Alliance for Regenerative Medicine

SECTOR SNAPSHOT

APRIL 2024

ADVANCES IN ENGINEERED CELL THERAPY

In this edition…

- An updated 2024 clinical pipeline outlook
- Review of the cell therapy clinical landscape
- Trends driving cell therapy development

The 2024 regulatory pipeline

- First-ever adoptive cell therapy for solid tumor already approved in the US
- Potentially unprecedented year for US approvals
- Another surge of approvals for gene therapies to treat rare genetic disease

	Therapy	Therapy (Indication)	Status
Approved therapies	**Casgevy** *(Vertex Pharmaceuticals & CRISPR Therapeutics)*	Gene Editing Therapy (Sickle cell disease and beta-thalassemia)	Jan 16: Approved in the US (Beta-thalassemia) Feb 13: Approved in the EU (Both indications)
	Lifileucel *(Iovance Biotherapeutics)*	Cell Therapy (Metastatic melanoma)	Feb 16: Approved in the US MAA submission anticipated in 2024
	Lenmeldy *(Orchard Therapeutics)*	Gene Therapy Metachromatic leukodystrophy)	March 18, 2024: Approved in the US
Regulatory decision scheduled	**Fidanacogene Elaparvovec** *(Pfizer)*	Gene Therapy (Hemophilia B)	April 27, 2024 (FDA) MAA accepted; 2024 decision possible (EU)
	Kresladi *(Rocket Pharmaceuticals)*	Gene Therapy (Severe leukocyte adhesion deficiency type 1)	June 30, 2024 (FDA)
	Afami-cell *(Adaptimmune Therapeutics)*	Cell Therapy (Advanced Synovial sarcoma)	August 4, 2024 (FDA)
	Human Acellular Vessel *(Humacyte)*	Tissue Engineering (Vascular trauma)	August 10, 2024 (FDA)
	Obe-cel *(Autolus Therapeutics)*	CAR-T Cell Therapy (B-Cell acute lymphoblastic leukemia)	November 16, 2024 (FDA) MAA submission possible in 2024
	Vyjuvek *(Krystal Biotech)*	Gene Therapy (Dystrophic Epidermolysis Bullosa)	MAA accepted; 2024 EU approval decision possible in H2 2024
	RP-L102 *(Rocket Pharmaceuticals)*	Gene Therapy (Fanconi anemia)	FDA BLA submission possible in 2024 MAA accepted; 2024 decision possible (EU)
BLA or MAA submitted or submission expected in 2024	**Upstaza** *(PTC Therapeutics)*	Gene Therapy (AADC deficiency)	BLA submitted; FDA decision possible in 2024
	Tab cel *(Atara Biotherapeutics)*	Cell Therapy (Epstein-Barr virus-associated post-transplant lymphoproliferative disorder)	FDA BLA submission possible in 2024
	Elevidys *(Sarepta Therapeutics and Roche)*	Gene Therapy (Duchenne Muscular Dystrophy)	2024 EMA MAA submission possible
	Giroctocogene fitelparvovec *(Pfizer)*	Gene Therapy (Hemophilia A)	FDA BLA and EMA MAA submissions possible in 2024
	Remestemcel-L *(Mesoblast)*	Cell Therapy (Steroid-refractory acute graft versus host disease)	FDA BLA submission possible in 2024

View our latest sector data

GlobalData.

GlobalData is ARM's data partner.

Cell And Gene Therapy Sector Data Q4 2023

2023	North America	Asia Pacific	Europe	Total
Developers (Snapshot Value)	1,184	925	568	2,762*
Clinical Trials (Snapshot Value)	978	805	360	1,920*
Investment (Aggregate Value)	$8.3B	$2.1B	$1.2B	$11.7B*

*Totals refer to unique quantities and includes data from other regions not shown

Access our full data at alliancerm.org or use the QR code.

2024 - A banner year for cell therapy?

With the approval of five therapies for rare genetic diseases, including the first-ever approval of a CRISPR gene editing therapy, 2023 was the biggest year yet for gene therapy. While more gene therapies are poised to receive approval this year, 2024 is already shaping up to be the year of cell therapy.

