Alliance *for* Regenerative Medicine

Q3 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.

www.alliancerm.org

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Letter from ARM's Chairman

The accelerated growth of the industry has continued over the past few years, led by the launches of products like Kymriah, Yescarta, and LUXTURNA, and supported by positive news and successful capital raises across therapeutic platforms and in major markets around the world. The sector has never been stronger or more globally connected.

Two years ago, with a few pivotal approvals approaching, the industry was on the cusp of drastic change—a true inflection point that hinged on the regulatory success of these products. 2017 didn't disappoint, and products powered through the approval process driven by their transformative results for patients. However, we recognized, more than ever, that the commercial environment, while maturing, hadn't quite kept up with the speed at which these products showed their clinical potential. That environment includes the coordinated infrastructure to provide for the regulation, reimbursement, legislation, and manufacture of these products. By all measures, the lessons we've learned over the past year indicate what needs be done to ensure commercial success of those and future products. If, that is, we listen to and keep the patient at the core of our mission.

With products now reaching the global market, our ability to deliver these medicines to patients is under intense scrutiny, and the healthcare marketplaces are testing our ability to manufacture, deliver, pay for, and profit from these therapies at scale, recognizing their tremendous potential to transform the medical landscape. It's truly showtime.

ARM's activities have contributed to, and, in many cases, led these advances in the field. To prepare for the new demands associated with its role, ARM has evolved as an organization, and will continue to cultivate its leadership position as the preeminent go-to multi-stakeholder advocacy group in the regenerative medicine sector.

It has been an honor to have the opportunity to serve as Chairman of ARM throughout this extraordinary time of global growth, change, and momentum.

Robert Preti, Ph.D.
President & CEO,
Hitachi Chemical Advanced Therapeutics Solutions;
General Manager,
Hitachi Chemical Regenerative Medicine Business Sector

Current Regulatory & Legislative Priorities

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

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

Industry Overview

Q3 Summary Overview

Companies developing regenerative medicine and advanced therapies continue to move preclinical and clinical candidates forward. Cellerant's Romyelocel-L for infection and Audentes's AT132 for X-linked myotubular myopathy received RMAT designation from the FDA, bringing the total number of products with the designation up to 27. In addition, bluebird bio's Lenti-D for CALD received the EMA's PRIME designation, with a total of 45 therapies granted this designation since its 2016 launch.

Partnerships remain a key factor in the growth of the sector. Fate Therapeutics signed a substantial deal with ONO Pharmaceuticals, worth as much as $1.22 billion, to use Fate's iPSC platform to develop CAR-T therapies. Gritstone Oncology will use its EDGE AI platform as part of a deal with bluebird bio, potentially raising $1.25 billion, including potential milestone payments. Precision BioSciences will use their genome editing platform to develop nucleases targeting hepatitis B for Gilead; milestone payments could generate up to $445 million. Other notable deals included Genmab and Immatics, CRISPR Therapeutics and ViaCyte, Mesoblast and Tasly, Editas Medicine and Allergan, Cellular Biomedicines and Novartis, and many more.

The parade of regenerative medicine companies lining up with public offerings continued in Q3 as 16 companies filed or completed successful IPOs and secondary offerings. Rubius Therapeutics raised $277.3 million in a successful IPO, with Allogene, Gamida, and LogicBio all filing for IPOs to be completed in Q4. Secondary offerings this quarter raised more than $1.2 billion, including offerings from bluebird bio ($632.50 million), REGENXBIO ($201.8 million), CRISPR Therapeutics ($200 million), Fate Therapeutics ($143.80 million), and Adaptimmune ($100 million).

In venture financing rounds, Ambys Medicines, Akouos, Recombinetics, Mammoth Biosciences, CODA Biotherapeutics, and CureGenetics all had positive Series A rounds, with Abmys and Akouos leading the pack with $60 Million and $50 million raised, respectively. Series B funding was led by 4D Molecular, who raised $90 million. Other Series B investments went to VAXIMM and Nohla Therapeutics. Orchard Therapeutics raised $150 million and SQZ Biotechnologies secured $72 million in their respective Series C financings, with SCM Lifescience raising $35 million in their Series C.

