Alliance *for* Regenerative Medicine

SECTOR SNAPSHOT

AUGUST 2024

THE EMERGING VALUE OF CELL AND GENE THERAPY

In this edition…

- 2024 clinical pipeline update
- A snapshot of our Q2 2024 sector data
- ARM's updated value framework for gene therapy and a new value framework for CAR-T cell therapy

The 2024 Regulatory Pipeline

- Up to 8 possible approvals in the US
- Up to 6 possible approvals in the EU

	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 (Expanded label: 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 pending
	Lenmeldy *(Orchard Therapeutics)*	Gene Therapy (Metachromatic leukodystrophy)	March 18: Approved in the US
	Fidanacogene Elaparvovec *(Pfizer)*	Gene Therapy (Hemophilia B)	April 27: Approved in the US July 25: Approved in the EU
	Tecelra *(Adaptimmune Therapeutics)*	Cell Therapy (Advanced synovial sarcoma)	Aug 1: Approved in the US
Regulatory decision scheduled	**Human Acellular Vessel** *(Humacyte)*	Tissue Engineering (Vascular trauma)	Additional time required to review BLA; The original PDUFA date was Aug 10, 2024, and the new date is TBD
	Upstaza *(PTC Therapeutics)*	Gene Therapy (AADC deficiency)	November 13, 2024 (FDA)
	Obe-cel *(Autolus Therapeutics)*	CAR-T Cell Therapy (B-Cell acute lymphoblastic leukemia)	November 16, 2024 (FDA) MAA accepted, 2024 EU decision possible
	NT-501 *(Neurotech Pharmaceuticals, Inc.)*	Cell Therapy (Macular Telangiectasia Type 2)	December 17, 2024 (FDA)
	Remestemcel-L *(Mesoblast)*	Cell Therapy (Steroid-refractory acute graft versus host disease)	January 7, 2025 (FDA)
	Tab cel *(Atara Biotherapeutics)*	Cell Therapy (Epstein-Barr virus-associated post-transplant lymphoproliferative disorder)	January 15, 2025 (FDA)
	RP-L102 *(Rocket Pharmaceuticals)*	Gene Therapy (Fanconi anemia)	FDA BLA submission possible in 2024 MAA accepted, 2024 EU decision possible
	Vyjuvek *(Krystal Biotech)*	Gene Therapy (Dystrophic epidermolysis bullosa)	MAA accepted, 2024 EU decision possible
	UM171 *(ExCellThera)*	Cell Therapy (Hematological malignancies in patients who lack a readily available suitable donor)	MAA accepted, 2024 EU decision possible
BLA or MAA submitted or submission expected in 2024	**Elevidys** *(Sarepta Therapeutics and Roche)*	Gene Therapy (Duchenne muscular dystrophy)	2024 EMA MAA submission possible
	UX111 *(Ultragenyx)*	Gene Therapy (Sanfilippo Syndrome Type A)	2024 FDA BLA submission possible
	RGX-121 *(REGENXBIO)*	Gene Therapy (Mucopolysaccharidosis Type II)	2024 FDA BLA submission possible
	Giroctocogene fitelparvovec *(Pfizer)*	Gene Therapy (Hemophilia A)	FDA BLA and EMA MAA submissions possible in 2024

Q2 2024 Sector Data

GlobalData is ARM's data partner.

2024	Developers (Snapshot Value)	Clinical Trials (Snapshot Value)	Investment (Q2 2024 Total)
North America	1,243	974	$3.8B
Asia Pacific	1,000	784	$0.1B
Europe	579	341	$0.3B
Total	2,919*	1,851*	$4.2B*

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

More data breakdowns available at www.alliancerm.org/data

A Strengthening Value Proposition

Cell and gene therapy has often made headlines due to its nontraditional cost model but the value of this transformative medicine is often overlooked. ARM unveiled its Gene Therapy for Patients and Society (GPS) framework this year at the Biotech Showcase during JP Morgan's 2024 Healthcare Conference, demonstrating how these advanced medicines are poised to provide incredible value. This edition of the Sector Snapshot updates the GPS framework and introduces a similar framework for CAR-T cell therapies.

Gene Therapy for Patients and Society (GPS)	CAR-T Therapy for Patients and Society (CAR-PS)
Target devastating, often deadly diseases	Save the lives of blood cancer patients who have no alternatives
Target expensive diseases	Increasingly more effective than the standard of care
Are highly effective	Can reduce or replace a costly and toxic standard of care
Provide strong value for healthcare systems	Are sustainable for the healthcare system
Are sustainable	Drive revolutions in breakthrough therapies

Gene Therapy for Patients and Society

TARGET DEVASTATING, OFTEN DEADLY DISEASES

The average life expectancy for rare diseases targeted by FDA-approved gene therapies is **<40 years – HALF** the normal lifespan.

