



Alliance *for* Regenerative Medicine

Innovation in the Time of COVID-19

*ARM Global Regenerative Medicine &
Advanced Therapy Sector Report*

**H1
2020**



Alliance *for* Regenerative Medicine

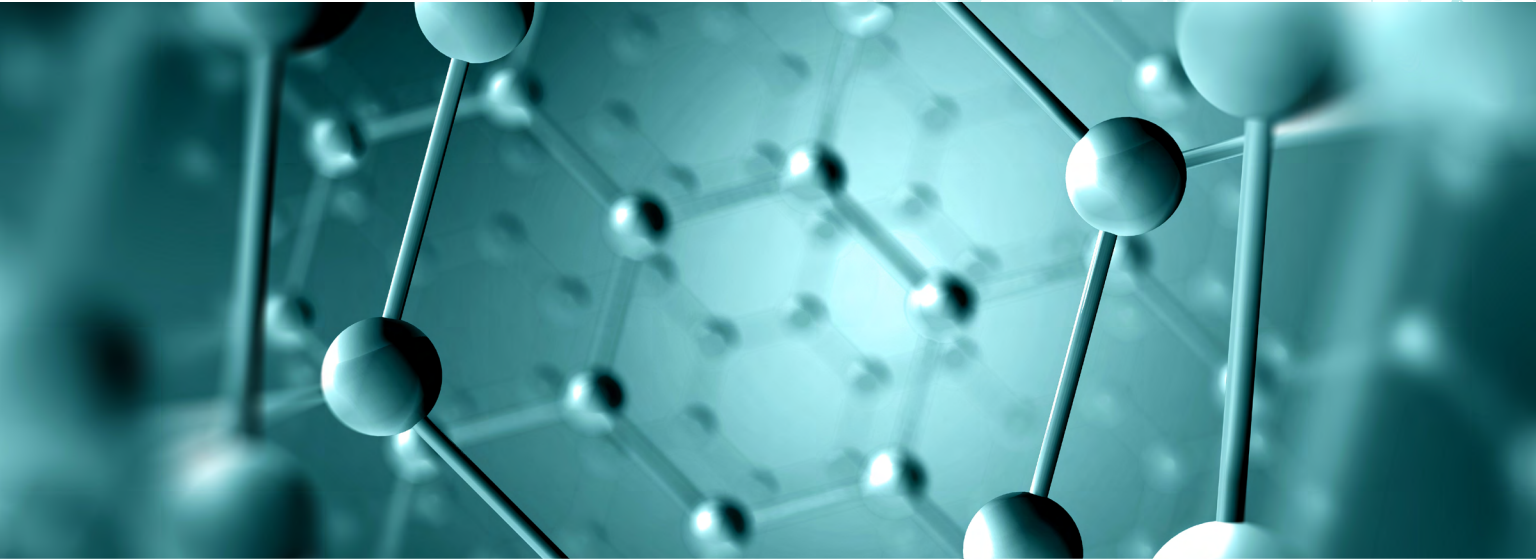
The Alliance for Regenerative Medicine (ARM) is the leading international advocacy organization dedicated to realizing the promise of regenerative medicines and advanced therapies. ARM promotes legislative, regulatory and reimbursement initiatives to advance this innovative and transformative sector, which includes cell therapies, gene therapies and tissue-based therapies.

Early products to market have demonstrated profound, durable and potentially curative benefits that are already helping thousands of patients worldwide, many of whom have no other viable treatment options. Hundreds of additional product candidates contribute to a robust pipeline of potentially life-changing regenerative medicines and advanced therapies.

In its 11-year history, ARM has become the voice of the sector, representing the interests of 360+ members worldwide, including small and large companies, academic research institutions, major medical centers and patient groups.

To learn more about ARM or to become a member, visit www.alliancerm.org.

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Letter from the CEO

Despite unprecedented global challenges, the regenerative medicine and advanced therapy sector demonstrated remarkable resilience in the first half of 2020. Patients continued to benefit from the cell and gene therapies currently on the market and in trials. Investment in the sector was robust, and we made important gains in improving market access policy. Clinical progress also continued, albeit with new obstacles caused by the pandemic and its effects.

In the first half of 2020, our sector raised \$10.7B globally, exceeding the total amount raised in all of 2019. Across the board, public and private financings are on pace to match or exceed recent years, with total financings likely to outstrip the \$13.5B record for financings set in 2018. And for the first time ever, there are more than 1,000 therapeutic developers active in this space worldwide.

In the US and Europe, we achieved some important policy successes this spring. After lobbying efforts by ARM and others, the Centers for Medicare and Medicaid Services (CMS) announced a proposed and long sought Medicare Severity-Diagnosis Related Group (MS-DRG) for chimeric antigen receptor T cell (CAR-T) therapies. This should significantly improve reimbursement for providers of CAR-T therapies and therefore patient access. In addition, CMS proposed a new rule allowing state Medicaid programs to enter into outcomes-based arrangements with therapeutic developers. In Europe, the European Commission (EC) released a proposal to temporarily relax regulations on clinical trials of products utilizing genetically modified organisms (GMOs) to treat or prevent COVID-19. This is an important first step in streamlining requirements for gene therapy clinical trials in Europe to facilitate innovation and patient access.

On the clinical front, several academic research centers and therapeutic developers are investigating the application of regenerative medicine technologies to treat COVID-19 in the short term and address related complications in the future. In addition, therapeutic developers continue to advance clinical programs in a wide variety of indications with unmet medical needs not related to COVID-19. Notably, over the past few months, we've seen initial clinical efficacy data for pioneering gene-editing technologies and longer-term durability data for approved and late-stage gene therapies. Additionally, late-stage product candidates continue to advance to market, including product launches in Europe and Japan. And the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) continue to provide pathways for expedited approval for regenerative medicines and advanced therapies, with seven FDA Regenerative Medicine Advanced Therapy (RMAT) designations and two EMA PRIority MEDicine (PRIME) designations granted so far this year.

At the same time, however, we have seen disruptions to the development of non-COVID-19 related regenerative medicines. Many global regenerative medicine companies reported challenges in clinical trial execution, including patient recruitment, enrollment, data collection and/or follow-up. In addition, given that managing and reacting to the ongoing public health crisis caused by COVID-19 has become the priority for many policymakers, regulators, and public sector payors, we have seen new demands for regulators that could result in delays for cell, gene, and tissue-based therapy product candidates outside of the COVID-19 space. Both developers and regulators recognize that interruptions can have devastating consequences for patients who rely on timely access to treatments, and regulators have shown a willingness to be flexible while retaining a high standard for health and safety.

One thing is for sure, this has been a year like no other. The following pages further detail the state of the regenerative medicine and advanced therapy landscape and ARM's role in advancing the sector.

Now more than ever, we are grateful for the ongoing efforts and support of our members. We are committed to doing everything we can to ensure that patients will be able to access these profound, durable and potentially curative therapies.



Janet Lambert
Chief Executive Officer
Alliance for Regenerative Medicine

The Martin Family: Fighting MLD with Gene Therapy



Lynda Martin with her sons Ciaran (left) and Cathal (right).



Les Martin with his son Ciaran, age 4, three years after receiving gene therapy.

