Q1

ALLIANCE for Regenerative Medicine

2018

Quarterly 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.

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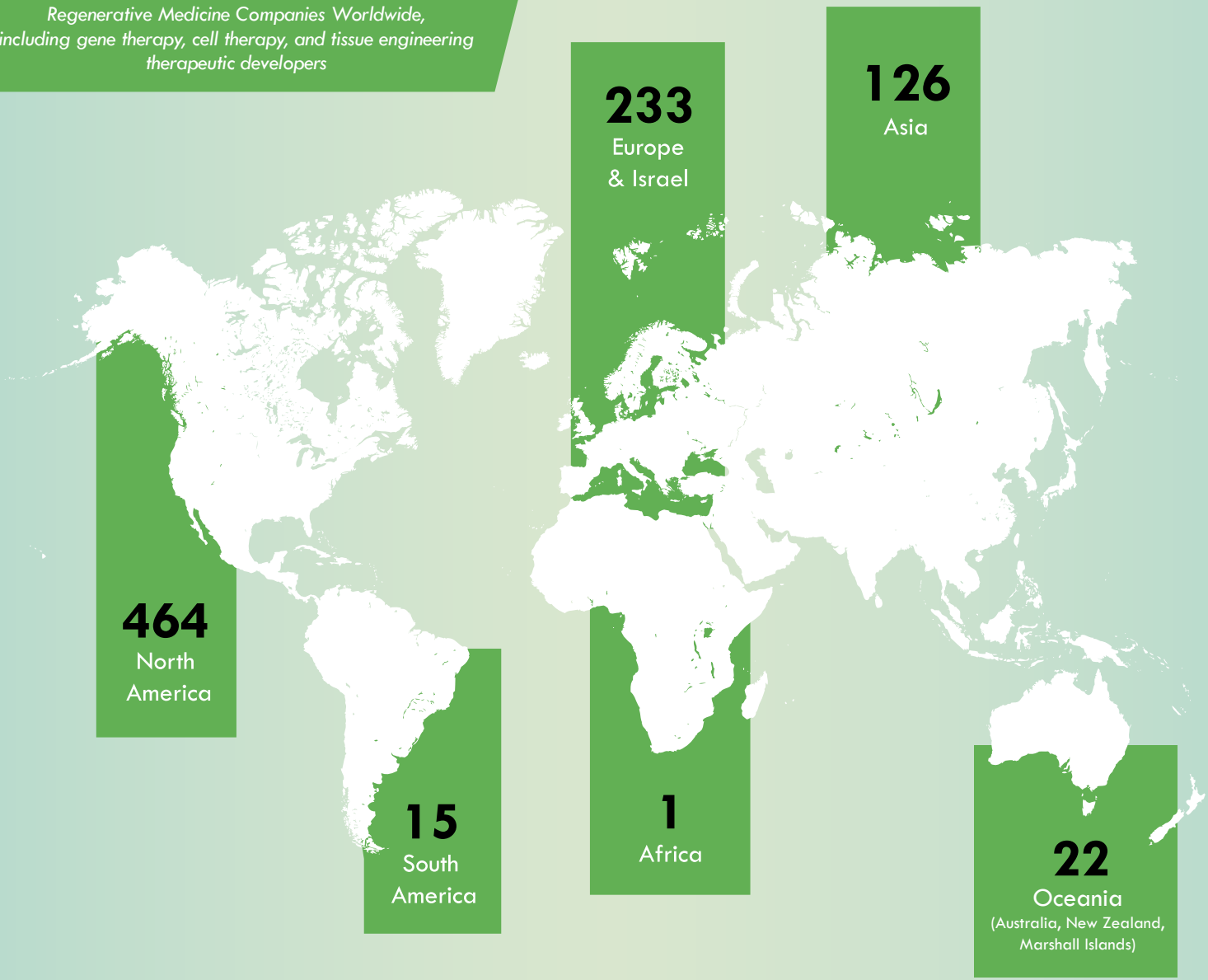
Global Landscape

861+

Regenerative Medicine Companies Worldwide, including gene therapy, cell therapy, and tissue engineering therapeutic developers



Industry Overview

The first quarter jump-started 2018 with large gains for advanced therapies and headline-making IPOs, finance rounds, and partnership agreements. Investors signaled their willingness to invest early, with several companies raising funds in Series A. Most recently, Allogene Therapeutics, founded by former top execs at Kite, raised a remarkable $300 million in a Series A and announced the acquisition of Pfizer's allogeneic CAR-T portfolio. The deal with Pfizer includes collaborating with Cellectis on UCART19 and gives Pfizer a 25% stake in Allogene. In addition, Tmunity Therapeutics had a $100 million mega-round to advance their novel TCR and CAR-T cell therapies. Shanghai's JW Therapeutics, founded by Juno Therapeutics and the WuXi AppTec Group in 2016, completed a $90 million Series A. Prevail Therapeutics raised $75 million in Series A for gene therapies for neurodegenerative diseases, including Parkinson's therapy PR001.

