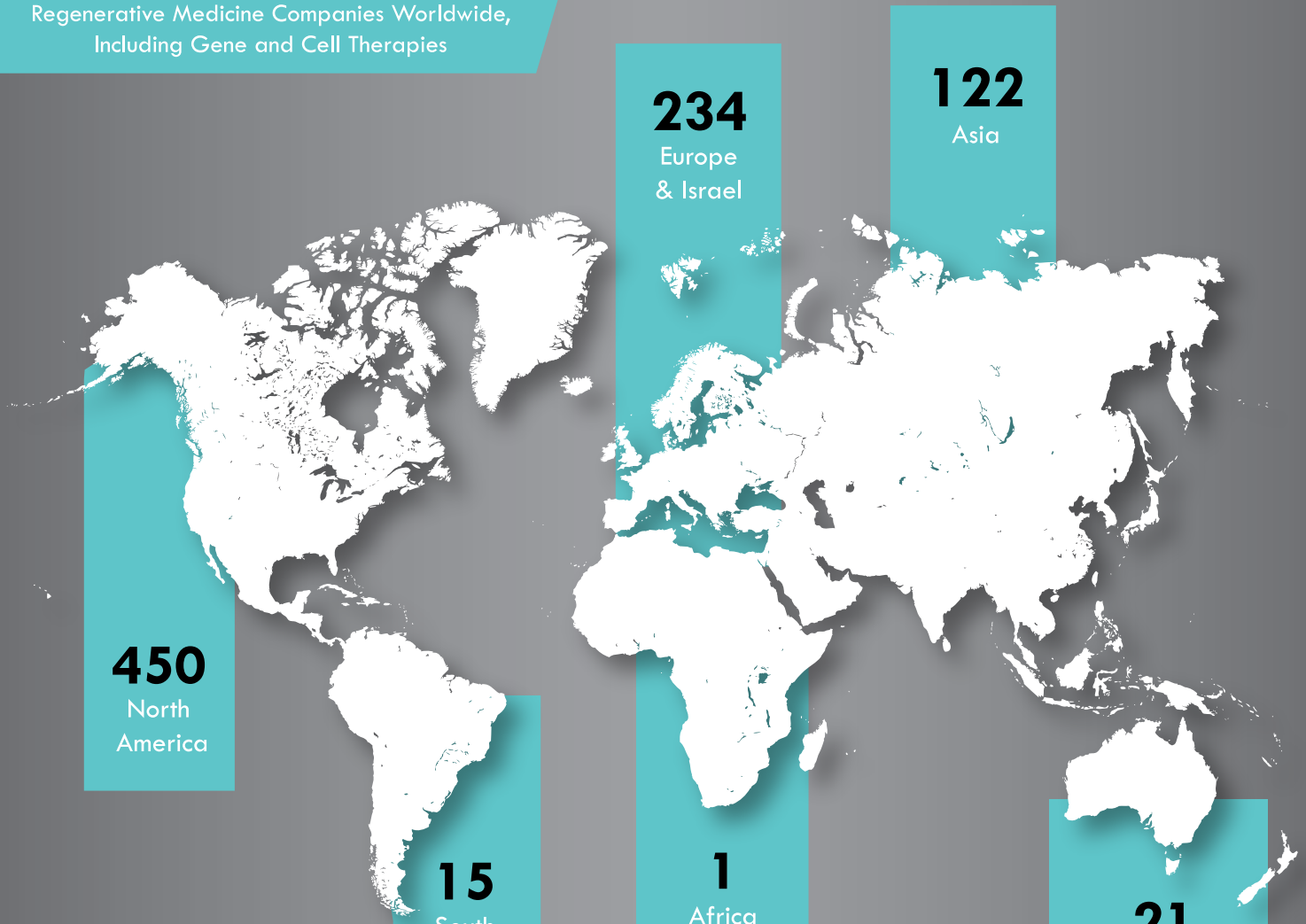
*By leveraging the expertise of its membership, ARM empowers multiple stakeholders to promote legislative, regulatory and public understanding of, and support for, this expanding field.*

*www.alliancerm.org*

# Table of Contents

# Global Landscape

**843+**
Regenerative Medicine Companies Worldwide, Including Gene and Cell Therapies



# Industry Overview

It's impossible to write about Q3 2017 without highlighting two landmark U.S. FDA approvals that have rocked both Q3 and the start of Q4. In late August, Novartis' CAR-T therapy Kymriah was approved for relapsed/refractory acute lymphoblastic leukemia for pediatric and young adult patients the first cell-based immunotherapy to make it across the finish line in the United States. Gilead completed its acquisition of Kite Pharma for almost $12B in early October and only had to wait until October 18 to see Kite's CAR-T therapy Yescarta approved for adult patients with relapsed/refractory large B cell lymphoma after two or more lines of systemic therapy.