Les and Lynda Martin's oldest son, Cathal, was just two and a half years old when they received the news that no parent wants to hear. "At about 18 months, he started showing symptoms — he wasn't hitting his growth and motor function milestones. He wasn't really progressing to walking by himself," Les Martin of Wicklow, Ireland remembers. Over the next year, Cathal was referred to a series of doctors. His symptoms progressively worsened for months before receiving a diagnosis of metachromatic leukodystrophy (MLD). This rare and historically fatal metabolic disease causes progressive neurological problems and motor, behavioral, and cognitive regression. "It's a devastating diagnosis. It's beyond words," says Les.

During Cathal's diagnostic odyssey, the Martins' second son, Ciaran, was born. Ciaran was only nine months old when Cathal was diagnosed with MLD. Because MLD is genetic, the Martins knew that Ciaran might have the disease as well. Though he was not yet showing symptoms, Ciaran was tested and also diagnosed with MLD.

Through their research, the Martins found a new gene therapy in development by San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy. Cathal was unable to participate due to the advanced state of his disease. However, Ciaran — who was still pre-symptomatic — was eligible to receive the experimental therapy. The Martins moved to Milan, where they lived for nine months while Ciaran received treatment. "Both of our boys had just been diagnosed as terminally ill. We were in a very difficult and dark place," Les says. "In our minds, we were leaving Ireland to go to a foreign country where one of our boys might die and the other — we were fighting to save his life."

In Milan, the Martins met several other families who were receiving gene therapy. Many had received a terminal MLD diagnosis for an older child and were desperate for the chance to save their younger children from the same fate. "That slowly brought about the realization that we weren't alone or singled out for some sort of terrible punishment in life," says Les.

Since receiving gene therapy in 2017, Les reports that Ciaran's disease has not progressed any further. He wears splints for his legs, sometimes needs to use a wheelchair, and has some damage to his white matter tissue, which allows different parts of the brain to communicate with one another. The long-term impact of that damage for Ciaran is still unknown. But Ciaran's original terminal diagnosis is no longer certain, and the difference between Ciaran and Cathal is staggering. "The contrast between our two boys tells the story of how gene therapy is so effective. One of our boys was completely paralyzed at age two and a half, and our other boy is running around [...] and has apparently been saved by the treatment that he received," Les says. "We have hope where we didn't have hope before."

Les is optimistic about the future of the gene therapy field. "The potential and the development in the gene therapy area — from small and large companies all across the world — there will be breakthroughs every couple of months. Treatments for diseases like MLD will be coming out very fast." And with development accelerating rapidly, policymakers need to ensure the entire healthcare system is keeping pace.

Back in Ireland, Les is actively advocating for expanded newborn screening for many severe genetic disorders. Many of these diseases may already have potential therapies in the pipeline, but time is of the essence for progressive disorders. "There was never really a chance for treatment for Cathal because he was too old when he was diagnosed," Les says. At age six, Cathal is in the late stage of MLD. Individuals with the form of MLD that Cathal has typically do not survive past childhood.

With several gene therapy approvals anticipated worldwide for an array of serious diseases in the coming months, it is more important than ever to establish a robust infrastructure for patient access to these innovative and potentially life-saving therapies.



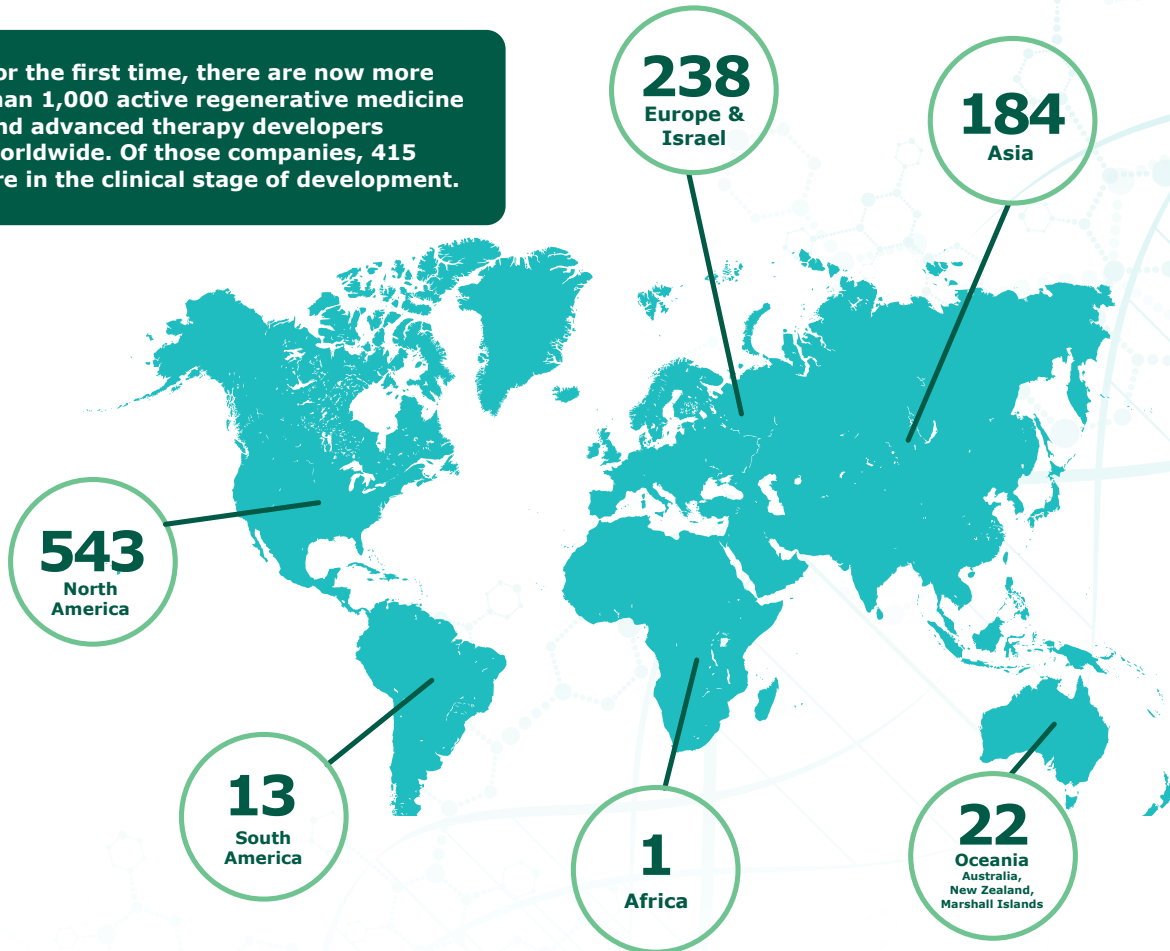
Les and Lynda Martin, along with their three children, Holly, Cathal, and Ciaran, meet with Irish President Michael D. Higgins to advocate for expanded newborn screening.

Sector Growth

1,001+

Regenerative medicine and advanced therapy companies worldwide, including gene, cell, and tissue-based therapeutic developers

For the first time, there are now more than 1,000 active regenerative medicine and advanced therapy developers worldwide. Of those companies, 415 are in the clinical stage of development.