There were a several key acquisitions this quarter: Takeda completed the acquisition of TiGenix for $624 million; PTC Therapeutics will pay $200 million upfront and up to $535 million in milestones to acquire Agilis Biotherapeutics, whose gene therapy for AADC deficiency is set to go before the FDA next year. Astellas announced it acquired Quethera for $109.4 million; and Sangamo Therapeutics began the $84 million acquisition of TxCell, which was completed in the beginning of Q4.

The fourth quarter will likely round out a very successful year for advanced therapies. We will look to see if 2018 year-end totals will outshine all previous years in company, products, and financial growth.

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

Global Financings

Total Q3 2018 Global Financings

TOTAL GLOBAL FINANCINGS

$2.8 Billion raised in Q3 2018
59% increase from Q3 2017

$10.7 Billion raised YTD 2018
40% increase year-over-year

GENE & GENE-MODIFIED CELL THERAPY

$2.1 Billion raised in Q3 2018
35% increase from Q3 2017

$7.8 Billion raised YTD 2018
34% increase year-over-year

CELL THERAPY

$1.8 Billion raised in Q3 2018
73% increase from Q3 2017

$6.0 Billion raised YTD 2018
32% increase year-over-year

TISSUE ENGINEERING

$1.5 Million raised in Q3 2018
91% decrease from Q3 2017

$785.6 Million raised YTD 2018
213% increase year-over-year

*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.

Examples of Key Financings: Q3 2018

Public offerings:

- bluebird bio raises $632.5 million in follow-on financing – July 27
- Rubius Therapeutics raises $277.3 million in initial public offering – July 23
- REGENXBIO raises $201.8 million in follow-on financing – August 14
- CRISPR Therapeutics raises $200 million in follow-on financing – September 19
- Fate Therapeutics raises raises $144 million in follow-on financing – September 25
- Adaptimmune raises $100 million in follow-on financing – September 7

Corporate partnerships and other financings:

- Orchard Therapeutics raises $150 million in Series C financing – August 13
- Allogene Therapeutics raises $120 million in venture financing – September 6
- bluebird bio receives $100 million in private placement of shares – August 6
- 4D Molecular Therapeutics secures $90 million in Series B funding – September 5
- SQZ Biotechnologies secures $72 million in Series C funding – August 8
- Ambys Medicines secures $60 million in Series A funding – August 8
- Genmab signs $54 million upfront agreement with Immatics – July 12
- Akouos secures $50 million in Series A funding – August 7

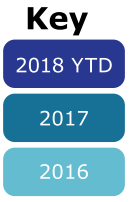
M&A Activity:

- Takeda Pharmaceutical acquires TiGenix NV for $626.4 million upfront – July 31
- PTC Therapeutics acquires Agilis Biotherapeutics for $200 million upfront – August 23
- Astellas Pharma acquires Quethera for $109.4 million upfront – August 10
- Amicus acquires Celenex for $100 million upfront – September 20

Global Financings

Total Global Financings by Type, by Year

Mergers & Acquisitions: Upfront Payments



Commentary: Cell & Gene Meeting on the Mesa 2018

ARM's recently held 2018 Cell and Gene Meeting on the Mesa was the biggest yet, with more than 1,200 attendees, 70 company presentations, and nearly 2,200 scheduled one-on-one meetings. Speakers, including the U.S. FDA CBER Director Peter Marks, addressed a number of pertinent topics in the regenerative medicine field, including pricing and reimbursement of products, regulatory convergence, gene therapy approaches for rare disease, and more.

The meeting began in 2006 as a one-day Scientific Symposium, expanding to include the industry's first-ever investor and partnering forum in 2011. The growth of the meeting, from a small scientific gathering with a few hundred attendees to the sector's premier annual event it is today, reflects the growth of the regenerative medicine sector. Since the first full meeting, the number of therapeutic developers in the space has increased from approximately 200 to now nearly 900 (an increase of more than 300%); financings have increased from $1.5 billion in 2010 to more than $10 billion year-to-date (an increase of 566%); and the number of ongoing clinical trials has increased from 301 to 1,003 (an increase of 233%). ARM as an organization has grown as well, from its 17 founding member organizations to now more than 300.