In Q3 regulatory news, the FDA granted two Regenerative Medicine Advanced Therapy (RMAT) designations: Mallinckrodt's regenerative skin tissue product StrataGraft and Kiadis Pharma's cell-based immunotherapy product ATIR101. M&A activity in Q3 was brisk. CSL Bering acquired Calimmune, which focuses on the development of *ex vivo* hematopoietic stem cell gene therapy, for an upfront payment of $91M and milestones that could add up to an additional $325M. Acer and Opexa completed their merger in September, raising $15.7M in capital to move lead asset EDSIVO through NDA submission with the FDA in the 1H 2018. This quarter also saw a bidding war for rare disease gene therapy developer Dimension Therapeutics: REGENXBIO made the first move, but was outbid by Ultragenyx Pharmaceutical, which offered $151M.

Notable partnerships in Q3 included Celgene's license of bluebird bio's CAR-T therapy bb21217, targeting B cell maturation antigen, for $15M plus milestones. Bone Therapeutics entered into a licensing agreement with Asahi Kasei for development and commercialization of its autologous bone cell therapy product PREOB(R) in Japan. The upfront payment of around $2M will include royalties of roughly $8.8M. Gene therapy company Spark Therapeutics entered into a licensing agreement with Genethon, a French R&D non-profit, for the development and commercialization of an AAV gene therapy targeting the liver to address a rare genetic disease.

There was also a wave of sizeable public financing rounds this past quarter. Juno Therapeutics, bluebird bio and Spark Therapeutics all closed their public offerings of common stock, raising $287M, $460M and $402M, respectively, to advance their clinical pipelines. In addition, Krystal Biotech raised $45.6M, the sector's only initial public offering this quarter.

2017 continues to be a success-filled year for this sector. We are now on the doorstep of other significant advances coming to market and to patients worldwide. We look forward to following all of this sector's accomplishments as we head into year's end.

–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 Q3 2017 Global Financings

### TOTAL GLOBAL FINANCINGS

**$1.85 Billion raised in Q3 2017**

*102% increase from Q3 2016*

**$6.12 Billion raised in first three quarters of 2017**

*19% increase compared to full-year 2016*

### GENE & GENE-MODIFIED CELL THERAPY

**$1.62 Billion raised in Q3 2017**

*167% increase from Q3 2016*

**$3.68 Billion raised in first three quarters of 2017**

### CELL THERAPY

**$1.08 Billion raised in Q3 2017**

*295% increase from Q3 2016*

**$3.8 Billion raised in first three quarters of 2017**

### TISSUE ENGINEERING

**$17 Million raised in Q3 2017**

*-79% decrease from Q3 2016*

**$313.3 Million raised in first three quarters of 2017**

## Examples of Key Financings: Q3 2017

**Public offerings:**

- bluebird bio raises $460M in public offering – July 30, 2017
- Spark Therapeutics raises $402M in public offering – August 9, 2017
- Juno Therapeutics raises $287.6M in follow-on offering – September 26, 2017
- Inovio Pharmaceuticals raises $75M in public offering – July 25, 2017
- Krystal Biotech raises $45.6M initial public offering – September 22, 2017

**Corporate partnerships, acquisitions and other financings:**

- CSL Behring acquires Calimmune for $416M, including $91M upfront – August 28, 2017
- Homology Medicines raises $83.5M in Series B financing – August 1, 2017
- Adaptimmune exercises $62.6M option agreement with GSK – September 7, 2017
- Mesoblast raises A$50.7 Million in private placement – September 15, 2017

**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.*

# Total Global Financings by Type, by Year

# Commentary: CAR-T Commercialization

***Commentary taken from ARM's recently held Cell and Gene Meeting on the Mesa 2017: Plenary Session: Implications of Commercialization: What Does Approval Mean?***

***On innovative and outcomes-based pricing for high-value therapies:***

"When it came to Kymriah, we thought from the beginning we had to be innovative; not only in bringing this transformative therapy to patients, which involves many challenges in general, but also, how can we ensure patient access?

"Every therapy, every disease, every indication will lead to a different type of approach, but the idea is the same: how can we align with different stakeholders on the type of outcome we're trying to reach, and how can we align ourselves to reach that outcome. But the system is not organized for such, and that's where we have to work."

*–Pascal Touchon*
*SVP and Global Head, Cell and Gene*
*Novartis Oncology*

Plenary Session: Implications of Commercialization: What Does Approval Mean?

"It's a watershed event with CMS, as companies like Juno want to understand the details…We're at the threshold now where the products are becoming expensive, they're extremely personalized, and this all comes together with pay-for-performance, getting value for the dollars you're spending. I think CMS made a step forward with Novartis, and now we'd love to see the details so we can start thinking about how to operationalize such an arrangement, not only with Medicare, but also how to do it with commercial payers, and how that may or may not impact price."

