Alliance for Regenerative Medicine

SECTOR SNAPSHOT

DECEMBER 2023

GENE THERAPIES POISED TO REACH MORE PATIENTS

In this edition...

- **Q3 data and 2024 pipeline outlook**
- **Gene therapy indications that are driving higher patient populations**
- **Impact of the first gene therapies for sickle cell disease**

Q3 2023 Sector Data

	North America	Asia Pacific	Europe	Total
Developers	1,115	861	514	2,575
Clinical Trials	940	747	340	1,804
Investment	$1.1B	$0.9B	$0.1B	$2.2B

To access our full data with different visualizations, visit www.alliancerm.org/data or scan the QR code.

Clinical Pipeline Update

The UK's MHRA became the first regulatory agency globally to approve a CRISPR therapy – for sickle cell disease and TDT – on November 16, and the EMA CHMP delivered a positive opinion for the same therapy on December 15

The FDA approved the first two gene therapies for sickle cell disease on December 8, including the first CRISPR gene editing therapy

The FDA approved five gene therapies for rare genetic diseases in 2023 alone

PDUFA dates have already been set for five new therapies in the first five months of 2024

Pipeline Outlook

	Therapy	Therapy *(Indication)*	Status
Regulatory decision scheduled	**Lifileucel** *(Iovance Biotherapeutics)*	Cell Therapy (Metastatic melanoma)	February 24, 2024 (FDA) EMA MAA submission possible in H1 2024
	Libmeldy *(Orchard Therapeutics)*	Gene Therapy (Metachromatic leukodystrophy)	March 18, 2024 (FDA)
	Casgevy (Vertex Pharmaceuticals & CRISPR Therapeutics)	Gene Editing Therapy (Sickle cell disease and Beta-thalassemia)	FDA decision for β-thalassemia set for March 30, 2024 EU decision for sickle cell disease and β-thalassemia anticipated in Q1 2024
	Kresladi *(Rocket Pharmaceuticals)*	Gene Therapy (Leukocyte Adhesion Deficiency-I)	March 31, 2024 (FDA)
	Fidanacogene Elaparvovec *(Pfizer)*	Gene Therapy (Hemophilia B)	April 27, 2024 (FDA) MAA accepted; 2024 decision possible (EU)
	Pz-cel *(Abeona Therapeutics)*	Cell Therapy (Dystrophic epidermolysis bullosa)	May 25, 2024 (FDA)
BLA or MAA submitted or submission expected in 2023. 2024 decision possible.	**Afami-cell** *(Adaptimmune Therapeutics)*	Cell Therapy (Advanced synovial sarcoma)	2024 FDA approval decision possible
	Vyjuvek *(Krystal Biotech)*	Gene Therapy (Dystrophic Epidermolysis Bullosa)	2024 EU approval decision possible
	Obe-cel *(Autolus Therapeutics)*	CAR-T Cell Therapy (R/R B-cell acute lymphoblastic leukemia	2024 FDA approval decision possible EMA MAA submission possible in H1 2024
	Upstaza *(PTC Therapeutics)*	Gene Therapy (AADC deficiency)	2024 FDA approval decision possible
	Elevidys *(Sarepta Therapeutics and Roche)*	Gene Therapy (Duchenne Muscular Dystrophy)	2024 EU approval decision possible
BLA or MAA submission possible in 2024	**RP-L102** *(Rocket Pharmaceuticals)*	Gene Therapy (Fanconi anemia)	FDA BLA and EMA MAA submissions possible in H1 2024
	Tab cel *(Atara Biotherapeutics)*	Cell Therapy (Epstein-Barr virus-associated post-transplant lymphoproliferative disorder)	BLA submission possible in H1 2024
	Giroctocogene fitelparvovec *(Pfizer)*	Gene Therapy (Hemophilia A)	BLA and MAA submissions possible in H1 2024
	ExoFlo *(Direct Biologics)*	Exosome (COVID-induced acute respiratory distress syndrome)	BLA submission possible in H1 2024

Is the patient population increasing for gene therapies?

With the approval of two new gene therapies to treat sickle cell disease on December 8, 2023, the FDA has now approved a total of 10 gene therapies for rare genetic diseases. The European Union (EU) also has eight rare genetic disease gene therapies approved for market use, while three were approved but then withdrawn from the market. As the clinical pipeline matures, innovative therapies are targeting diseases with larger patient populations.