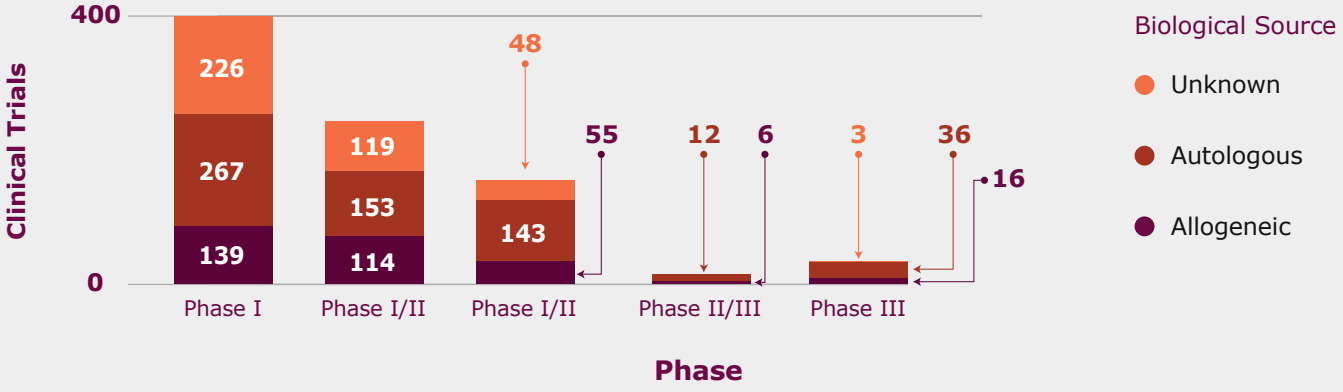
Cell therapy saw a hot start to investments this year, with $1.2 billion+ in deals and investments already having taken place. What is driving the interest? If we peer into the clinical pipeline, we can see three trends that outline promising developments for this innovative science.

- Increased effectiveness in treating blood cancer
- Accelerating progress in treating solid tumors
- Clinical breakthroughs in treating autoimmune diseases

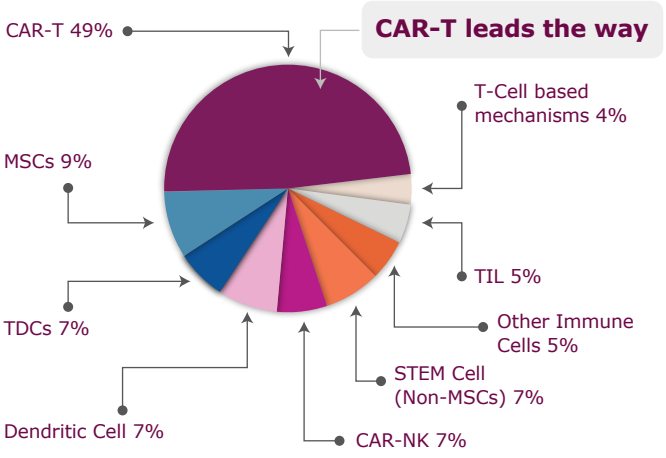
Review of the cell therapy clinical landscape

Cell/CBIO therapy breakdown: 1,336 ongoing trials globally

Cell-based Immuno-Oncology (CBIO) is a sub-set of cell therapy that leverages a cell type from the body's immune system as a therapeutic agent

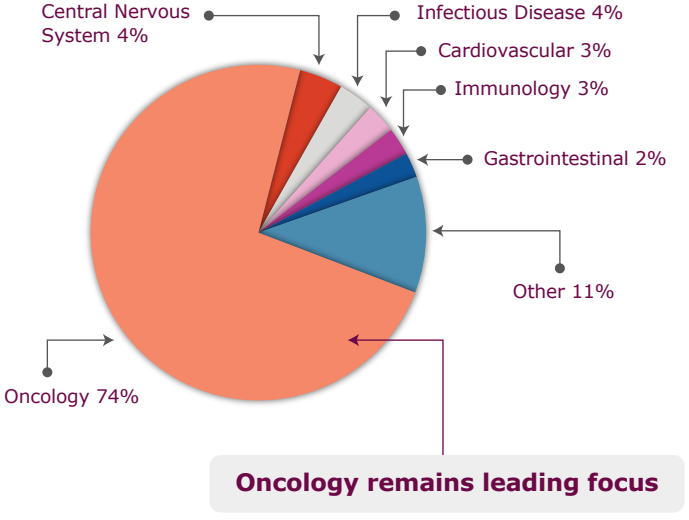


Cell type used



Included in the figure are Mesenchymal stem/stromal cells (MSCs), Terminally Differentiated Cells (TDCs), Tumor-Infiltrating Lymphocytes (TIL). An example of TDCs are Red Blood Cells. An example of Immune Cells are Macrophages. An example of T-cell based mechanisms is T-cell receptor (TCR)-engineered cells.