As the sector continues to grow, events like the Cell and Gene Meeting on the Mesa will play an important role, allowing sector stakeholders across the globe to convene and promote innovation and collaboration to address some of humankind's most devastating diseases and disorders.

"The evolution of this meeting of course mirrors the growth of the sector overall. We've come a great distance from when this meeting began […] The progress in this sector has obviously been driven by huge numbers of people and many, many organizations."

Janet Lambert
CEO, Alliance for Regenerative Medicine
Meeting on the Mesa Welcome Remarks

Commentary: Cell & Gene Meeting on the Mesa 2018

Peter Marks, M.D., Ph.D.
Director, Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

Featured Talk: FDA's Efforts to Advance the Development and Approval of Cellular and Gene Therapies

"We're constantly looking for ways to do things better […] We're here obviously to make sure that products that are safe and effective make it to market, but we want to do whatever we can to help you who are making those products be able to get them to people in a timely manner because otherwise we're not going to make the progress we'd like to see."

(From left to right) Chair: Robert Preti, Ph.D., President and CEO, Hitachi Chemical Advanced Therapeutics Solutions; GM, Hitachi Chemical Regenerative Medicine Business Sector
Panelists: David Lennon, Ph.D., President, AveXis; Ron Philip, SVP, Head of Global Commercial, Spark Therapeutics; Pascal Touchon, SVP and Global Head, Cell and Gene, Novartis Oncology

Plenary Session: Charting the Path – Lessons from the Pioneers of Cell and Gene Therapy Commercialization

"Pricing and reimbursement is an area that has been truly transformative and we've seen huge progress in the way payers have started to consider these types of transformative therapies. When [Novartis] started a year and a half ago, there were a lot of challenges about this idea of one-off cost and how you can pay so much one-off for one-time therapies, so we were very clear that we were winning value to the patients, value to the medical community, value to the health care system, and value to society […] If you engage early with payers and you really educate them to show the value of these one-time transformative therapies and you back that with strong cost-effectiveness data, you can find a way, you can transform the way they look at that."

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

Commentary: Cell & Gene Meeting on the Mesa 2018

"We really need to reshape, probably at the senior-most government levels, perceptions of how these therapies can transform their healthcare systems and generate willingness at a government level—not just the payer components of government, but really the legislators themselves—to really support the industry on the commercialization side and not just the regulatory side."

–David Lennon, Ph.D., President, AveXis

(From left to right) Chair: Keith Thompson, CEO, Cell and Gene Therapy Catapult
Panelists: Max Colao, Chief Commercial Officer, Abeona Therapeutics; Geoff MacKay, President & CEO, AVROBIO; Matthew Patterson, Co-Founder and CEO, Audentes Therapeutics; Alvin Shih, M.D., CEO, Enzyvant

Panel: Opportunities and Challenges in Rare Disease

"Pricing and reimbursement really is the final frontier. We live in such an amazing time, where there's just such a confluence of positive factors. We have numerous tailwinds, you know, the scientific and clinical piece, the regulatory piece, and the technical elements are all in the process of getting solved or answered but the issue of access to these therapies and how they're going to be reimbursed still has not yet been decided […] I think the key is for us to have a dialogue as an industry, an open and honest discussion around the value that these therapies are bringing."

–Alvin Shih, M.D., CEO, Enzyvant

"We have to innovate in commercial issues just like we're innovating in R&D, and it requires creative thinking. This is a huge challenge. The good news is good dialogue has started, everyone is talking about it […] We need to show that we can succeed in getting these products to patients globally. Let's agree that we can live in a world where some sort of payment over time can be an option, because it's absolutely going to increase the speed with which patients get access to products."