The first eight US gene therapies for rare genetic diseases approved by the FDA have a combined estimated eligible patient population approaching 18,000, while in the EU, the estimated number approaches 16,000. The two recently approved gene therapies to treat sickle cell disease, one of which also treats transfusion-dependent beta-thalassemia (TDT), will expand the number of treatable patients significantly. Casgevy is up for approval in the EU to treat sickle cell disease and TDT in early 2024.

EMA-Approved Rare Genetic Diseases Gene Therapies	**<16,000 patients**	Estimated EU eligible patient population
FDA–Approved Rare Genetic Diseases Gene Therapies	**<18,000 patients**	Estimated U.S. eligible patient population
Sickle Cell Disease Gene Therapies	**25,000 patients**	Estimated U.S. and EU eligible patient population

Estimates based on developer reports and press releases.
CVS Health, Gene Therapy Pipeline 3Q 2021-2H 2025; CVS Health, Gene Therapy Pipeline 2Q 2022-4Q 2025
PharmExec, Vertex Pharmaceuticals Touts Potential of CRISPR Gene Editing Therapy

In Focus: Sickle cell disease

On December 8, 2023, the FDA approved two gene therapies to treat sickle cell disease, marking a seminal moment in the history of biotechnology and human health. Casgevy, developed by CRISPR Therapeutics and Vertex Pharmaceuticals, represents the first-ever approval of a gene-editing medicine in the United States (it was previously approved in the United Kingdom and Bahrain). Lyfgenia, developed by bluebird bio, joins Casgevy as the first two gene therapies ever approved in the United States to treat sickle cell disease.

An estimated 15,000 people in the UK and 100,000 people in the US have sickle cell disease, making it among the most prevalent rare genetic diseases in both countries. Up to 2,000 patients in the UK will be eligible for treatment, along with 25,000 in the US and EU, according to Vertex Pharmaceuticals. According to bluebird bio, there are up to 20,000 eligible patients for its therapy in the US.

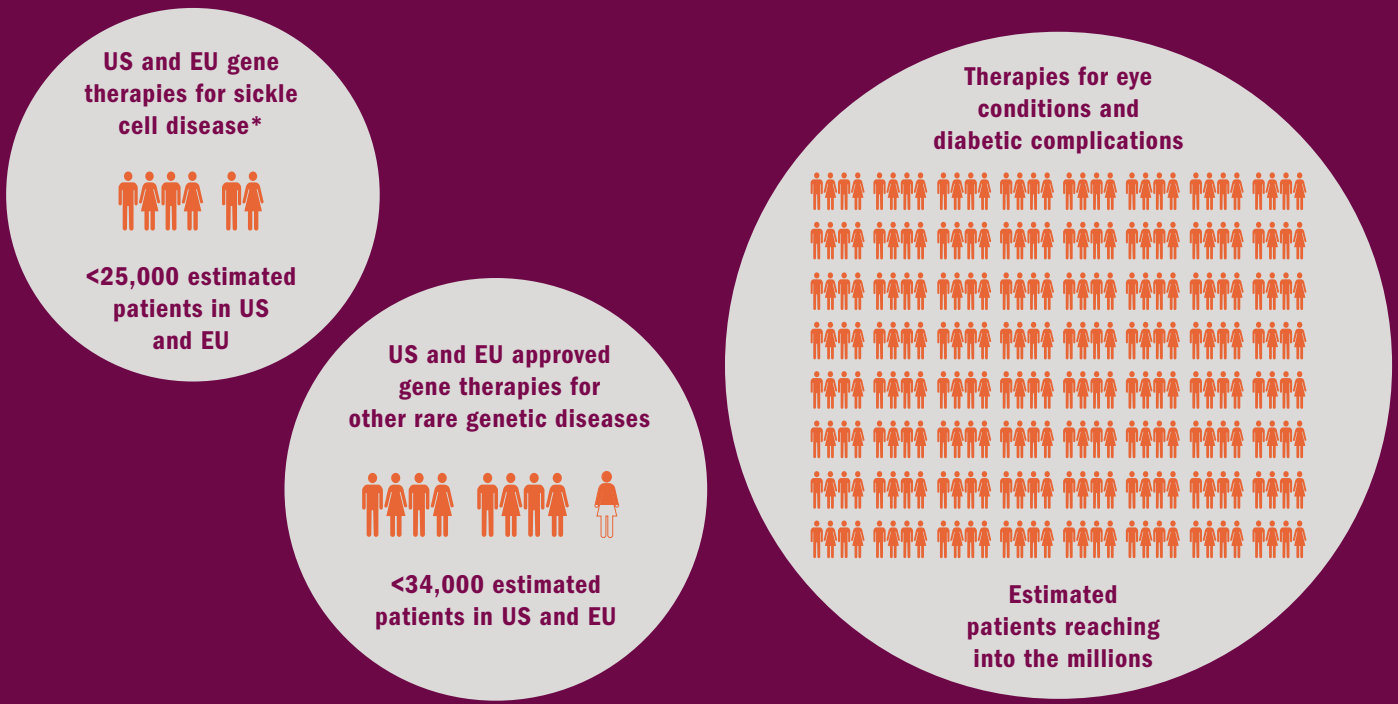
Potential patient populations for therapy in the US. sickle cell disease