Clinical focus



The outlook for blood cancer treatments

For the past decade, treating hematologic malignancies (blood cancers) has been and remains one of the main indications targeted by engineered cell therapies. Leading the charge are chimeric antigen receptor T-cell (CAR-T) therapies, which have engineered receptors that target cancer cells. Currently, six CAR-T cell therapies for blood cancers are approved in the United States (US) and the European Union. (EU) However, many more cell therapies for blood cancers, including non-CAR-T approaches, are in the clinical pipeline. Of the ten most explored indications in cell therapy, nine fall within the scope of blood cancer.

Commonly explored cell therapy indications (Q4 2023)

Indication	# Of Trials
Diffuse large B-cell lymphoma	161
Various solid tumors	157
Non-Hodgkin lymphoma	145
Acute Lymphocytic leukemia	126
Follicular lymphoma	120
B-cell non-Hodgkin lymphoma	104
Multiple myeloma	103
Acute myelocytic leukemia	103
Primary mediastinal B-cell lymphoma	90
B-cell acute lymphocytic leukemia	85

Improved safety

Scientific advancement is driving these therapies to new heights for safety and effectiveness. A handful of the authorized therapies were approved as a last line of treatment, meaning a patient must endure several treatments before being eligible. Since 2022, the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) have approved some of these cell therapies for earlier lines of treatment based on robust safety and efficacy data.

Therapy	Indication	Original lines of treatment authorized	Revised lines of treatment authorized
Abecma (Bristol Myers-Squibb & 2seventybio)	Multiple myeloma	5th line treatment (2021) 5th line treatment (2021)	Decision date for 3rd line treatment pending 3rd line treatment (2024)
Carvykti (Legend Biotech & Janseen)	Multiple myeloma	5th line treatment (2022) 4th line treatment (2022)	April 5, 2024, decision date for 2nd line use authorization EMA CHMP recommended 2nd line treatment, EU Commission approval pending
Breyanzi (Bristol Myers-Squibb)	Large B-cell lymphoma	3rd line treatment (2021) 3rd line treatment (2022)	2nd line treatment (2022) 2nd line treatment (2023)
Yescarta (Kite, A Gilead Company)	Large B-cell lymphoma	3rd line treatment (2017) 3rd line treatment (2018)	2nd line treatment (2022) 2nd line treatment (2022)

Progress toward solid tumors

While cell therapies have made incredible progress against blood cancers, solid tumors have been a challenge. For one, solid tumors create a hostile environment in the body that is hard for immune cells to penetrate. Another issue is heterogeneity. Compared to blood cancers, tumors are often comprised of cells that express a variety of targets. These combined challenges have traditionally stumped many researchers, but recent progress shows that science is starting to overcome these hurdles.

2024 breakthroughs

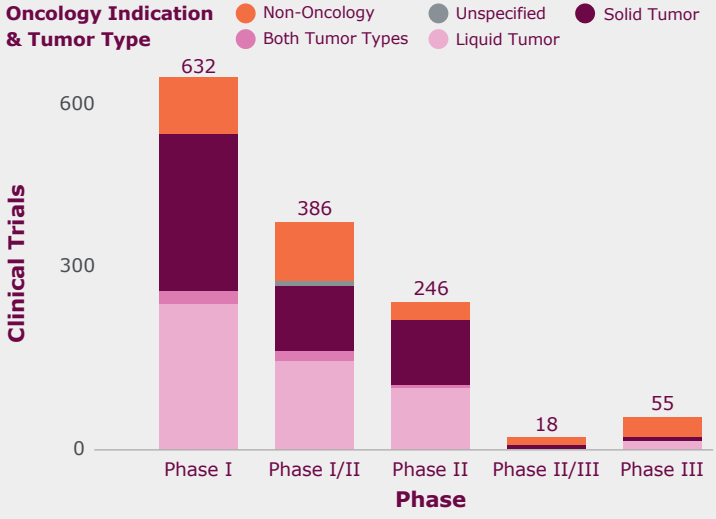
Tumor-infiltrating lymphocyte (TIL) therapies	T-cell receptor (TCR) therapies
Amtagvi (Iovance Biotherapeutics)	Afami-cel (Adaptimmune Therapeutics)
TIL therapy involves harvesting immune cells that have shown initial penetration of the tumor, expanding them in large numbers in vitro culture, and then reinfusing them back into the patient to more efficiently attack the tumor.	TCR therapy involves leveraging edited T-cells to boost a body's immune response to target specific types of cancer, such as tumors. Utilizing the TCR also allows targeting intracellular tumor antigens.