There were multiple successes in secondary financing rounds as well. In January, bluebird bio raised a staggering $651.3 million from their public offering. Ultragenyx and Iovance each had successful financing rounds garnering $250 million and $172.5 million, respectively. Generation Bio announced a $100 million Series B financing to move their first two gene therapies through IND studies. TCR2 Therapeutics followed in March with a $125 million Series B round to move their TCR therapies through human proof-of-concept.

In March, Homology Medicines' IPO raised $144 million for their novel gene editing technology. Unum Therapeutics raised $69.6 million, which includes an estimated $20 million to finish a Phase I combo trial of ACTR087 and rituximab for patients with B-cell NHL.

Significant partnership deals announced this quarter included Sangamo and Gilead/Kite's partnership to develop and commercialize cell therapies in cancer. Sangamo will receive $150 million upfront and will be eligible for up to $3.01 billion in milestones. AbbVie and Voyager signed an agreement to develop therapies for Alzheimer's disease, with Voyager receiving $69 million upfront with an additional $155 million for preclinical and Phase I options, as well as a potential $895 million in milestones. bluebird bio and Celgene entered into an agreement to co-develop and co-promote CAR-T therapy bb2121 for multiple myeloma. bluebird bio will receive up to $70 million in milestone payments, and the companies will split U.S. profits.

Several therapies received the FDA's RMAT designation this quarter: Abeona's gene therapy for recessive dystrophic epidermolysis bullosa, Capricor's cell therapy CAP-1002 for Duchenne's muscular dystrophy, and MiMedx's AmnioFix Injectable for osteoarthritis of the knee.

We will watch this dynamic sector closely as we move into Q2 with a keen eye on whether momentum can be sustained in a more volatile market environment.

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

Global Financings

Total Q1 2018 Global Financings

TOTAL GLOBAL FINANCINGS

$3.8 Billion raised in Q1 2018

135% increase from Q1 2017

GENE & GENE-MODIFIED CELL THERAPY

$3.1 Billion raised in Q1 2018

248% increase from Q1 2017

CELL THERAPY

$1.9 Billion raised in Q1 2018

42% increase from Q1 2017

TISSUE ENGINEERING

$363.1 Million raised in Q1 2018

1,347% increase from Q1 2017

Examples of Key Financings: Q1 2018

Public offerings:

- *bluebird bio raises $651.3M in follow-on financing – January 8*
- *AveXis raises $431.9M in follow-on financing – January 22*
- *Audentes Therapeutics raises $231.4M in follow-on financing – January 29*
- *Iovance raises $172.5M in follow-on financing – January 29*
- *CRISPR Therapeutics raises $130.8M in follow-on financing – January 9*

Corporate partnerships, acquisitions and other financings:

- *Sangamo & Kite enter into $3.2B collaboration, including $150M upfront – February 20*
- *AbbVie signs $1.12B agreement with Voyager Therapeutics, including $69M upfront – February 16*
- *REGENXBIO and AveXis announce $260M expansion of previous relationship, including $80M upfront – January 8*
- *Celularity secures $250M in venture financing – February 15*
- *Spark Therapeutics signs $170M licensing agreement with Novartis, including $105M upfront – January 24*
- *Sangamo & Pfizer enter into $162M collaboration, including $12M upfront – January 3*
- *TCR2 raises $125M in venture financing – March 21*
- *Tmunity raises $100M in venture financing – January 23*

M&A activity:

- *Celgene acquires Juno Therapeutics for $9B – March 6*
- *Astellas acquires Universal Cells for $102.5M – February 14*
- *Celularity acquires Alliqua BioMedical for $29M – January 5*

**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.*

Total Global Financings by Type, by Year

Commentary: Commercializing Cell & Gene Therapies

Commentary from ARM's State of the Industry presentation and panels, held January 8, 2018 in San Francisco at the JP Morgan Biotech Showcase.

Panel: Next Generation CARs and Other Cell-Based Immunotherapies
Presenters (left to right): Robert Preti (Hitachi Chemical Advanced Therapeutics Solutions); Manuel Litchman (Mustang Bio); James Noble (Adaptimmune); Pascal Touchon (Novartis Oncology); Scott Wolchko (Fate Therapeutics); and Bob Azelby (Juno Therapeutics)

Pascal Touchon, SVP & Global Head, Cell & Gene, Novartis Oncology:

"It all started with partnering and I think it's going to continue with partnering [...] with the number of questions we have to solve, the number of challenges we have in front of us, this can only be done with partnering. And I think academic teams and small companies can bring unique features to this field in the term of constructs, technologies, facilitating the supply and logistics, as well as making sure we can deliver at scale to many patients around the world. [...] The field is immense, and I don't see even a company like Novartis being able to do everything by itself so we are going to rely on partnering."

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"[CAR-T] is so new and so transformative as a therapy, we couldn't just go in with a traditional view of access, which I think is the key issue. The key issue isn't pricing, it's access, and making sure we can organize the access of patients in different geographies...It was very nice to see that many parts of the U.S. system, first and foremost CMS, were able to engage in a dialogue with us and find ways to address the unique features of that kind of transformative therapy."

"The medical need is immense and the need to address solid tumors as well as other liquid tumors is great."

