International Society
ISCT
Cell & Gene Therapy®

CELL AND GENE THERAPY GLOBAL REGULATORY REPORT

H1 2024

DATA PARTNER: CITELINE
a norstella company

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OVERVIEW OF REPORT & AUTHORS

SECTION 1

OVERVIEW OF REPORT

Welcome to the third biannual Cell and Gene Therapy Global Regulatory Report from ISCT and Citeline. This report provides a global overview of the cell and gene therapy regulatory landscape, including pipeline, late-stage (Phase III and pre-registration), and approved products. It covers Cell, Genetically-Modified Cell, and Gene Therapies.

Over the last few years, the regulatory agencies have been updating legislation and frameworks to keep up with the rapidly advancing cell and gene therapy space. As a result, ISCT and Citeline have collaborated to highlight some of these changes and offer commentary on the updates and their effects.

In this report, we see that year-over-year, non-genetically modified cell therapies continue to make up the majority of all approved products (68%). However, the pipeline for genetically modified cell therapies continues to be larger with 1,008 therapies in development, compared to 902 non-genetically modified cell therapies and 938 gene therapies.

Meanwhile, ISCT continues to track regulatory changes and events and provide comments on Key Global Legislative/Framework Changes including US FDA draft guidance in potency assurance for CGT products and EMA reflection paper on the use of Real-World Data in Non-Interventional Studies to Generate Real-World Evidence.

ABOUT THE AUTHORS

The International Society for Cell & Gene Therapy (ISCT) is the global leader focused on pre-clinical and translational aspects of developing cell and gene-based therapeutics, thereby advancing scientific research into innovative treatments for patients. ISCT offers a unique collaborative environment that addresses three key areas of translation: Academia, Regulatory, and Commercialization. Through strong relationships with global regulatory agencies, academic institutions, and industry partners, ISCT drives the advancement of research into a standard of care.

Comprised of over 4,000 cell and gene therapy experts across five geographic regions and representation from over 60 countries, ISCT members are part of a global community of peers, thought leaders, and organizations invested in cell and gene therapy translation. For more information about the organization, visit ISCT.

A special thanks to the ISCT Global Regulatory Task Force for their contribution. The ISCT GRTF works to address challenges and opportunities in established and evolving global regulatory environments

Citeline (formerly Pharma Intelligence) powers a full suite of complementary business intelligence offerings to meet the evolving needs of life science professionals to accelerate the connection of treatments to patients and patients to treatments. These patient-focused solutions and services deliver and analyze data used to drive clinical, commercial, and regulatory related-decisions and create real-world opportunities for growth.

Our global teams of analysts, journalists and consultants keep their fingers on the pulse of the pharmaceutical, biomedical and medtech industries, covering it all with expert insights: key diseases, clinical trials, drug R&D and approvals, market forecasts and more. For more information on one of the world's most trusted life science partners, visit Citeline.

REPORT HIGHLIGHTS

SECTION 2

REPORT HIGHLIGHTS

	H1 2024 REPORT (JUNE 2024)	H2 2023 REPORT (DECEMBER 2023)
GLOBAL PIPELINE	**2848** Therapies in Pipeline **(-3.8%)**	**2960** Therapies in Pipeline
	35% *genetically modified* | ***33%*** *gene therapies* | ***32%*** *non-genetically modified*	
APPROVED PRODUCTS	**100** Approved Products Globally	**96** Approved Products Globally
ACQUIRED FIRST APPROVALS	**3** Products received their first approvals globally **(-50%)**	**6** Products Received their First Approvals Globally
PRODUCTS UNDER REGULATORY REVIEW	**85** Products are Under Regulatory Review **(+6.2%)** Of Which **77** Products are in Phase III Clinical Trials **(+8.4%)**	**80** Products are Under Regulatory Review Of Which **71** Products are in Phase III Clinical Trials
GLOBAL LEGISLATIVE/ FRAMEWORK CHANGES	British Pharmacopoeia, EMA, ICH, NIH, and US FDA.	EMA, ICH, NZ Ministry of Environment, and US FDA.

