Alliance *for* Regenerative Medicine

SECTOR SNAPSHOT

APRIL 2023: A NEW VISION

THE ALLIANCE FOR REGENERATIVE MEDICINE (ARM) IS THE LEADING INTERNATIONAL ADVOCACY ORGANIZATION CHAMPIONING THE BENEFITS OF ENGINEERED CELL THERAPIES AND GENETIC MEDICINES FOR PATIENTS, HEALTHCARE SYSTEMS, AND SOCIETY.

As a community, ARM builds the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and advancing the narrative with data and analysis. We actively engage key stakeholders to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from durable, potentially curative treatments.

As the global voice of the sector, we represent more than 475 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations.

GlobalData.

THANK YOU TO OUR DATA PARTNER, GLOBALDATA.

GlobalData is a trusted and authoritative intelligence provider to the world's largest industries. We cover a broad spectrum of the pharmaceutical, medical technology and healthcare value systems with in-depth analysis, forecasts, exclusive news, and robust databases all available through a fully integrated platform.

MOVING TO A NEW FORMAT

If you're a regular reader of our content, you know ARM has traditionally released our data and recap of the cell and gene therapy sector through our annual reports, published in early spring, and our H1 Reports, published in early fall.

We have decided to discontinue these formats to bring you a more consistent and digestible flow of content about the cell and gene therapy sector – The Sector Snapshot. Here is what you can expect moving forward.

More Frequent Sector Perspectives

The Sector Snapshot will provide sector trends, spotlight stories and commentary.

New Home for Our Data

Our new format will provide you snapshots of important trends, but will not be exhaustive. A full breakdown of current sector data, updated quarterly, can be accessed below!

ACCESS OUR DATA ON CLINICAL TRIALS, INVESTMENT, AND DEVELOPERS BELOW.

ALLIANCERM.ORG/DATA ↗

Since joining ARM in September 2022, I have crossed paths with hundreds of individuals working toward a single goal – transforming patients' lives. In my first six months, here's a recap of what I saw as some of the significant events that shaped the sector.

TIM HUNT ARM CHIEF EXECUTIVE OFFICER

A NEW VISION

What stood out in 2022?

The past year can be characterized by momentous regulatory approvals:

- **THREE NEW GENE THERAPIES APPROVED** FOR RARE DISEASES, A NEW RECORD FOR THE SECTOR!
- **THREE CAR-T CELL THERAPIES WERE EXPANDED AS TREATMENT OPTIONS AGAINST DIFFERENT CANCERS**, WITH TWO APPROVED AS EARLIER-LINE TREATMENTS.
- THE FIRST-EVER 'OFF-THE-SHELF' **T-CELL THERAPY APPROVED GLOBALLY**

But 2022 wasn't without challenge. After two record-breaking years of investment, economic headwinds produced a difficult financing environment. Despite these obstacles, the sector is poised to make unprecedented progress this year.

What can we anticipate for the rest of 2023?

The next wave of cell and gene therapies is arriving fast. In the United States (US) alone, we are looking in the range of 10 regulatory decisions this year on cell and gene therapies. This includes decisions on:

- **SEVERAL GENE THERAPIES FOR RARE DISEASES**, INCLUDING TWO FOR SICKLE CELL DISEASE – AND THE **FIRST-EVER CRISPR GENE EDITING THERAPY**.
- THE **FIRST-EVER ADOPTIVE CELL THERAPY** FOR A SOLID TUMOR.
- THE FIRST GENE THERAPY FOR **DUCHENNE MUSCULAR DYSTROPHY**

One thing is clear – a larger patient population is on the horizon, and we need to collectively act to ensure that healthcare systems are ready to deliver the future of medicine.

THE WAY FORWARD

The future we want for patients must be built on collaboration. ARM convenes the cell and gene therapy sector, hosting first-in-class conferences, workshops, and policymaker briefings to enable the exchange of thought-provoking ideas among regulators, policymakers, and industry leaders. We are a community focused on building the future of medicine – and I look forward to what we can accomplish together.