Gene therapy: 515



Cell therapy: 632



Tissue engineering /
biomaterials: 136

Extraordinary Times in Cell and Gene Therapy

The first half of 2020 has been extraordinary for many reasons, the most conspicuous of which is, of course, the COVID-19 pandemic and the disruption it has caused in all areas of life and business, including the cell and gene therapy sector. Even with many experiencing clinical trial delays, regulatory slow-downs, and the challenge of running research and development enterprises from home, companies still have been able to attract investors and raise significant financing for their programs.

In fact, global fundraising by cell and gene therapy developers during the first half of 2020 more than doubled compared with the first half of 2019. Between January and June, these companies raised \$10.7B — a 120% increase year-over-year, according to Biomedtracker.

Initial public offerings totaled \$1.4B in the first half of 2020, which is 2.5 times the IPO total for all of 2019. Similarly, follow-on public offerings totaled \$1.6B, surpassing the \$1.5B raised in FOPOs last year. Even private companies are bringing in massive sums with \$3B in venture capital raised in the first half of 2020 versus \$4.1B in VC investment for all 12 months of last year.

However, one segment of cell and gene therapy financing has fallen: mergers and acquisitions totaled just \$3.4B in the first half of this year. At an average of \$1.7B per quarter, M&A is far below the quarterly averages of \$2.8B in 2019 and \$4.7B in 2020, but those years were notable for multibillion-dollar transactions, including Roche's \$4.3B acquisition of gene therapy specialist Spark Therapeutics last year.

With investment capital for cell and gene therapies high and rising, companies may feel less pressure to do a deal – or at least they're financed well enough to hold off on M&A until their development programs progress and their values rise even higher. Also, with cell and gene therapy companies' values at elevated levels even during a pandemic, buyers may be more selective about executing big deals.

Nevertheless, investment has not abated in the third quarter. IPOs, FOPOs, VC rounds and other types of financing are continuing at a robust pace as everyone gets used to the new normal of doing due diligence over e-mail and Zoom, instead of at conferences, in office buildings or in research laboratories. Deals are being signed with virtual handshakes and confidence that business in the biopharmaceuticals industry will continue as usual no matter how unusual the circumstances become.



Mandy Jackson
Managing Editor, US Commercial News
Scrip/The Pink Sheet
Pharma intelligence | informa

Global Financings Poised to Break Records Despite the Pandemic

Despite the immense economic challenges presented by the COVID-19 pandemic, investors remain bullish on the potential of cell and gene therapies — and the sector as a whole is on track for a record-breaking year. Regenerative medicine and advanced therapy developers have raised \$10.7B in financing in the first half of 2020, a 120% increase from the first half of 2019. The public market for cell and gene therapies has been particularly strong. Five companies have gone public since the beginning of the year — including three in the second quarter, in spite of COVID-19 — raising more than \$1.4B, with an additional \$4B raised in follow-on offerings. In general, the market has been extremely strong, with life sciences stock indices such as the NASDAQ Biotech Index already having made up for any losses incurred during the first weeks of the pandemic.

In May, ARM hosted a webinar on [fundraising in the midst of COVID-19](#), featuring insights from public and private investors on the current and future funding landscape for cell and gene therapies. Speakers emphasized that companies looking to finance this year will need to demonstrate: upcoming value-driven milestones; management's proactive approach to contingency planning for potential COVID-19 related issues or delays; and how a company's therapeutic approach fits into the modern healthcare system.

"We are being more rigorous in looking at how COVID could potentially impact that company specifically — are they reliant on a study that's ongoing, that's accessing a lot of academic centers in areas that are particularly affected by COVID? Is it a situation where they need to come in for multiple administrations of a therapeutic in a hospital setting? I think all of those things raise the risk of potential delays. Now, that doesn't make those companies completely unappealing, but it makes it so that we need to work with the companies to ensure that they have a financing put together, a plan put together, that will ensure that with the current round that they're raising, they can still hit the value inflection points that they're looking to see.



"Biotech is actually fairly well positioned to weather these kinds of events because you're not relying on day-to-day consumer spending. You're relying on meaningful clinical catalysts at the end of the day to really generate value, and that's still going to be there in this environment."

— Jason Pitts, Principal, Private Equity, Sofinnova Investments

"From my perspective, the delays so far in the cell and gene therapy space have not been as meaningful as they could have been. A lot of the companies we follow — certainly if they're going after life-threatening diseases, especially late line oncology or late lung cancers — we're actually seeing pretty modest delays for the companies that have to enroll and produce results [...] What I do think is unappreciated is the ability for one-time treatments to actually mitigate some of these issues in the future, and that's what gene therapy is all about. You treat a patient once and they're done."



— Gbola Amusa, Partner, Director of Research and Head of Healthcare Research, Chardan

While the COVID-19 pandemic is far from over — and the long-term impacts on the sector remain to be seen — the first half of 2020 has been, without a doubt, the strongest half for regenerative medicine and advanced therapies fundraising to date. As the sector continues to grow, ARM is excited to continue to facilitate valuable connections between our members and the investor community. We're looking forward to seeing the sector advance — bolstered by this new wave of public and private financings.



TOTAL GLOBAL FINANCING

\$10.7B
raised in H1 2020

120% increase YoY from H1 2019

\$3.2B raised in Q1 2020

\$7.5B raised in Q2 2020



GENE & GENE-MODIFIED CELL THERAPY

\$7.9B
raised in H1 2020

*81% increase
YoY from H1 2019*

\$2.9B raised in Q1 2020

\$5.0B raised in Q2 2020



CELL THERAPY

\$7.5B
raised in H1 2020

*387% increase
YoY from H1 2019*

\$1.8B raised in Q1 2020

\$5.7B raised in Q2 2020



TISSUE ENGINEERING

\$84M
raised in H1 2020

*25% increase
YoY from H1 2019*

\$64M raised in Q1 2020

\$20M raised in Q2 2020

*Total amount raised represents sector-wide figures; please note that some companies utilize multiple technology types, and financings for those companies are included in each of the applicable categories. As a result, the total financing amount does not equal the sum of the individual technology categories.

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

In spite of the economic challenges of COVID-19, 2020 is on track to be a record-breaking year for regenerative medicine and advanced therapy financings. Therapeutic developers raised more in the first half of 2020 than in all of 2019 (\$10.7B in H1 2020 versus \$9.8B total in 2019). Compared to 2018, the best year on record for cell and gene therapy financings (\$13.5B total raised), therapeutic developers have already raised nearly 80% of the full-year total for 2018.