KEY TAKEAWAYS

THREE NEW APPROVALS HIGHLIGHT IN H1 2024

- Amtagvi (*lifileucel*)
- CT-053 (*zevorcabtagene autoleucel*)
- Beqvez (*fidanacogene elaparvovec*)

H1 2024 WAS A GROWTH PERIOD PARTICULARLY FOR NON-GENETICALLY MODIFIED CELL THERAPIES

- There is a 4% increase in the number of non-genetically modified cell therapies in the pipeline from H2 2023.
- The non-genetically modified cell category continues to have the most therapies under phase III or in pre-registration phase with a total of 46 therapies in H1 2024.
- The non-genetically modified cell therapies continue to make up the majority of all approved products (68%)

GLOBAL OVERVIEW OF PIPELINE PRODUCTS, RECENT APPROVALS & REGULATORY REVIEWS

SECTION 2

GLOBAL OVERVIEW OF PIPELINE PRODUCTS

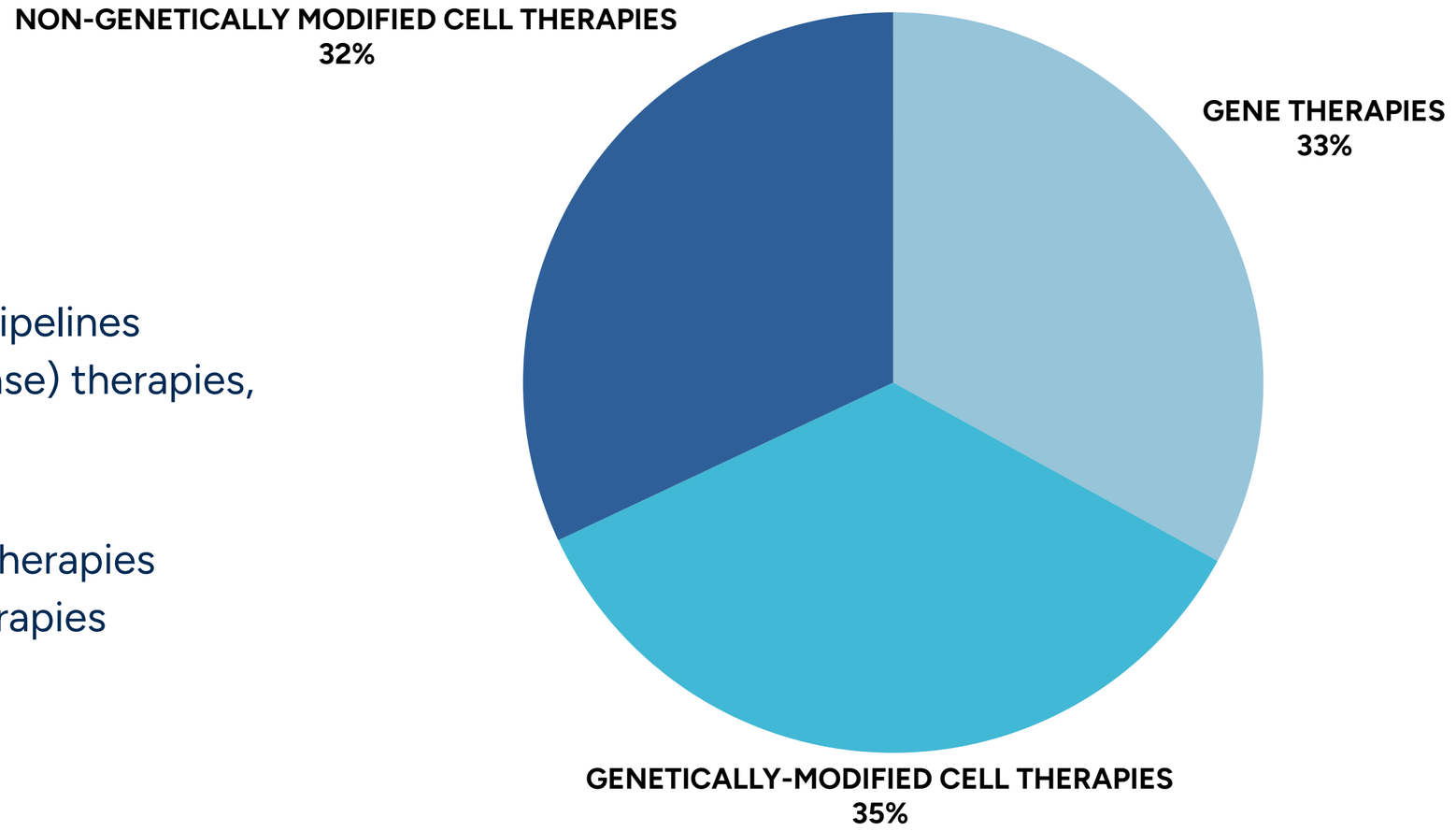
CELL, GENETICALLY-MODIFIED CELL, AND GENE THERAPIES