	Therapy :	Stage :	Potential patient population :
01	Casgevy CRISPR Therapeutics and Vertex Pharmaceuticals	Approved for market use on November 16, 2023	2,000 in the United Kingdom (Source: Vertex Pharmaceuticals)
02	Casgevy CRISPR Therapeutics and Vertex Pharmaceuticals	Approved by the FDA on December 8, 2023	25,000 in the United States and EU (Source: Vertex Pharmaceuticals)
03	Lyfgenia bluebird bio	Approved by the FDA on December 8, 2023	20,000 in the United States (Source: bluebird bio)

The patient population for approved non-oncology gene therapies could grow considerably in the coming years.

Several gene therapies are in the pivotal stage of the clinical pipeline and could receive a regulatory decision during 2024-2026. If approved, they could thrust non-oncology gene therapy into the mainstream and reach millions of patients. Several new treatments aim to target more prevalent conditions, such as eye conditions and diabetic complications.

Possible patient population growth for non-oncology gene therapies



*As of December 2023, there are two therapies for sickle cell disease approved in the US, and one in the EU awaiting approval

A look into the pipeline

Prevalent eye conditions and diabetic complications

Eye conditions found in millions of patients, such as wet age-related macular degeneration (AMD), retinitis pigmentosa, and diabetic retinopathy, are targeted by a growing number of therapies in the late-stage pipeline.

Additionally, there are over 37 million Americans with some form of diabetes according to the American Diabetes Association. For many, diabetes comes with other health complications, such as foot ulcers and nerve damage. Gene therapies are increasingly targeting these diabetic-related conditions.

Example indications in late-stage clinical trials

Diabetic Retinopathy	Wet AMD	Diabetic Peripheral Neuropathy
Therapy: RGX-314 (REGENXBIO) Possible patient population = 20 million in the US, EU and Japan (Source: REGENXBIO)	**Therapy:** RGX-314 (REGENXBIO) Possible patient population = 5.7 million in the US, EU and Japan (Source: REGENXBIO)	**Therapy:** Engensis (Helixmith) Possible patient population = 4 million in the US (Source: Helixmith)

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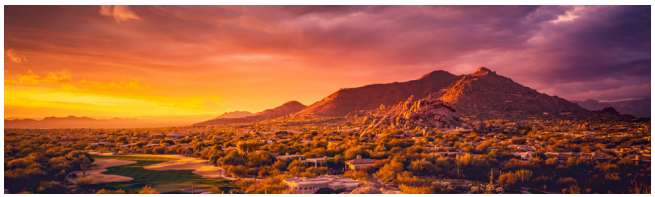
Events



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 9-11, 2024

Meetingonthemed.com ↗

Get Involved

ARM has opened a new governance structure and decision model to support our 2023-2025 Strategic Plan. We introduced Membership Forums in June 2023 for broader member engagement, discussion, and information sharing. To get involved in a forum, please get in touch with Elaine Blauser at eblauser@alliancerm.org

Stay engaged

BECOME A MEMBER

Contact: Robin Muthig, rmuthig@alliancerm.org ↗

MEDIA INQUIRIES

Contact: Stephen Majors, smajors@alliancerm.org ↗

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