Global Financings Poised to Break Records Despite the Pandemic

Total Global Financings by Type and Year

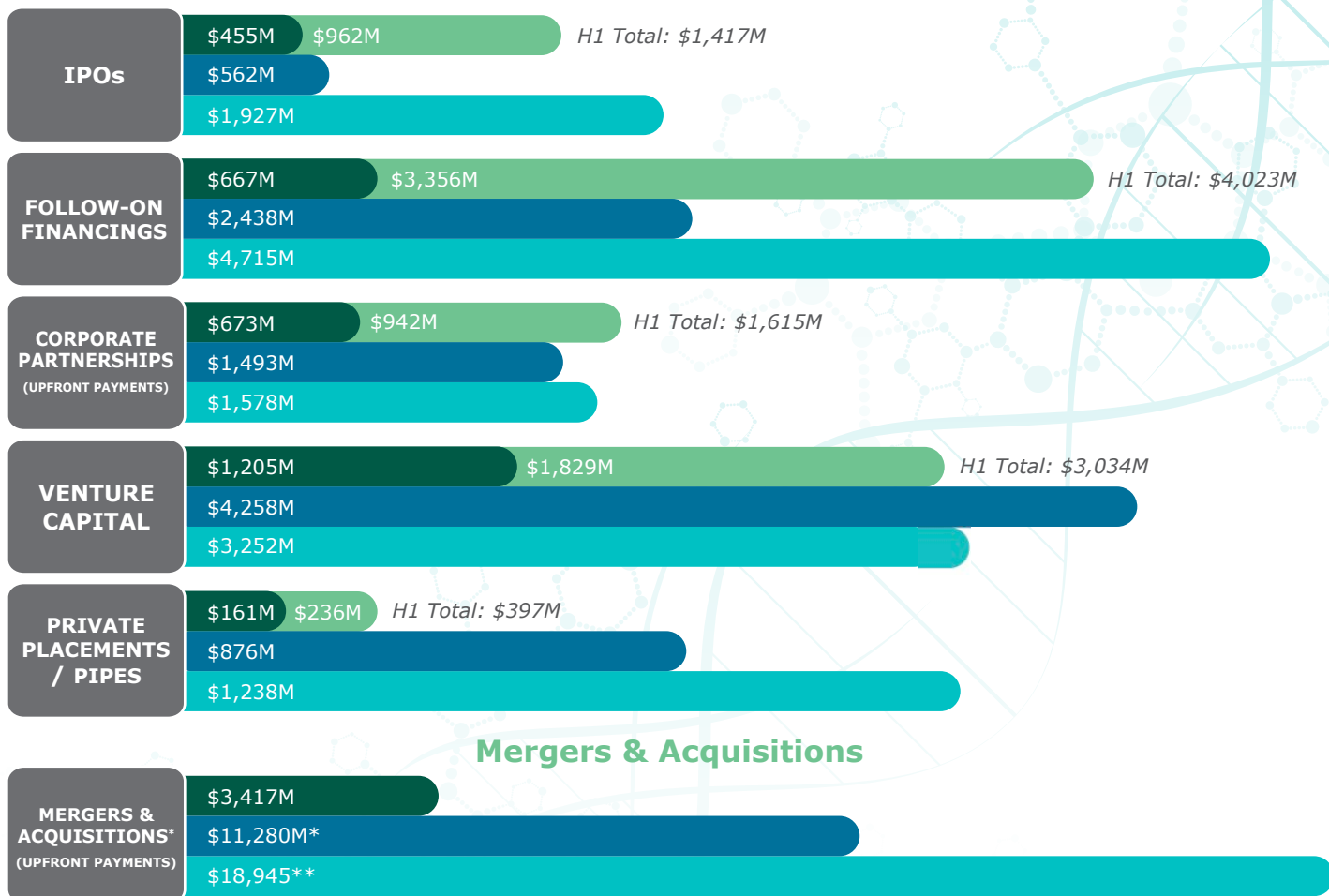
LEGEND

Q1 2020

Q2 2020

2019

2018



Mergers & Acquisitions

*This includes Roche's \$4.3B acquisition of Spark Therapeutics

**This includes Celgene's \$9B acquisition of Juno and Novartis's \$8.7B acquisition of AveXis

2020 is on track to outpace previous years in nearly every category of financing, with the exception of Private Placements / PIPES and Mergers & Acquisitions.

A multitude of regenerative medicine and advanced therapy developers attracted financings in excess of \$100M to advance their product candidates towards patients in need.

IPOs

- Legend Biotech — \$487M (June 9)
- Passage Bio — \$284M (February 3)
- Akouos — \$244M (June 25)
- Generation Bio — \$230M (June 12)
- Beam Therapeutics — \$207M (February 11)

Follow-On Offerings

- Iovance Biotherapeutics — \$604M (June 2)
- bluebird bio — \$575M (May 18)
- Allogene — \$550M (June 1)
- Adaptimmune Therapeutics — \$259M (June 4)
- Editas Medicine — \$216M (June 23)
- Atara Biotherapeutics — \$202M (June 24)
- Fate Therapeutics — \$201M (June 11)
- Adverum Biotechnologies — \$150M (February 14)
- Krystal Biotech — \$125M (May 18)
- IVERIC bio — \$125M (June 17)
- Intellia Therapeutics — \$115M (June 5)
- Replimune — \$115M (June 8)
- AVROBIO — \$100M (February 18)

Private Financings

- Sana Biotechnology — \$700M (June 23)
- Orca Bio — \$192M (June 17)
- Elevate Bio — \$170M (March 30)
- Legend Biotech — \$150M (April 1)
- Freeline Therapeutics — \$120M (June 30)
- Poseida Therapeutics — \$110M (June 25)
- Generation Bio — \$110M (January 10)
- Akouos — \$105M (March 3)
- JW Therapeutics — \$100M (June 9)

Corporate Partnerships

(Upfront Payments)

- uniQure & CSL Behring — \$450M (June 24)
- Biogen & Sangamo — \$350M (February 27)
- bluebird & Bristol-Myers Squibb — \$200M (May 11)
- UltraGenyx & Daiichi Sankyo — \$125M (March 31)
- Fate Therapeutics & Janssen — \$100M (April 2)
- Regeneron & Intellia — \$100M (June 1)

Of the 33 financings in excess of \$100M in the first half of 2020, 27 were announced following the first stay-at-home order in the US, enacted by California on March 19.

*All amounts listed are gross proceeds.

ARM Advances Value-Based Models for Innovative Therapies

A growing pipeline of late-stage regenerative medicines and advanced therapies are poised to come to market over the next three to five years, with the potential to provide profound, durable, and potentially curative benefits to patients with a variety of serious diseases and disorders. With this new wave of transformative therapies rushing towards us, payors, policymakers, and other stakeholders must implement the infrastructure necessary to ensure broad patient access and appropriate value-based reimbursement.

Despite the challenges presented by the COVID-19 pandemic, the Centers for Medicare and Medicaid Services (CMS) has proposed two key policy initiatives in the first half of 2020 to support patient access to regenerative medicines and advanced therapies:

- CMS' [FY21 Inpatient Prospective Payment System \(IPPS\) proposed rule](#) included a provision establishing a separate Medicare-Severity Diagnosis-Related Group (DRG) for chimeric antigen receptor T-cell (CAR-T) therapies. ARM [applauds](#) this proposal as an important step toward ensuring that Medicare providers are appropriately and sustainably reimbursed for administering these life-saving therapies.
- CMS also proposed a [rule](#) that would modify Medicaid average manufacturer price (AMP) and Best Price requirements, allowing state Medicaid programs to enter into value-based purchasing agreements with therapeutic developers.

"CMS' proposal to create a new CAR-T specific DRG in the Medicare Hospital inpatient system is a tremendous achievement for patient access to cell therapies. This highest-paying DRG in the Medicare system demonstrates CMS' recognition of the value of these therapies for Medicare patients. With an increasing number of regenerative medicines and advanced therapies likely to be approved in the US within the next few years, it's important that payors and policymakers ensure these therapies are appropriately reimbursed and incentivize innovation. ARM's Market Access and Value committee will continue to engage stakeholders from across the sector to further this goal."