GLOBAL PIPELINE OVERVIEW – BY CATEGORY

2,848 PIPELINES

As of June 25, 2024, from the global pipelines (from preclinical to preregistration phase) therapies, there are:

- 938 gene therapies
- 902 non-genetically modified cell therapies
- 1,008 genetically-modified cell therapies

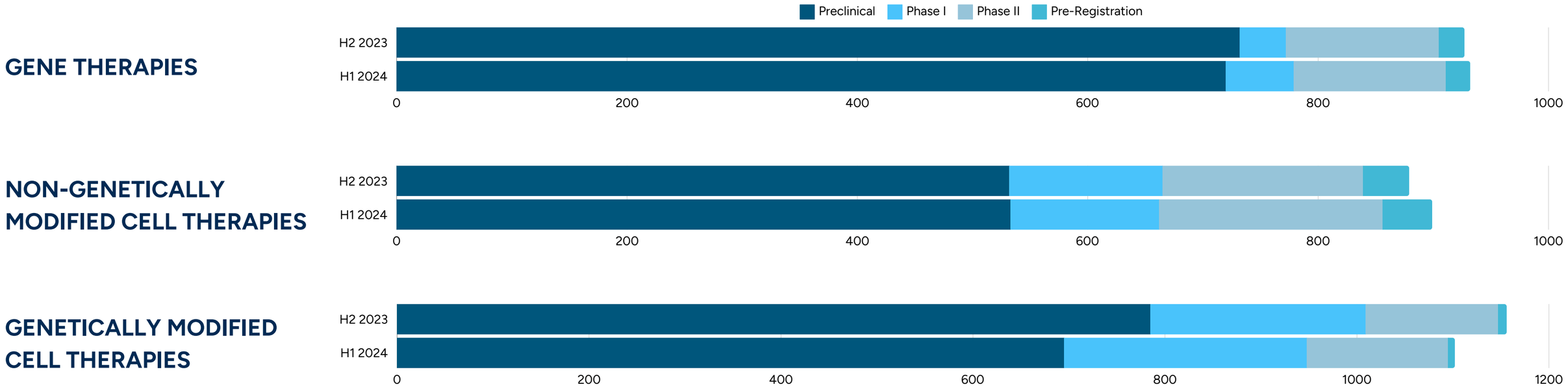


Source: Pharmaprojects | Citeline, June 2024

GLOBAL PIPELINE OVERVIEW – BY PHASE

AS OF JUNE 25, 2024, THE MAJORITY OF THERAPIES ARE IN PRECLINICAL DEVELOPMENT

- Non-genetically modified cell category has the most therapies under regulatory review with 46 therapies in Phase III or in pre-registration
- Gene therapy category has the greatest absolute number of therapies in preclinical development (720 therapies), as well as the greatest proportion of preclinical development (77%)