–Max Colao, Chief Commercial Officer, Abeona Therapeutics

Clinical Trials

1003
Clinical trials underway worldwide by end of Q3 2018

Ph. I: 330
Ph. II: 580
Ph. III: 93

Number of Clinical Trials Utilizing Specific RM/AT Technology: Q3 2018

Gene Therapy

Total: 351
Ph. I: 114
Ph. II: 204
Ph. III: 33

Gene-Modified Cell Therapy

Total: 328
Ph. I: 145
Ph. II: 168
Ph. III: 15

Cell Therapy

Total: 283
Ph. I: 61
Ph. II: 189
Ph. III: 33

Tissue Engineering

Total: 41
Ph. I: 10
Ph. II: 19
Ph. III: 12

Clinical Trials by Indication: Q3 2018

- 57% (573) 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.
- 7% (69) are in cardiovascular disorders, including congestive heart failure, myocardial infarction, critical limb ischemia, heart disease, and others.
- 6% (58) are in musculoskeletal disorders, including spinal muscular atrophy, osteoarthritis, muscular dystrophies, cartilage defects, and bone fractures and disorders.

Select Significant Clinical & Data Events: Q3 2018

Gene Therapy & Genome Editing Programs

- Spark's LUXTURNA for the treatment of biallelic RPE65-mediated inherited retinal disease received positive CHMP opinion – September 21
- Adverum Biotechnologies received Fast Track designation of ADVM-022 for the treatment of wet age-related macular degeneration – September 19
- bluebird bio presented updated data from Phase II/III Starbeam study of investigational Lenti-D gene therapy for CALD – September 5.
    - An additional 12 patients have received Lenti-D in the Phase 2/3 Starbeam study. While these patients have not reached the primary endpoint of 24-month follow-up, there have been no MFDs reported as of April 25, 2018.
- Fibrocell announced FDA Fast Track designation of FCX-013 for treatment of moderate to severe localized scleroderma – September 5
- Reflection Biotechnologies announced that the FDA granted Orphan Drug Designation to ReflectionBio's RBIO-101 program, an AAV-based gene therapy product for treating Bietti's Crystalline Dystrophy – August 29
- MeiraGTx announced the FDA has granted rare pediatric disease designation to the company's gene therapy product candidate AAV-CNGA3 for the treatment of patients with achromatopsia due to mutations in the CNGA3 gene – August 27
    - The product also received Orphan Drug Designation from the FDA – August 13
- Adverum Biotechnologies announced that the FDA granted Orphan Drug Designation to ADVM-053, a preclinical gene therapy candidate for the treatment of hereditary angioedema – August 24
- Krystal Biotech announced that the FDA granted a Rare Pediatric Disease Designation to the company's gene therapy candidate KB105 for the treatment of patients with TGM-1-deficient autosomal recessive congenital ichthyosis – August 23
- Audentes Therapeutics announced that the FDA granted RMAT designation to AT132 for the treatment of X-linked Myotubular Myopathy – August 21

Select Significant Clinical & Data Events: Q3 2018

Gene Therapy & Genome Editing Programs (cont.)

- MeiraGTx announced that the FDA granted Fast Track designation for its AAV-CNGB3 gene therapy product candidate for the treatment of achromatopsia caused by mutations in the CNGB3 gene – August 20
- bluebird bio announced that its investigational LentiGlobin gene therapy for the treatment of adolescent and adult patients with transfusion-dependent β-thalassemia and a non-β0/β0 genotype was granted an accelerated assessment by CHMP for its upcoming marketing authorization application – July 26

Cell-Based Immuno-Oncology Programs

- Novartis received Health Canada approval of Kymriah for use in pediatric and young adult patients three-25 years of age with r/r B-cell acute lymphoblastic leukemia and for the treatment of adult patients with r/r large B-cell lymphoma after two or more lines of systemic therapy – September 6
    - Novartis also received EC approval of Kymriah for the treatment of pediatric and young adult patients up to 25 years of age with r/r B-cell acute lymphoblastic leukemia and for the treatment of adult patients with r/r diffuse large B-cell lymphoma after two or more lines of systemic therapy – August 27
- Kite, a Gilead Company, announced that the EC granted Marketing Authorization for Yescarta as a treatment for adult patients with r/r diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma, after two or more lines of systemic therapy – August 27

Cell-Based Therapy Programs

- Pluristem announced that the FDA granted Orphan Drug Designation to PLX-R18 for the treatment of insufficient hematopoietic recovery following bone marrow transplantation – September 28, 2018
- BioCardia announced positive data from its Phase III trial of CardiAMP – September 24
    - Nine-month results from the 10-patient roll-in cohort of the trial showed clinically meaningful improvements in symptoms, quality of life, and exercise capacity.