*–Bob Azelby*
*EVP and Chief Commercial Officer*
*Juno Therapeutics*

# Commentary: CAR-T Commercialization

Pascal Touchon
SVP and Global Head, Cell and Gene
Novartis Oncology

***On managing CAR-T's complex delivery issues:***

"It's complex. It's manageable. Just get the right team in the right place to do it. We did it progressively, and I think that was a good thing to do in two different steps: one was to move from one center, UPenn, to treating patients in many centers, so how do you manage that? Then, to move from one country, the U.S., to doing studies in multiple countries, different continents. We've done studies now in DLBCL in 27 centers across the world, and in pediatric ALL in 25 centers across the world, from Japan, Australia, to Canada, Europe and the U.S. By moving progressively, we've learned how to manage complexity.

"Now we're moving into our first country with the first approval, in a relatively small [patient] population, that's also a learning phase…then we'll move into other types of therapies, where we're going to treat thousands of patients, then we're going to move to other countries, so it's a progression of complexity that we've been able to manage so far."

*–Pascal Touchon*
*SVP and Global Head, Cell and Gene*
*Novartis Oncology*

"We're at the very early stages of the science; we're going to continue to understand the type of cells that go into the product and how they impact the patient, as well as how do we improve the toxicity profile so you can democratize access to these products, as 80 percent of patients reside outside of these Centers of Excellence."

*–Bob Azelby*
*EVP and Chief Commercial Officer*
*Juno Therapeutics*

"One of the complexities from a supply-chain standpoint is that with autologous cell therapies, every patient is a lot. In traditional pharmaceuticals and biologics, you go through the manufacturing and release process for a lot that will treat potentially thousands of patients. Here, you're doing it every time for every patient…The complexity is almost mind-boggling, but obviously doable."

*–Nick Colangelo*
*President and CEO*
*Vericel Corporation*

**934**
Clinical trials underway worldwide by end of Q3 2017

Ph. I: 307
Ph. II: 548
Ph. III: 79

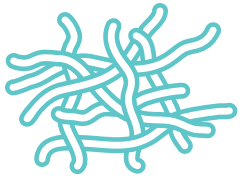
## Number of Clinical Trials Utilizing Specific RM/AT Technology: Q3 2017

### Gene Therapy & Gene-Modified Cell Therapy

**Total: 566**
Ph. I: 212
Ph. II: 315
Ph. III: 39

### Cell Therapy

**Total: 607**
Ph. I: 192
Ph. II: 370
Ph. III: 45



### Tissue Engineering

**Total: 18**
Ph. I: 6
Ph. II: 8
Ph. III: 4

**Total number of clinical trials represents sector-wide figures; please note that products employing cell-based immunotherapy are accounted for in both the gene therapy & gene-modified cell therapy and cell therapy sectors. As a result, the total number of clinical trials does not equal the sum of the trials within the individual technology groups.*

## Clinical Trials by Indication: Q3 2017


- 492 (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.
- 85 (Nearly 10%) are in cardiovascular disorders, including congestive heart failure, myocardial infarction, critical limb ischemia, heart disease and others.
- 58 (6%) are in diseases of the central nervous system, including multiple sclerosis, Alzheimer's disease, Parkinson's disease, traumatic brain injury, ALS and others.

# Examples of major milestones and key data events: Q3 2017

## Cell-Based Immuno-Oncology Programs

- Kiadis Pharma blood cancer receives U.S. FDA Regenerative Medicine Advanced Therapy designation for cell-based immunotherapy product ATIR101 for the treatment of blood cancer – September 20, 2017
- Novartis receives first-ever U.S. FDA approval for a CAR-T cell therapy, Kymriah (CTL019), for children and young adults with relapse/refractory B-cell ALL – August 30, 2017
- Kite files CAR-T marketing authorization application with EMA for Axicabtagene Ciloleucel – July 31, 2017
  *Note: In Q4, Kite's Yescarta CAR T-cell therapy is approved by U.S. FDA for treatment of adult patients with relapsed/refractory large B-cell lymphoma after two or more lines of systemic therapy*

## Gene Therapy & Genome Editing Programs

- Audentes Therapeutics announces Rare Pediatric Disease and Fast Track designations for AT132 for the treatment of X-Linked Myotubular Myopathy – September 27, 2017
- Editas Medicine receives EMA's Orphan Medicinal Product designation for EDIT-101 for the treatment of Leber Congential Amaurosis type 10 – September 26, 2017
- Voyager Therapeutics announces positive results from ongoing Phase 1b trial of VY-AADC01 for advanced Parkinson's disease, demonstrating durable improvements across patients' motor function after a one-time administration – September 6, 2017
- Abeona Therapeutics receives U.S. FDA Breakthrough Therapy designation for EB-101 gene therapy program for Recessive Dystrophic Epidermolysis Bullosa – August 29, 2017
- Orchard Therapeutics announces ADA-SCID gene therapy OTL-101 receives designation as Promising Innovative Medicine by UK Medicines and Healthcare Products Regulatory Agency – August 22, 2017
- AGTC announces U.S. FDA Orphan Drug Designation for gene therapy product candidate to treat X-linked retinitis pigmentosa caused by mutations in RPGR gene – August 3, 2017