Example Disease	Life Expectancy
Sickle Cell Disease	45 to 55 years
Cerebral Adrenoleukodystrophy	10 years
Duchenne Muscular Dystrophy	22 years

Sources: Serjeant, The Natural History of Sickle Cell Disease, The Stop ALD Foundation, Broomfield J., Hill M., Guglieri M., Crowther M., Abrams K., Life Expectancy in Duchenne Muscular Dystrophy:Reproduced Individual Patient Data Meta-analysis

TARGET INCREDIBLY EXPENSIVE DISEASES

The lifetime cost to manage most rare diseases targeted by approved gene therapies is **several million dollars.**

Example Disease	Estimated Lifetime Cost
Severe Sickle Cell Disease	$4-6 million
Transfusion-Dependent Beta-Thalassemia	$5.4 million
Severe Hemophilia B	$20 million+

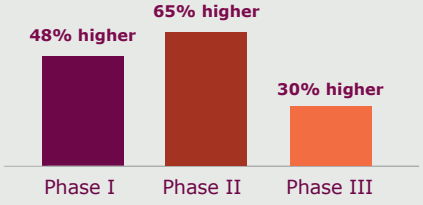
Sources: Vertex Pharmaceuticals, Vertex and CRISPR Therapeutics Announce US FDA Approval of CASGEVY™ (exagamglogene autotemcel) for the Treatment of Sickle Cell Disease, Udeze C., Maruszczyk K., Atter M., Lopez A., Projected lifetime economic burden of transfusion-dependent beta-thalassemia in the United States, Li N. et al., Adult lifetime cost of hemophilia B management in the US: payer and societal perspectives from a decision analytic model

GENE THERAPIES ARE HIGHLY EFFECTIVE

Evidence shows that gene therapies for rare diseases display high effectiveness in clinical trials. Orphan gene therapies are **3.5 times more likely to be approved** once entering Phase 1 trials than average drugs included in BIO's New Clinical Development Success Rates 2011-2020 Report. Similar results were found in comparing gene therapy success rates with average drugs according to IQVIA.

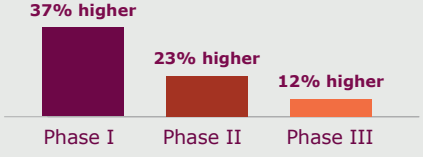
BIO: New Clinical Development Success Rates 2011-2020 Report

Orphan gene therapy success rate by phase compared to average drugs



IQVIA: Global Trends in R&D 2023

Gene therapy success rate by phase compared to average drugs



In focus: Efficacy examples of recently approved gene therapies for sickle cell disease

Casgevy: 97% of Phase II/III clinical trial patients were free of vaso-occlusive crises for 12 months or more

Lyfgenia: 94% of clinical trial patients did not experience any severe vaso-occlusive events between 6 and 18 months after treatment

PROVIDE STRONG VALUE FOR THE HEALTHCARE SYSTEM

Discussions about gene therapy often focus on the price but overlook its value. An analysis performed by ICER confirms that gene therapies deliver high value for rare diseases like spinal muscular atrophy, sickle cell disease, and metachromatic leukodystrophy.

ICER's health benefit price benchmark for gene therapies to treat the following conditions:

- **Spinal muscular atrophy:** **~$2 million**
- **Sickle cell disease:** **~$2 million**
- **Metachromatic leukodystrophy:** **~$4 million**

An illustrative case: FDA-approved gene therapies for hemophilia A and hemophilia B give significant savings back to the system, according to ICER analysis.

Hemophilia A

Cost-effective at **$6.7 million**

Gene therapy list price **$2.9 million**

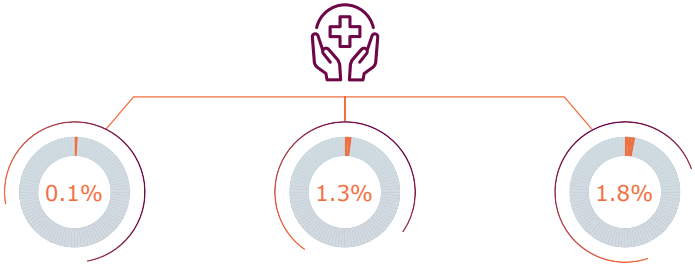
Hemophilia B

Cost-effective at **$9.9 million**

Gene therapy list price **$3.5 million**

GENE THERAPIES ARE SUSTAINABLE

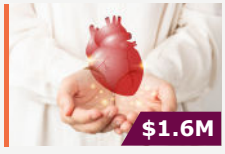
Some have expressed concerns about the budget impact these transformative therapies will have on the healthcare system. However, the data show that gene therapies are sustainable. For example, NEWDIGS projects US durable gene therapy spending will reach $7.5 billion in 2030. For comparison, this is:



- **of projected healthcare spending in 2030**
- **of projected prescription drug spending in 2030**
- **of the economic burden of rare diseases in the US in 2019**

Sources: NEWDIGS, CMS Office of the Actuary, Peterson/CMS, and the EveryLife Foundation

In the US, we are already accustomed to the cost of transplants, which amounts to $1.6M for a heart transplant (3,500 per year) and **$1M+** for an allogeneic bone marrow transplant (9,950 per year) in 2020.