Source: Pharmaprojects | Citeline, June 2024

APPROVED PRODUCTS

CELL, GENETICALLY-MODIFIED CELL, AND GENE THERAPIES

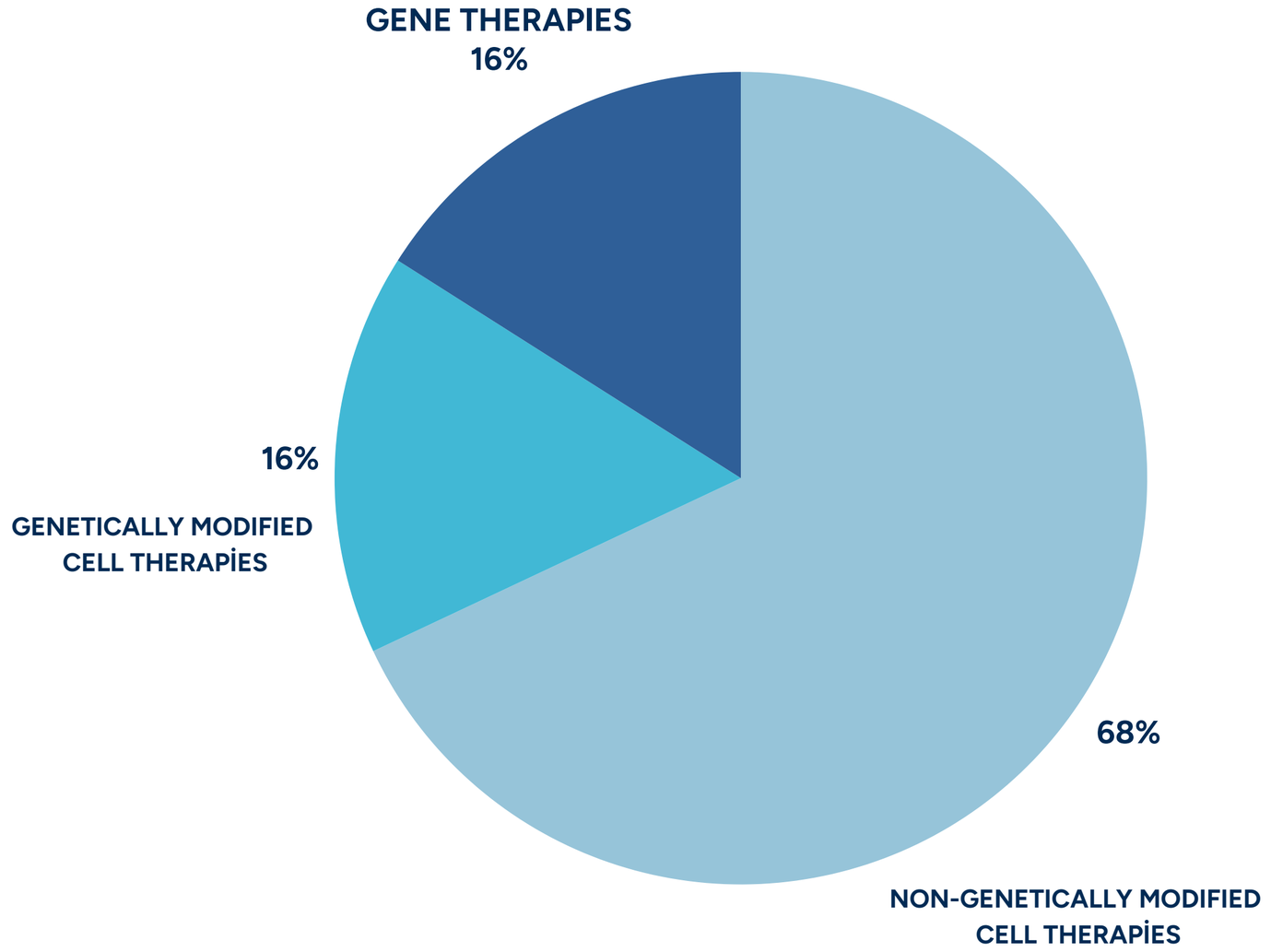
OVERVIEW OF APPROVED PRODUCTS – BY CATEGORY

100 PRODUCTS

As of June 25, 2024, 100 products are approved globally:

- 16 gene products
- 68 non-genetically modified cell products
- 16 genetically-modified cell products

Since H2 2023 (July 1 – December 31), there have been 1 gene products, 2 non-genetically modified cell products, and 1 genetically modified cell products approved