IN FOCUS: THE SECTOR IN 2022

	NORTH AMERICA	ASIA-PACIFIC	EUROPE	OTHER REGIONS	TOTAL
DEVELOPERS	686	492	244	35	1,457
CLINICAL TRIALS	964	848	403	139	2,220
INVESTMENT	$10.8B 339 DEALS	$2.2B 147 DEALS	$3.2B 118 DEALS	$3.6B 124 DEALS	$12.6B 478 DEALS

Note: The totals for clinical trials and upfront investment may appear lower than the total value of each region added together. This is to account for overlap between regions.

APPROVED THERAPIES IN 2022

NEW THERAPIES APPROVED

Carvykti (CAR-T)
LEGEND BIOTECH & JANSSEN - US AND EU

Roctavian (Gene Therapy)
BIOMARIN PHARMACEUTICAL - EU

Upstaza (Gene Therapy)
PTC THERAPEUTICS - EU

Hemgenix (Gene Therapy)
UNIQURE AND CSL BEHRING - US

Adstiladrin (Gene Therapy)
FERRING PHARMACEUTICALS - US

Ebvallo (Cell Therapy)
ATARA BIOTHERAPEUTICS - EU

THERAPIES APPROVED IN NEW GEOGRAPHIES OR NEW INDICATIONS

Breyanzi (CAR-T)
BRISTOL-MYERS SQUIBB - US AND EU

Kymriah (CAR-T)
NOVARTIS - US

Yescarta (CAR-T)
KITE PHARMA (GILEAD) - US AND EU

Zynteglo (Gene Therapy)
BLUEBIRD BIO INC. - US

Skysona (Gene Therapy)
BLUEBIRD BIO INC. - US

WHAT'S IN THE PIPELINE FOR 2023?

POSSIBLE REGULATORY DECISIONS IN 2023

UNITED STATES

AFAMI-CEL (CELL THERAPY)
Adaptimmune Therapeutics
Advanced synovial sarcoma

BB1111 (GENE THERAPY)
bluebird bio
Sickle cell disease

B-VEC (GENE THERAPY)
Krystal Bio
Dystrophic epidermolysis bullosa

CTX001 (GENE EDITING THERAPY)
Vertex Pharmaceuticals & CRISPR Therapeutics
Sickle cell disease, ß-thalassemia

HPC CORD BLOOD (CELL THERAPY)
StemCyte
Unrelated donor hematopoietic progenitor cell transplantation

LIFILEUCEL (CELL THERAPY)
Iovance
Metastatic melanoma

OMIDUBICEL (CELL THERAPY)
Gamida Cell
Hematological malignancies

REMESTEMCEL-L (CELL THERAPY)
Mesoblast
Steroid-refractory Acute Graft Versus Host Disease

ROCTAVIAN (GENE THERAPY)
BioMarin Pharmaceutical
Hemophilia A

SRP-9001 (GENE THERAPY)
Sarepta Therapeutics
Duchenne muscular dystrophy

TAB-CEL (CELL THERAPY)
Atara Biotherapeutics
Epstein-barr virus associated post transplant lymphoproliferative disorder (EBV-PTLD)

EUROPE

HEMGENIX (GENE THERAPY)
CSL Behring and UniQure
Hemophilia B

APPROVED, FEBRUARY 2023

CTX001 (GENE EDITING THERAPY)
CRISPR Therapeutics & Vertex Pharmaceuticals
Sickle cell disease, ß-thalassemia

Note: CSL Behring and UniQure's gene therapy to treat hemophilia B was approved by the EU in February 2023.

TREND TO WATCH

Gene editing—entering the mainstream?