— Greg White, Senior Director, Global Market Access Policy, Janssen, Pharmaceutical Companies of Johnson and Johnson; Co-Chair, US Market Access and Value Committee, ARM

"We're encouraged by the continued efforts from the Centers for Medicare and Medicaid Services (CMS) to promote a positive environment for patient access to regenerative medicines and advanced therapies in the United States even during the unprecedented health crisis caused by COVID-19. We look forward to continuing to work with policymakers and payors in the United States and to advocating for the immediate and long-term needs of the thousands of patients who could potentially benefit from these innovative therapies."

— Kristin Wolff, Senior Director, Global Government Affairs & Public Policy, bluebird bio; Co-Chair, US Market Access and Value Committee, ARM

Regenerative medicines and advanced therapies continue to demonstrate the potential for long-term cost savings to health care systems. In January of this year, the Marwood Group, with support from ARM, published a [report](#) that demonstrates the cost-saving potential of a durable cell or gene therapy in treating rare blood diseases. The report used a novel value model to calculate the potential cost savings to the healthcare system of a durable cell or gene therapy to treat patients with multiple myeloma, hemophilia A, or sickle cell disease.

Key findings include:

- The total potential savings of cell and gene therapies range from 18% to 30% in annual total disease costs and productivity. This represents an aggregate cost savings of more than \$33B over ten years.
- Innovative financing models, such as subscription models, payment-over-time, and value-based payments, are needed to help payors offset the potentially high upfront costs of these therapies and realize longer term cost-savings.

ARM hosted a [webinar](#) with the National Association for Managed Care Physicians (NAMCP) and Evidera that convened experts in the commercial payor setting to discuss market access for innovative cell, gene and tissue-based therapies in a post-COVID world. Participants highlighted the need for strong value stories for regenerative medicines and advanced therapies and the implementation of innovative financing models:

“The biggest impact [of COVID-19] is going to be the economic impact on the healthcare system. There are going to be very difficult decisions that are going to have to be made in terms of what [commercial and employer] plans can afford... This whole [industry] begs for innovative solutions to the payment mechanisms for [cell and gene therapy] treatments.”

— *Jim Cross, former National Medical Director of a top commercial plan*

“[Payors] will really stretch to accommodate... services [for patients in the oncology and devastating pediatric disease arena], but as [disease states addressed by cell and gene therapies] become... more discretionary, I think tougher decisions will certainly have to be made... and I think [payor] scrutiny is going to be very strenuous.”

— *Richard Powell, Chief Medical Officer, MedPOINT Management*

“I think the issue of potentially pushing for more realistic outcomes that correlate with what physicians are seeing... and longer-term outcomes where we can really see whether [a therapy] is transformative or curative will be more important before dispensing dollars.”

— *Michael Ackerman, Medical Director, Anthem Blue Cross/Blue Shield of Virginia*

Improving patient access by implementing innovative, value-based models for evaluating, pricing, and reimbursing regenerative medicines and advanced therapies continues to be a key priority for ARM and our member companies moving forward. We are working with policymakers both in the US and Europe to ensure the immense promise of these innovative therapies is realized.

Robust Pipeline Targets Hundreds of Devastating Diseases

1,078

Clinical Trials Currently Ongoing Worldwide

Ph. I: 394

Ph. II: 587

Ph. III: 97

Number of Clinical Trials by Technology Type: 2020



Gene Therapy

Total: 359

Ph. I: 109

Ph. II: 215

Ph. III: 35



Cell-Based IO

Total: 471

Ph. I: 230

Ph. II: 225

Ph. III: 16



Cell Therapy

Total: 204

Ph. I: 49

Ph. II: 125

Ph. III: 30



Tissue Engineering

Total: 44

Ph. I: 6

Ph. II: 22

Ph. III: 16

There are currently **11** ongoing clinical trials worldwide utilizing regenerative medicines and advanced therapies to treat COVID-19.



Musculoskeletal
58



Central
Nervous
System
52



Oncology
665



Endocrine,
Megabolic, &
Genetic Disorders
55



Cardiovascular
45

Hematology
37



Infectious
Diseases
33



Dermatology
22



Ophthalmology
35



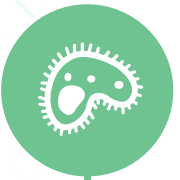
Immunology
& Inflammation
30



Genitourinary
Disorders
14



Geriatric
Diseases
3



Gastroenterology
17



Respiratory
10



Lymphatic
Diseases
2

Cutting-Edge Technologies Celebrate New Milestones

Despite challenges presented by COVID-19, therapeutic developers active in the regenerative medicine and advanced therapies space continued to advance clinical programs in a wide variety of indications with unmet medical needs. From expedited pathways to marketing authorizations to new first-in-human applications of these innovative technologies, here is a list of key development milestones from the first half of 2020.

Therapeutic developers continue to advance late-stage product candidates to market, including in China and Japan:

- Mallinckrodt completed their rolling Biologics License Application in the US for StrataGraft, a tissue-based product for the treatment of severe burns — June 9
- AveXis, a Novartis company, received EMA approval for Zolgensma, a gene therapy to treat spinal muscular atrophy — May 19; and approval from Japan's Ministry of Health, Labour and Welfare — March 19
- Mesoblast was granted priority review from the FDA for their BLA for Ryoncil, a cell therapy to treat graft versus host disease — April 1
- Marketing authorizations were submitted in Japan and China for Kite/Gilead's Yescarta for the treatment of B-cell lymphomas:
 - Licensee Daiichi Sankyo submitted the application for Yescarta in Japan — March 30
 - Fosun Kite, a cooperative enterprise of Kite and Fosun Pharma, submitted the application for Yescarta in China — February 24
- Bristol-Myers Squibb received priority review from the FDA for their CAR-T therapy liso-cel for the treatment of adult patients with relapsed or refractory large B-cell lymphoma — February 13
- Kite received priority review from the FDA for their second CAR-T therapy, KTE-X19, for the treatment of relapsed or refractory mantle cell lymphoma KTE-X19 — February 10*
 - The EMA also validated Kite's marketing authorization application (MAA) for KTE-X19 in Europe — January 28
- PTC Therapeutics submitted an MAA in Europe for their gene therapy PT-AADC for the treatment of AADC deficiency — January 13

Late-stage and approved gene therapies continued to demonstrate long-term durability several years post-treatment:

- Valoctocogene roxaparvovec for hemophilia A (BioMarin): During the four years following treatment, participants experienced an average 95% reduction in annualized bleed rates — June 17
- Zolgensma for spinal muscular atrophy (AveXis, a Novartis company): Data from a long-term follow up study shows that, of the of the 10 patients who received the targeted therapeutic dose of Zolgensma, all are alive and free of permanent ventilation and no previously achieved motor milestone was lost — March 24

**The FDA announced the approval of Tecartus (KTE-X19) in the US on July 24.*

Gene Therapy for Life-Threatening Disorder Reaches Patients in Europe & Japan

The first half of 2020 brought significant milestones in bringing Zolgensma® (onasemnogene abeparvovec-xioi) to more patients worldwide who can benefit from the treatment of spinal muscular atrophy (SMA). In January, we launched a global Managed Access Program. Under this first-of-its-kind program, we are making 100 doses of Zolgensma available in 2020 to eligible patients with SMA under the age of two in countries where Zolgensma is not approved. The program has enabled children across Asia, Australia, Europe and North America, who would not have otherwise had access to the therapy, to receive the treatment at no cost.