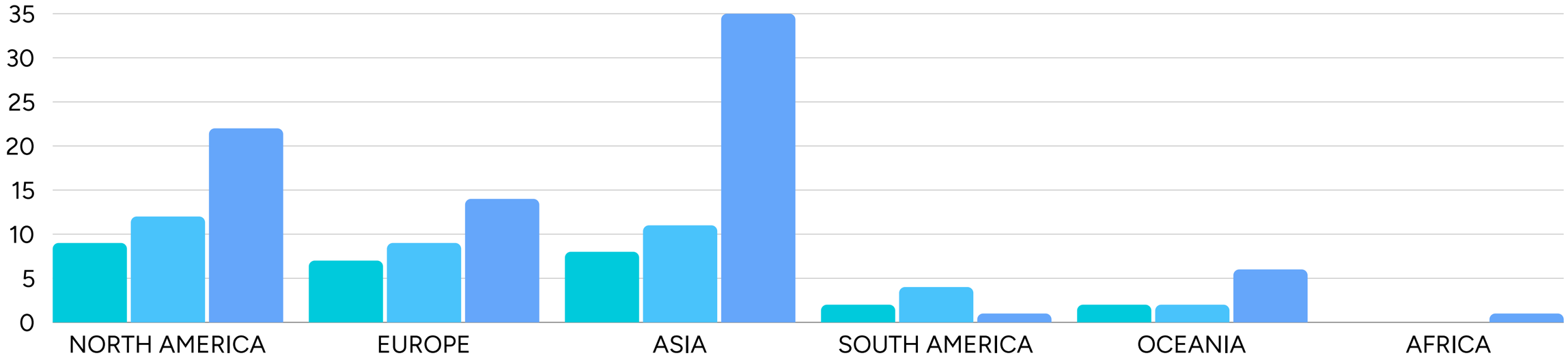


Source: Pharmaprojects | Citeline, June 2024

OVERVIEW OF APPROVED PRODUCTS – BY REGION

As of June 25, 2024, there is a similar approval distribution pattern between North America, Europe, and Asia

- Gene products – the least approved product category in all regions except South America and Oceania (where it is tied with genetically modified cell therapies). There is currently no approval in Africa
- Non-genetically modified cell products – the most approved product category in all regions besides South America
- Genetically modified cell products – the second most approved product category in North America, Europe, and Asia. There is an equal number of approved genetically modified cell therapies and gene therapies in Oceania. There is currently no approval in Africa



**Approvals by regions do not necessarily represent the approvals from one or more countries in the regions.*
**Oceania includes Australia and New Zealand.*

Source: Pharmaprojects | Citeline, June 2024

APPROVED NON-GENETICALLY MODIFIED CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Cupistem	Autologous Adipose-derived Stem Cell Therapy	2014	Anal Fistula	South Korea	Bukwang Pharmaceutical
HiQCell	Adipose-derived Stromal Vascular Fraction For Osteoarthritis	2014	Arthritis, Osteo	Australia	Regeneus
Ortho-ACI	Autologous Chondrocyte Implantation	2014	Regeneration, Cartilage, Unspecified	Australia	Orthocell
Ortho-ATI	Autologous Tenocyte Implantation	2014	Regeneration, Ligament	Oceania, Hong Kong	Orthocell
Spherox	Spheroids Of Human Autologous Matrix-associated Chondrocytes	2014	Regeneration, Cartilage, Orthopedic Lesion	EU, Switzerland, Iceland Liechtenstein, Norway, UK	co.don
Holoclar	Autologous Corneal Epithelial Cells	2015	Limbal Stem Cell Deficiency; Corneal Injury	EU, UK, Iceland, Liechtenstein, Norway	Holostem Terapie Avanzate
Astrostem	Human Adipose Mesenchymal Stem Cells	2015	Arthritis, Osteo	Japan	K-StemCell
TCD-51073	Autologous Myoblast Cell Therapy	2015	Heart Failure	Japan	Precigen
Lenzumestrocel	Autologous Bone Marrow Mesenchymal Stem Cells	2015	Amyotrophic Lateral Sclerosis	South Korea	Corestem
Stempeucel	Allogeneic Mesenchymal Stem Cells	2016	Ischaemia, Limb; Arthritis, Osteo	India	Stempeutics
AlloStem	Allogeneic Adipose-derived Mesenchymal Stem Cells	2016	Regeneration, Bone, Unspecified	US	AlloSource
Cartil-S	Autologous Mesenchymal Stem Cells	2016	Arthritis, Osteo	UK	Theracell Advanced Biotechnology
Chondroseal	Autologous Stem Cell Implantation	2016	Regeneration, Cartilage, Orthopedic Lesion	UK	Theracell Advanced Biotechnology