## Gene Therapy & Genome Editing Programs (cont.)

- Spark Therapeutics submits marketing authorization application to EMA for LUXTURNA (voretigene neparvovec) – July 31, 2017
- Spark Therapeutics' BLA for LUXTURNA accepted for filing by U.S. FDA – July 17, 2017

  *Note: In Q4, U.S. FDA Advisory Committee unanimously recommends approval of Spark Therapeutics' LUXTURNA for biallelic RPE65-mediated inherited retinal disease*

## Cell-Based Therapy Programs

- Bone Therapeutics announces all patients meet primary endpoint in allogeneic bone therapy product ALLOB Phase I/IIA delayed-union study interim analysis – September 20, 2017
- U.S. FDA grants Fast Track designation to Pluristem's PLX-PAD for the treatment of critical limb ischemia – September 18, 2017
- Enzyvant receives U.S. FDA Rare Pediatric Disease designation for investigational therapy RVT-802 for the treatment of primary immune deficiency associated with complete DiGeorge Syndrome – September 5, 2017
- Mesoblast announces positive results of its Phase IIa trial for prevention of radiographic and clinical features of knee osteoarthritis after injury, demonstrating a single intra-articular injection of product candidate MPC-75-IA reduced cartilage loss and bone changes by six months, and improved pain and function for over two years, when compared to controls – August 16, 2017
- Capricor Therapeutics receives Rare Pediatric Disease designation from U.S. FDA for CAP-1002 for treatment of Duchenne Muscular Dystrophy – July 18, 2017
- Korea Ministry of Food and Drug Safety awards marketing approval to TissueGene Asia licensee Kolon Life Science's Invossa-K for degenerative arthritis – July 12, 2017

## Tissue-Engineered Product Programs

- U.S. FDA issues Regenerative Medicine Advanced Therapy (RMAT) designation to Mallinckrodt's regenerative skin tissue product StrataGraft – July 18, 2017

# Current Regulatory & Legislative Priorities

**Global reimbursement issues –**

- Building and promoting a strong value story for regenerative products through evidence collection: case studies, framework development, coverage criteria and external stakeholder engagement.
- Securing favorable coverage and reimbursement policies for cell and gene therapies and other regenerative medicine products.
- Breaking down barriers to adoption of new, innovative payment and financing models, driving value-based payment reform and addressing core challenges to enable payments over time.

**U.S. regulatory issues –**

- Continuing to engage with U.S. FDA on the Regenerative Medicine Advanced Therapy (RMAT) designation, which optimizes a pathway to market for cell therapy, certain gene therapy, and other regenerative medicine products.
- Coordinating with U.S. FDA to improve communication between the agency and sponsors.
- Working with the Standards Coordinating Body to complete landscape analysis of standards for regenerative medicine and advanced therapies to support standards requirements discussions with the U.S. FDA and the National Institute of Standards and Technology (NIST).
- Identifying opportunities to improve global regulatory convergence.

**European regulatory issues –**

- Along with the main EU trade organizations in Europe, continuing to advocate for improvements of GMO requirements for clinical trials with gene therapies in Europe.
- Identifying ways to foster development and improve patient access to Advanced Therapy Medicinal Products (ATMP) in Europe, with emphasis on several aspects such as R&D, including standards development; regulatory processes, including GMO requirements; guidance on the structure of applications; and market access. ARM is currently drafting a position paper outlining proposed solutions to the identified barriers, to be published in Q4 2017.
- Leading regional legal analysis, advocacy and stakeholder engagement regarding Hospital Exemption (HE), enabling EU ATMP developers to improve their understanding of the legal resources available and to identify possible country-specific improvements to ensure fair implementation of HE across France, Germany, Italy, Spain and the U.K.

**Genome editing & related bioethics issues –**

- Broadening stakeholder awareness and acceptance of somatic cell approaches to treatments and cures, as most genetic diseases manifest in and can be treated in non heritable cells. It is ARM's view that patients will benefit more immediately from resources being directed towards somatic applications of genome editing technologies.
- ARM applauds and supports the continued and accelerated efforts to convene the appropriate stakeholder groups from around the world, including patients, scientists, bioethicists, regulatory authorities, governments, etc. to approach this matter from a rigorous, science-based and global perspective.

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