THE BIG PICTURE: CRISPR HAS ARRIVED

ZFN and TALEN set the early foundation for gene-editing and were the dominant approaches in clinical trials until about 2018. At that point, the number of CRISPR trials overtook the earlier approaches.

NEW TECHNOLOGY, LARGE IMPACT

The first regulatory decision for a CRISPR therapy is set for this year, for sickle cell disease. This is a significantly larger patient population than diseases targeted by previously approved gene therapies.

A SHIFTING PIPELINE

Within the clinical pipeline, CRISPR has risen in prominence. The total number of TALEN and ZFN trials, the other two prominent platforms for gene editing, has dropped by 41% since 2017.

SPURRING INNOVATION

CRISPR is a versatile tool with potential applications across the sector. The ability to use this technique to alter cells has led to developers devising improvements to CAR-T, Natural Killer, and other cell therapies that target different cancers.

Disease areas with the most CRISPR clinical trials: Oncology, blood disorders, dermatological, and ocular/vision disorders

*Available data sources on clinical trials do not always specify gene-editing or the type of gene-editing approach

A BRIEF TIMELINE OF CRISPR

2010s
CRISPR harvested for genome editing

2015-2016
CRISPR expands into agriculture

2018-2020
CRISPR sees widespread use in clinical trials

CRISPR AND NEXT GENERATION APPROACHES TO GENE EDITING

CRISPR | BASE EDITING | PRIME EDITING | EPIGENETIC EDITING

CRISPR's effectiveness

CRISPR is showing early success against different blood diseases. Exacel, the CRISPR therapy developed by Vertex Pharmaceuticals and CRISPR Therapeutics to treat sickle cell disease, is up for approval this year in the US, European Union, and United Kingdom (UK). Other developers like Editas Medicine and Intellia Therapeutics aim to submit their own license applications and proofs-of-concept for various blood conditions.

CRISPR in the clinic

While the potential approval of the first CRISPR therapy is exciting, it is just the beginning. The sector is also making gradual steps towards different applications of these medicines to treat a variety of diseases. For example, in vivo forms of CRISPR to treat ATTR amyloidosis (Intellia Therapeutics) and Leber congenital amaurosis (Editas Medicine) are generating evidence of effectiveness.

As the sector continues to innovate, more advanced forms of gene editing are emerging to improve accuracy and efficiency. **Base editing**, which allows for precise modifications to individual DNA letters in a sequence, is already being tested in clinical trials in the UK and New Zealand. One such example is Verve Therapeutic's base editing therapy to treat heterozygous familial hypercholesterolemia, a source of heart disease that remains a leading cause of death in the US.

What does the future hold?

Other advanced forms of gene editing are beginning to take form. Early clinical research is exploring **prime editing**, a technique that can alter longer lengths of DNA. This would have the potential to make wholesale changes to disease-causing DNA at one time.

Other researchers are investigating **epigenetic editing**, which can potentially control gene expression, and thereby fix harmful mutations without making any direct changes to the DNA.

2023
First regulatory decision on a CRISPR therapy

NEAR-TERM
Promising applications for in vivo gene editing

AND BEYOND...
Prime and epigenetic editing

A COMMUNITY FOCUSED ON BUILDING THE FUTURE OF MEDICINE

APRIL 12-14

CELL AND GENE MEETING ON THE MEDITERRANEAN

Barcelona, Spain

meetingonthemed.com ↗

MAY 9-10

CELL AND GENE CONGRESSIONAL FLY-IN

Washington, DC

alliancerm.org/arm-event/dcforum ↗

OCTOBER 10-12

CELL AND GENE MEETING ON THE MESA

Carlsbad, CA

meetingonthemesa.com ↗

STAY ENGAGED

BECOME A MEMBER

Contact: Erica Wilhide, ewilhide@alliancerm.org ↗

MEDIA INQUIRIES

Contact: Stephen Majors, smajors@alliancerm.org ↗

Alliance *for* Regenerative Medicine

STAY CONNECTED

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