Select Significant Clinical & Data Events: Q3 2018

Cell-Based Therapy Programs (cont.)

- Mesoblast announced survival outcomes through Day 180 in children with steroid refractory acute GvHD treated with the company's Phase 3 product candidate remestemcel-L – September 20
- Histogenics announced top-line results from a Phase 3 clinical trial of NeoCart in patients with knee cartilage damage, demonstrating statistically significant and clinically meaningful improvements six months after treatment on nearly all pain and function measures compared to microfracture one and two years after treatment – September 5
- Nohla Therapeutics announced that the FDA granted Fast Track designation to dilanubicel (NLA101) for patients with high-risk hematologic malignancies receiving an allogeneic cord blood transplant – August 6
    - The product also received the FDA's Orphan Drug Designation – July 16
- Cellerant Therapeutics announced that the FDA granted RMAT designation to romyelocel-L for the prevention of serious bacterial and fungal infections in patients with de novo acute myeloid leukemia undergoing induction chemotherapy – July 2

Tissue-Engineered Product Programs

- Avita Medical announced FDA approval of its RECELL system for the treatment of severe burns – September 20
- Enzyvant announced that it has initiated its rolling submission of a Biologics License Application to the FDA for RVT-802, designed to treat the primary immune deficiency resulting from congenital athymia associated with complete DiGeorge Anomaly – July 9

Meeting on the Med 2019

The Cell & Gene Meeting on the Mediterranean is a two-day conference bringing together the entire cell and gene therapy community from Europe and beyond. Covering a wide range of commercialization topics from market access and regulatory issues to manufacturing and financing the sector, this program will feature expert-led panels, extensive one-on-one partnering capabilities, exclusive networking opportunities, and presentations by the leading publicly traded and privately held companies in the space. The event is modeled after the organization's highly successful Cell & Gene Meeting on the Mesa, which hosted more than 1,200 attendees this year.

Highlights include:

- Keynote address by Guido Rasi, Director General of the European Medicines Agency (EMA)
- 500+ one-on-one partnering meetings
- 250+ company executives, investors, patient advocates and large pharma representatives in attendance
- 50+ industry experts discussing topics ranging from go-to-market strategies to the latest discoveries in T-cell therapies
- 40+ presentations by the field's most prominent publicly traded and emerging private companies

Join ARM for what will be Europe's premier conference for advanced therapies.

Registration is open, with discounted early bird registration rates available now through January 15, 2019.

Registration is complimentary for investors and credentialed members of the media. To learn more and to register, please visit http://meetingonthemed.com.

Meeting on the Med 2019

Miguel Forte, M.D., Ph.D.
CEO, Zelluna Immunotherapy

"European cell and gene therapy stakeholders need an opportunity to convene to advance the overall competitiveness of the field with a perspective from this side of the Atlantic. At ARM's Meeting on the Med, I look forward to engaging in scientific and business discussions and networking with key industry and investor colleagues in this global community. This will be a great opportunity to support our individual, company, and collective efforts in bringing successful cell and gene therapy products to patients."

–Miguel Forte

Michael Hunt
Chief Financial Officer, ReNeuron

"ARM's inaugural Cell & Gene Meeting on the Mediterranean looks to bring together the best aspects of ARM's two previous European annual meetings, providing a single forum to discuss industry-related topics as well as interact with the European investor community. The event will replicate the resounding success of ARM's longstanding Cell & Gene Meeting on the Mesa, but with a distinct European flavor!"

–Michael Hunt

Annie-Virginie Eggimann
Vice President of Regulatory Science,
bluebird bio

"The value of the ARM Meeting on the Med will include the amazing opportunity to network with leaders in the field of cell and gene therapy, be part of a forum to generate and communicate the latest thinking on regenerative medicine including with regulators and payers, and to learn about ongoing innovative products in development from research to commercialization. There is no other event like this!"

–Annie-Virginie Eggimann

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