In March, our one-time gene therapy received approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) for SMA patients under the age of two and in May, we received approval from the European Commission for the treatment of patients with SMA and a clinical diagnosis of SMA Type 1 or SMA patients with up to three copies of the SMN2 gene.

In SMA, we say “time is neurons” because it is critical to begin treatment, including proactive supportive care, as early as possible to halt irreversible motor neuron loss and disease progression. Even under pandemic conditions, this urgent need remains a primary focus. Since approval in both Japan and the EU, we have seen immediate and accelerated access for patients. In Japan, reimbursement with the MHLW is already secured. Access in the EU is already in place in Germany and France via the Temporary Authorization for Use (ATU) program. The ATU provides early access to lifesaving medicines ahead of an official pricing and reimbursement agreement.

In the remainder of the EU we are well on track for accelerated access with the launch of our innovative “Day One” access program. Designed to work within existing pricing and reimbursement frameworks, yet recognizing the novel nature of a one-time gene therapy for a devastating and progressive disease, the “Day One” access program offers ministries of health and reimbursement bodies a variety of flexible options that can be implemented immediately. To date we have discussed the “Day One” access program with more than 100 stakeholder organizations and have agreements in place with a number of EU countries. These access agreements are aligned to our broader strategy of following local clinical and economic assessment processes, including deferred payments and installment options, outcomes-based rebates, robust training for treating institutions on administration and follow-up care, and access to RESTORE, a global registry of patients who have been diagnosed with SMA.

Our purpose is to serve SMA patients and we are committed to supporting immediate access for SMA patients all over the world. Additionally, we are pursuing registration for Zolgensma in close to three dozen countries — with regulatory decisions anticipated in Switzerland, Canada, Australia, Argentina, South Korea and Brazil in late 2020 or early 2021.

As we look ahead to the second half of the year, we are unwavering in our dedication to the SMA community. We will continue to collaborate with advocacy organizations, physicians, hospitals, and health systems to ensure treatment and care for SMA patients remains uninterrupted during these unprecedented times.



Lisa Deschamps
Senior Vice President
Chief Business Officer
AveXis, a Novartis Company

Cutting-Edge Technologies Celebrate New Milestones

The FDA and EMA continued to provide pathways for expedited approval for regenerative medicines and advanced therapies:

- CRISPR Therapeutics and Vertex Pharmaceuticals received the FDA's Regenerative Medicine Advanced Therapy (RMAT) designation for their gene-edited product candidate CTX001 for the treatment of sickle cell disease and beta-thalassemia — May 11
- Immunicum received RMAT designation for Ilixadencel, a cell therapy for the treatment of kidney cancer — May 6
- Novartis received RMAT designation for their CAR-T therapy Kymriah to treat follicular lymphoma — April 22
- TissueTech received the FDA's RMAT designation for TTAX02, their tissue-based product candidate for the in-utero fetal surgical repair of spina bifida — April 16
- MeriaGTX and Janssen received the EMA's PRIority MEDicine (PRIME) designation for their AAV-RPGR gene therapy for the treatment of X-linked retinitis pigmentosa — March 2
- Tessa Therapeutics received the FDA's RMAT designation for their CAR-T therapy for the treatment of relapsed or refractory CD30-positive classical Hodgkin lymphoma — February 27
- AlloVir received the EMA's PRIME designation for ViralyM-M, a cell therapy for the treatment of or the treatment of serious infections with BK virus, cytomegalovirus, human herpes virus-6, Epstein Barr virus, and/or adenovirus in immunocompromised patients — February 12

Gene-editing technologies continued to advance, and developers have begun to present data showing clinical efficacy:

- New data from CRISPR Therapeutics and Vertex showed that 9 months post-treatment with CRISPR therapy CTX001, the first sickle cell patient in the trial was free of VOCs, was transfusion independent — June 12
- Allogene Therapeutics and Gracell Biotechnology reported initial data from clinical trials of their respective gene-edited allogeneic CAR-T therapies:
 - ALLO-501 for relapsed or refractory non-Hodgkin lymphoma (Allogene): In an ongoing Phase 1 study with 19 evaluable patients, 37% of patients experienced a complete response and an additional 26% of patients experienced a partial response — May 29
 - GC007F for T-cell acute lymphoblastic leukemia (Gracell Biotechnology): In a Phase 1 study, four out of five patients experienced a complete response — April 28
- Editas and Allergan announced the dosing of the first patient to be treated with an in vivo CRISPR-based therapy in a trial to Leber congenital amaurosis 10 — March 4
- Locus Bio initiated the first clinical trial of a CRISPR-enhanced bacteriophage — January 8

In the second half of the year, we're looking forward to several potential approvals and additional submissions for new therapies; continued support from the FDA and EMA for priority review pathways for regenerative medicines and advanced therapies; and clinical data readouts from both late-stage product candidates and from new first-in-human approaches.

Cell Therapy Developers Fight COVID-19 with MSCs

In response to the ongoing global spread of COVID-19, several academic research centers and therapeutic developers have announced that they are investigating the application of regenerative medicine technologies to treat this disease in the short term and address related complications in the future. Approaches include therapies intended to promote immune response and manage inflammatory responses in patients with the disease, as well as approaches to repair tissues damaged by the disease in the long-term.

ARM is tracking 11 clinical trials using regenerative medicine and advanced therapy technologies to treat COVID-19, with an additional 25 programs in preclinical development. Many developers are utilizing mesenchymal stem cells (MSCs) and other stromal cells to treat Acute Respiratory Distress Syndrome, a severe complication of COVID-19.

On May 20, ARM [hosted a webinar](#) featuring representatives from Athersys and Pluristem Therapeutics, two companies developing stem cell therapies to treat ARDS caused by COVID-19.



"A small proportion [of COVID-19 patients] develop ARDS and have high mortality rates. PLX cells are allogeneic mesenchymal-like cells with immunomodulatory effects that may prevent or reverse the dangerous overactivation of the immune system and therefore maybe reduce the severity of COVID-19, pneumonia, and other lung complications, and improve the outcomes of these patients."

— *Racheli Ofir, Vice President, Research & Intellectual Property, Pluristem Therapeutics*



"We're working towards a commercial scale of manufacturing using a stirred tank bioreactor system. It would allow us to scale up quite dramatically to really large capacity in factoring to address the patient population that presents with moderate to severe ARDS. Certainly, there's the potential with cryopreservation and a long shelf life to actually stockpile a product for availability to roll out quite quickly with a new emergent outbreak. So, I think between those two attributes of the product [MultiStem] we could certain address even really dramatic pandemic presentations of high pathogen respiratory illnesses in the future."

— *Eric Jenkins, Senior Medical Director & Head of Clinical Operations, Athersys*

With several developers testing MSCs and other stromal cells to treat this severe and potentially fatal complication of COVID-19 in expanded access and compassionate use programs, as well as in clinical trials, we expect to see additional data in the second half of the year. The potential for cell therapies to treat this disease could provide a substantial benefit to patients as the pandemic continues.

As always, patient health and safety is paramount. There are currently no approved treatments for COVID-19, and patients should avoid unproven and potentially harmful therapies marketed by practitioners without appropriate regulatory oversight.