* * *

Deepak Srivastava, President, Gladstones Institute:

"I think one of the key issues going forward from a regulatory standpoint and from a production standpoint is how viable is a combination of vectors for a single therapy—how viable will that be and can it be taken forward toward clinical trials? [There are] safety issues, of course, and issues around delivery because in this situation you have to get high enough levels of gene expression to wholesale convert a cell from one cell type to another which it doesn't want to do […] So really local delivery, high enough levels of expression, production, and numbers of vectors are some of the key challenges we're facing."

* * *

Bill Lundberg, Chief Scientific Officer, CRISPR Therapeutics:

"There's been an intersection of a number of different discoveries and progress in significant scientific areas. One is in the field of cellular reprogramming & iPSCs […] Another is the increasing facility with which […] many, many different researchers and scientists, in industry and academia, can take the CRISPR toolkit and modify cells, and the third is a better understanding of the physiology of specific diseases. I would predict that over the coming years we will have significant opportunities to create regenerative medicine-based therapies using the marriage of these various different strands of work."

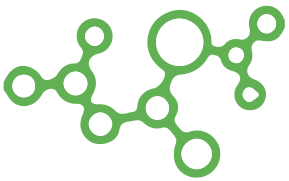
959
Clinical trials underway worldwide by end of Q1 2018

Ph. I: 320
Ph. II: 549
Ph. III: 90

Number of Clinical Trials Utilizing Specific RM/AT Technology: Q1 2018

Gene Therapy

Total: 319
Ph. I: 110
Ph. II: 174
Ph. III: 35



Gene-Modified Cell Therapy

Total: 284
Ph. I: 121
Ph. II: 152
Ph. III: 11

Cell Therapy

Total: 332
Ph. I: 84
Ph. II: 211
Ph. III: 37

Tissue Engineering

Total: 24
Ph. I: 5
Ph. II: 12
Ph. III: 7

**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: Q1 2018

- 509 (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 one in 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.

Select Significant Clinical & Data Events: Q1 2018

Cell-Based Immuno-Oncology Programs

- *Trillium's TTI-621 SIRPaFc fusion protein for treatment of cutaneous T-cell lymphoma received Orphan Drug designation from the FDA – March 20*

Gene Therapy & Genome Editing Programs

- *AveXis's AVXS-101 gene therapy for treatment of spinal muscular atrophy Type 1 received SAKIGAKE designation from Japan's MHLW – March 27*
- *Abeona's EB-101 gene-corrected autologous cell therapy for treatment of recessive dystrophic epidermolysis bullosa received RMAT designation from the FDA – January 29*

Tissue-Engineered Product Programs

- *MiMedx reported positive pain and foot function results from phase 2B clinical trial of AmnioFix Injectable in treatment of plantar fasciitis – March 26*
  - *Phase 2B IND clinical trial evaluating the use of AmnioFix Injectable for the treatment of plantar fasciitis demonstrated a clinically and statistically significant difference compared to patients in the Control Group in their reduction in the visual analog scale (VAS) score for pain ($p<0.0001$) and Foot Function Index-Revised (FFI-R) scores ($p=0.0004$) at 3 months compared to baseline.*
- *MiMedx's AmnioFix Injectable micronized amniotic tissue for treatment of osteoarthritis of the knee received RMAT designation from the FDA – March 9*

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Cell Therapy Programs

- *Cynata's CYP-001 mesenchymal stem cell product for treatment of graft versus host disease received Orphan Drug designation from the FDA – March 28*
- *Vericel reported publication of results from the Phase 3 SUMMIT Extension Study demonstrating sustained clinical benefit of MACI out to five years – March 23*
    - *Significantly greater improvements in Knee injury and Osteoarthritis Outcome Score (KOOS)1 pain and function scores for MACI versus microfracture shown in the two-year Phase 3 SUMMIT (Superiority of MACI Implant Versus Microfracture Treatment) study were maintained over the additional three-year follow-up in the SUMMIT Extension Study.*
- *Sigilon's SIG-003 genetically modified allogeneic cells for treatment of hemophilia B received ATMP designation from the EMA – March 14*
- *Primary endpoint successfully achieved in Mesoblast's Phase 3 cell therapy trial for acute graft versus host disease – February 22*
    - *In the 55 children enrolled in Mesoblast's open-label Phase 3 trial conducted across 32 sites in the United States, the Day 28 OR rate was 69%, a statistically significant increase compared to the protocol-defined historical control rate of 45% (p=0.0003).*
- *Capricor's CAP-1002 allogeneic cell therapy for treatment of Duchenne muscular dystrophy received RMAT designation from the FDA – February 5*
- *Nohla's NLA101 allogenic stem and progenitor cell therapy for use in hematopoietic stem cell transplantation received Orphan Drug Designation in the EU – January 23*
- *TiGenix's Alofisel (previously Cx601) allogeneic stem cell therapy for treatment of perianal fistulas in Crohn's received central marketing authorization from the European Commission – March 23*

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 other relevant 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 access and reimbursement for RM / AT products.

Industrialization and Manufacturing –

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

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