Source: 2020 Milliman Report

CAR-T Therapy for Patients and Society

SAVE THE LIVES OF BLOOD CANCER PATIENTS WHO HAVE NO ALTERNATIVES

There are around 60,000 patients with blood cancers for whom conventional treatments don't work. CAR-T cell therapy provides a durable and effective treatment option that can offer hope for many patients who are in later stages of cancer. Currently, 6 CAR-T cell therapies are approved in the US for aggressive forms of lymphoma, leukemia, and multiple myeloma.

Highlights

On average, 76% of all CAR-T patients achieve remission
Source: Blood Advances Journal

Overall survival is almost 9x higher than the standard of care for B cell lymphoma
Source: ISPOR Journal

Yescarta patients are 21% less likely to require subsequent treatment
Source: Vanderbilt University

INCREASINGLY MORE EFFECTIVE THAN THE CURRENT STANDARD OF CARE

CAR-T cell therapies are increasingly demonstrating superior safety and efficacy in comparison to the current standard of care. In head-to-head comparisons, CAR-T cell therapies:

Are 3X as likely to be approved when entering Phase I as the average oncology drug

Source: NEWDIGS

4 of the 6 FDA-approved CAR-Ts have recently been authorized as earlier line treatments in the US

Achieve over 50% reduction in the risk of disease progression or death, with most therapies reaching 60%-70%

Source: U.S. FDA

CAN REDUCE OR REPLACE A COSTLY AND TOXIC STANDARD OF CARE

Cancer patients, especially those who relapse, often must endure a series of arduous treatments. CAR-T therapies reduce collateral damage to healthy cells and minimize side effects compared to traditional treatments such as chemotherapy and radiation therapy.

B-Cell Lymphoma

CAR-T therapy requires 30% less staff time and has a treatment duration 18 days shorter than allogeneic stem cell transplants

Source: Lee Moffitt Cancer Study

Multiple Myeloma

Patients often relapse and require double- and triple-combination treatments **indefinitely**

Source: ASCO

4-drug combination of monoclonal antibodies = **$350,000-$600,000** per year

Source: ASCO

Proteasome inhibitors = **$260,000** a year

Source: ASCO

Bone marrow transplants = **$1 million**

Source: Milliman

ARE SUSTAINABLE FOR THE HEALTHCARE SYSTEM

According to NEWDIGS, durable oncology cell therapies -- which include CAR-T cell therapies -- may have close to zero net impact on overall US healthcare spending. Let's break this down in context.

$16.9B

Revenue from durable oncology cell therapies is expected to reach $16.9B in 2030

Source: NEWDIGS

7%

This represents 7% of the projected $240B the US will spend on cancer care in 2030

Source: American Association for Cancer Research

Multiple approved CAR-T therapies are cost-effective in the long term for specified indications

Source: ICER

DRIVE REVOLUTIONS IN BREAKTHROUGH THERAPIES

The early wave of CAR-T success is spurring innovation that can lower costs and provide new treatment options for diseases other than blood cancers.

01 Nearly 160 sites provide cell therapy services at outpatient facilities

Source: Foundation for the Accreditation of Cellular Therapies

02 Allogeneic approaches represent ~50% of Phase I cell therapy trials with known approaches

Source: ARM April 2024 Secor Snapshot

04 Reduction in cost of goods and shortened manufacturing schedules advance timely access

Source: ARM April 2024 Secor Snapshot

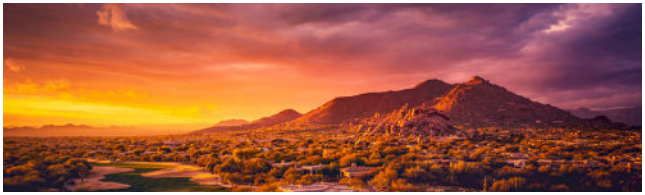
03 8 additional cell types are being studied in clinical trials; progress is being made in solid tumors and autoimmune disorders

Source: ARM April 2024 Sector Snapshot

Connect With ARM

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

Upcoming Events



Cell and Gene Meeting on the Mesa

Phoenix, AZ October 7-9, 2024

meetingonthemesa.com ↗

Cell and Gene Meeting on the Med

Rome, Italy April 15-17, 2025

meetingonthemed.com ↗

Get Involved

From Advisory Groups to Forums, there are many ways to get involved with ARM. This is your chance to influence the direction of the sector. Get in touch with our team today.

Contact: Elaine Blauser, eblauser@alliancerm.org

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BECOME A MEMBER

Contact: Robin Muthig, rmuthig@alliancerm.org ↗

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