Global Regulators Stay the Course Despite COVID

The COVID-19 pandemic has wreaked havoc globally, leaving myriad challenges for businesses including the broader pharmaceutical industry. Regulators have diverted considerable resources to the therapeutic response to the virus while working to maintain their normal slate of activities — all too aware that hanging in the balance is the health of patients with unmet medical needs unrelated to the crisis.

So far, they seem to be achieving that goal — the FDA announced on June 23 that the agency has “maintained the same pace of meeting its goals on review of applications for medical products during the pandemic that it has maintained in recent years.” Similarly, Guido Rasi, Executive Director of the European Medicines Agency (EMA), expressed reassurances that EMA will “continue to meet our mission to protect public and animal health during this quickly evolving crisis.”

In specific, the FDA granted seven product candidates Regenerative Medicine Advanced Therapy (RMAT) designation in the first half of 2020, while two advanced therapy products received the EMA’s PRiOritY Medicine (PRIME) designation, on par with past years. These efforts demonstrate a collective, continued commitment to advancing the development of novel therapies for a variety of serious diseases and disorders. AveXis, a Novartis company, received approval in Europe and Japan for its gene therapy for spinal muscular atrophy (a rare and potentially fatal genetic disorder), and Kite, a Gilead company, received FDA approval for its second CAR-T product in the beginning of the second half. Additional product candidates are slated for review in the US and Europe later this year. And the European Commission recently made the decision to relax GMO requirements for vaccines and therapies targeting COVID-19 — a positive step in opening an important dialogue about streamlining gene therapy trial requirements in a variety of indications.

However, as the number of confirmed COVID-19 cases continues to surge in many geographies, and with no end in sight, it’s important we acknowledge that our sector will likely begin to feel both the direct and indirect effects of the pandemic on clinical and regulatory operations. The FDA acknowledges that the pandemic may lead to delays in expected guidance for regenerative medicine and advanced therapy developers in the areas of neurodegenerative diseases, genome editing, and CAR-T therapies, as well as in their efforts to streamline the development of “N of 1” therapies for ultra-rare disorders. And despite the flexibility shown by international regulators in clinical trial protocols, the potential for the virus to disrupt patient identification, enrollment, dosage, and data collection in dozens — if not hundreds — of trials may contribute to delays in clinical development.

As the voice of the sector, ARM is executing against our regulatory priorities for 2020 and promoting the development of transformative therapies for patients worldwide. In the face of this unprecedented global health crisis, we continue to prioritize the appropriate resource allocation for cell and gene therapy regulators. We also support enhanced flexibility in clinical trial execution and efforts by the FDA, EMA and other international regulatory bodies to prevent the false marketing and sale of unproven, unsafe and potentially harmful products.

We look forward to continuing to work with our members to promote clear and harmonized regulatory pathways for regenerative medicines and advanced therapies in the second half of 2020.



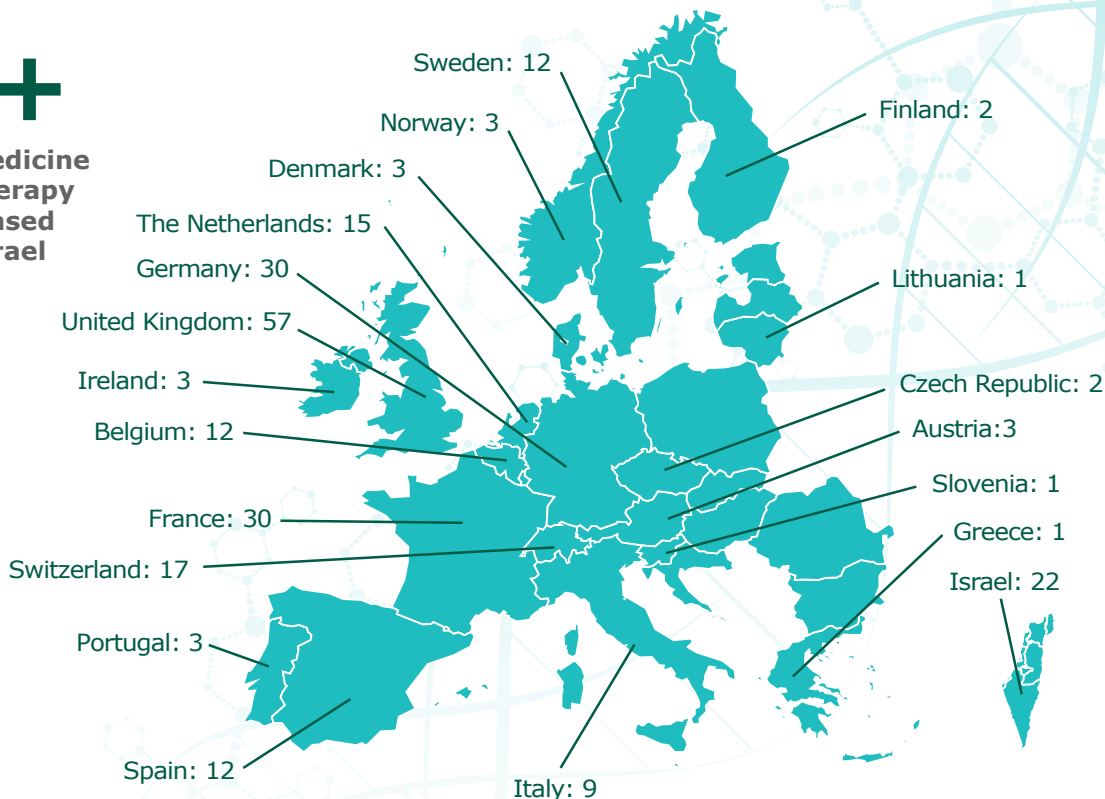
Paige Bischoff
Senior Vice President, Public Affairs
Alliance for Regenerative Medicine

Staying Competitive: Europe vs. the Global Pandemic

Mirroring the global sector landscape, the environment for advanced therapy medicinal products (ATMPs) in Europe was strong for the first half of 2020. While year-over-year growth in financings is somewhat more modest for European and Israeli companies compared to the global landscape — likely due to Europe's relatively strong fundraising performance in 2019 — total financings still doubled from the first half of 2019. Clinical development remains steady in Europe, with nearly half of all global Phase 3 trials sponsored by European and Israeli developers. And in positive regulatory news, European spinal muscular atrophy patients will soon be able to benefit from AveXis's gene therapy, Zolgensma, which was approved by the European Commission (EC) in May.

238+

**Regenerative Medicine
& Advanced Therapy
Developers Based
in Europe/Israel**



European/Israeli Developers by Technology:



Gene therapy: 111



Cell therapy: 142



Tissue engineering /
biomaterials: 39

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

Staying Competitive: Europe vs. the Global Pandemic

270

Ongoing Clinical Trials
Sponsored by European
& Israeli Developers

Ph. I: 52

Ph. II: 172

Ph. III: 46

On June 17, the EC released a proposal to relax regulations on clinical trials of vaccines and therapeutics utilizing genetically modified organisms (GMOs) to treat or prevent COVID-19. Traditionally, these same regulations have created burdensome requirements for gene therapy clinical trials, which may result in an overall lower rate of development for these therapies in Europe.