In February 2024, Iovance Biotherapeutics' TIL therapy to treat metastatic melanoma became the first adoptive cell therapy for a solid tumor to be approved by the FDA. Another approval to treat solid tumors could occur later this year. Adaptimmune's engineered T-cell receptor (TCR) therapy to treat advanced synovial sarcoma, a cancer found in soft tissue, will receive a regulatory decision from the FDA by August 4, 2024.

On the horizon

And this is just the beginning. Researchers like those from the National Institutes of Health and Penn Medicine have been developing new methods to augment cell therapies. Such published findings have included using mutated immune cells to supercharge CAR-T cells to attack tumors or engineering T-cells to carry proteins that boost their function. Within the clinical pipeline, cell therapies to treat solid tumors maintain a sizeable presence in early-stage trials, showing the potential for more therapies to reach the market in the years ahead.

Ongoing solid vs liquid tumor distribution for cell therapies



Autoimmune diseases and the future of cell therapy

While oncology has remained the primary clinical focus for cell therapies, a new wave of interest in treating autoimmune diseases is growing rapidly.

The publication of groundbreaking findings from the University Hospital Erlangen in 2023 sparked enthusiasm for this new approach. The study revealed that 15 patients with autoimmune disorders went into remission after receiving a CAR-T cell therapy. Earlier research from Mogrify also showed that regulatory T-cells, which play an integral role in suppressing the body's immune response, can be leveraged for therapeutic effect. The current therapies in clinical trials are primarily targeting indications like lupus, type 1 diabetes, myasthenia gravis, and multiple sclerosis, but the list is anticipated to grow.

ARM members with autoimmune disease therapies in clinical trials

Developer	Stage	Therapy Type	Indication
Cynata Therapeutics	Phase I	Allogeneic stem cell	Graft vs. host disease
Orca Biosystems Inc	Phase III	Allogeneic CAR-NK	Graft vs. host disease
Artiva Biotherapeutics	Phase I	Allogeneic NK cell	Lupus nephritis
Kyverna Therapeutics	Phase I	Autologous CD19 CAR-T	Lupus nephritis Systemic sclerosis Myasthenia gravis
ImmPACT Bio	Phase I/II	Autologous CD19/CD20 CAR-T	SLE Lupus nephritis
Cabaletta Bio	Phase I/II	Autologous CD19 CAR-T	SLE & Lupus nephritis Systemic sclerosis Myasthenia gravis
Miltenyi Biomedicine GmbH	Phase I/II	Autologous CAR-T	Lupus Nephritis SLE
Autolus Therapeutics	Phase I	Autologous CD19 CAR-T	SLE
Century Therapeutics	Phase I	Allogeneic CD19 CAR-iNK	SLE
Novartis Pharmaceuticals	Phase I/II	Autologous CD19 CAR-T	SLE
PolTREG	Phase II Phase I	Regulatory T-cell	Type 1 diabetes Multiple sclerosis
CRISPR Therapeutics	Phase I	Allogeneic stem cell	Type 1 diabetes
Vertex Pharmaceuticals	Phase I/II	Allogeneic stem cell	Type 1 diabetes
City of Hope	Phase I	Autologous dendritic cell	Type 1 Diabetes (Juvenile Diabetes)
Prokidney Corp	Phase I	Autologous TDC	Type 1 Diabetes (Juvenile Diabetes)

Autoimmune cont: Early investment interest

The race to cure autoimmune diseases is leading the hot start for cell therapy investing in 2024.

Kyverna Therapeutics	Autolus Therapeutics	Capstan Therapeutics
Successfully launched an IPO at $300+ million to support its extensive autoimmune pipeline.	Signed a $200+ million investment deal with BioNTech to support its autoimmune and oncology cell therapies pipeline.	Completed a $175 million Series B financing to develop CAR-T cell therapies to treat autoimmune diseases.

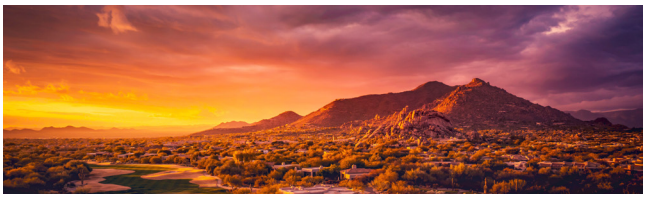
Stay engaged

Enjoy our Sector Snapshots? Here are a few ways to stay engaged with our network.

Cell and Gene Meeting on the Med

Rome, Italy April 9-11, 2024

meetingonthemed.com ↗



Cell and Gene Meeting on the Mesa

Phoenix, AZ October 7-9, 2024

meetingonthemesa.com ↗

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