ARM applauded the EC's proposal to temporarily lift certain requirements concerning clinical trials of therapies classified as GMOs to treat or prevent COVID-19. ARM strongly supports regulatory oversight and a high standard of patient safety and efficacy for ATMPs. However, the classification of certain genetic medicines as GMOs and the accompanying requirements for gene therapy clinical trials is an unintended consequence of the EC's GMO legislation, and is creating unnecessary delays in the development of, and patient access to, innovative therapies. A [report released last year](#) highlighted that clinical development of ATMPs in Europe is not on pace with growth rates in the rest of the world.

"Gene therapies hold immense promise for patients with many severe diseases and disorders. We commend the Commission for its recent decision to relax the GMO requirements in the case of therapeutics targeting COVID-19. We hope to see future work by the Commission to further streamline clinical trials and promote the development of innovative therapies for other patients with unmet medical needs."

— *Patrick Ginty, Head of Regulatory Affairs, Cell & Gene Therapy Catapult; Co-Chair, European Regulatory Committee, ARM*

"This decision by the EC is encouraging and could be an important step towards streamlining clinical trial requirements for investigational gene therapies in Europe. ARM's European Regulatory Committee is committed to working with policymakers to ensure a robust environment to support clinical development of, and ultimately patient access to, these life-changing therapies without compromising safety or environmental health."

— *Jill Morrell, Director, Regulatory Research & Intelligence and EU Policy, BioMarin; Co-Chair, European Regulatory Committee, ARM*

The EC's decision is a positive first step towards creating a much-needed dialogue on how to best facilitate the development of innovative therapies — like ATMPs — while maintaining strong regulatory precautions for patient safety.



FINANCING BY COMPANIES HQ'D IN EUROPE/ISRAEL

\$2.6 Billion (appx €2.2 Billion)

raised in H1 2020 across all technology types

103% YoY increase from H1 2019



GENE & GENE-MODIFIED CELL THERAPY

\$2.3 Billion

(appx €2.0 Billion)

raised in H1 2020

111% YoY increase from H1 2019



CELL THERAPY

\$1.8 Billion

(appx €1.5 Billion)

raised in H1 2020

196% YoY increase from H1 2019



TISSUE ENGINEERING

\$29 Million

(appx €25 Million)

raised in H1 2020

17% YoY decrease from H1 2019

*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.

Like much of the world, Europe's ATMP sector experienced a strong first half, despite challenges presented by COVID-19, with the potential for an even stronger environment that supports the development of and patient access to these innovative therapies. Just before midyear, the EC released a draft of the updated European Pharmaceutical Roadmap. ARM's [response](#) clearly identifies the priority areas needed to ensure innovative and life-changing ATMPs can continue to be brought to market.

"We really want to ensure that Europe remains a leader in ATMPs [...] We think the new pharma strategy is really an opportunity to get in and get this infrastructure right."

— Paige Bischoff, Senior Vice President, Public Affairs, ARM, in an interview with Pink Sheet

In the second half of 2020, ARM and its European members will be focusing on advancing many of the priorities highlighted in our response to the Roadmap, including developing a structure for fast-tracking the use of Real World Evidence (RWE) in ATMPs throughout Europe and a more harmonized and regulated approach to the implementation of the Hospital Exemption.

CELL GENE

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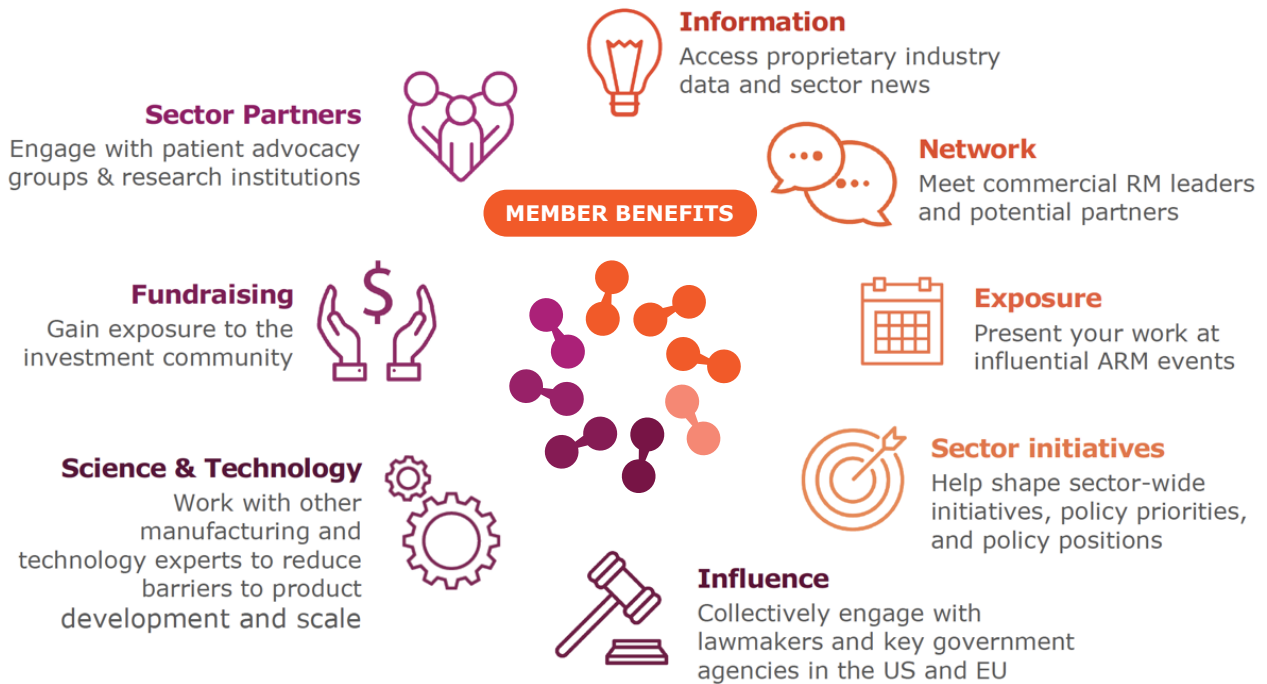
OCTOBER 12-16, 2020

The Cell & Gene Meeting on the Mesa is the sector's foremost annual conference bringing together senior executives and top decision-makers in the industry to advance cutting-edge research into cures. Tackling the commercialization hurdles facing the cell and gene therapy sector today, this meeting covers a wide range of topics from clinical trial design to alternative payment models to scale-up and supply chain platforms for advanced therapies.

The Alliance for Regenerative Medicine has announced a new virtual format for its annual Cell & Gene Meeting on the Mesa. The conference includes a digital form of the meeting's signature partnering system, expected to facilitate more than 3,000 one-to-one meetings between industry leaders. The program will include 15+ digital panels and workshops featuring key industry leaders discussing issues and trends in the regenerative medicine and advanced therapy sector, from market access to the latest discoveries in gene editing. Representatives from more than 100 prominent public and private companies will deliver on-demand presentations highlighting their clinical and commercial progress to interested partners and investors.

For more information, or to register, please visit www.meetingonthemesa.com.

The Alliance for Regenerative Medicine (ARM) is the leading international advocacy organization dedicated to realizing the promise of regenerative medicines and advanced therapies.



For more information about ARM and how to get involved, please contact Alyce Osborne, Director, Membership & Business Development at aosborne@alliancerm.org.

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Alliance *for* Regenerative Medicine

Alliance for Regenerative Medicine

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