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED NON-GENETICALLY MODIFIED CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Apceden	Autologous Dendritic Cells	2017	Cancer, Colorectal; Cancer, Lung, Non-small Cell; Cancer, Ovarian; Cancer, Prostate	India	APAC Biotech
Keraheal	Autologous Keratinocytes	2017	Burns	South Korea	Biosolution Co.
Rosmir	Autologous Fibroblast Therapy	2017	Nasojugal Lines	South Korea	Tego Science
Cellistem	Umbilical Cord Mesenchymal Stem Cells	2018	Arthritis, Osteo; Heart Failure	Chile	Cells for Cells
Alofisel	Darvadstrocel	2018	Anal Fistula; Crohn's Disease	EU, Israel, Japan, UK, Norway, Switzerland, Iceland, Liechtenstein, Serbia	Takeda
AmnioFix	Dhacm	2018	Plantar Fasciitis	Australia	MiMedx
Kyslecel	Autologous Pancreatic Islet Cell Therapy	2018	Pancreatitis	US	Orgenesis
Stemirac	Autologous Bone Marrow Mesenchymal Stem Cells	2018	Spinal Cord Injury	Japan	Nipro
CartiLife	Autologous Chondrocytes	2019	Arthritis, Osteo	South Korea	Biosolution Co.
FemCelz	Female Sexual Dysfunction Stem Cell Therapy	2019	Sexual Dysfunction, Female	US, UK, EU, Liechtenstein, Iceland, Norway	Creative Medical Technologies
Chondrosphere	Spheroids Of Human Autologous Matrix-associated Chondrocytes	2019	Regeneration, Cartilage, Orthopedic Lesion	EU, UK, Switzerland, Liechtenstein, Iceland, Norway	Codon
StemSpine	Autologous Stem Cell Therapy	2019	Pain, Musculoskeletal, Unspecified; Regeneration, Cartilage, Intervertebral Disc	US	Creative Medical Technologies

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED NON-GENETICALLY MODIFIED CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Nepic	Autologous Corneal Epithelium Cells	2020	Limbal Stem Cell Deficiency	Japan	Teijin Pharma
Holoderm	Autologous Keratinocyte Therapy	2020	Burns	South Korea	Tego Science
Kaloderm	Allogeneic Keratinocyte Therap	2020	Burns	Indonesia, Mongolia, South Korea	Tego Science
CardioCell	Mesenchymal Bone Marrow-derived Stem Cells	2021	Infarction, Myocardial	Kazakhstan	Stemedica
Stratagraft	Allogenic Skin Tissue Cells	2021	Wound Healing	US	Mallinckrodt
Ocural	Autologous Cultured Oral Mucosal Epithelium	2021	Limbal Stem Cell Deficiency	Japan	Teijin Pharma
Rethymic	Allogeneic Processed Thymus Tissue-agdc	2021	Digeorge Syndrome	US	Sumitomo Dainippon Pharma
Sakracy	Autologous Cultured Oral Mucosal Epithelium	2022	Limbal Stem Cell Deficiency	Japan	Hirosaki Lifescience Innovation
Tab cel	Tabelecleucel	2022	Post Transplant Lymphoproliferative Disorder	EU, UK, Iceland, Liechtenstein, Norway	Atara Biotherapeutics
MYJ-1633	Autologous Blood-derived NK, NKT, And T Cells	2022	Cancer, Breast	Japan, Malaysia, Vietnam	Immunisbio
Vyznova	Neltependocel	2023	Corneal Dystrophy	Japan	Aurion Biotech

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED NON-GENETICALLY MODIFIED CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Omisirge	Omidubicel	2023	Stem Cell Engraftment; Cancer, Haematological, Unspecified; Cancer, Leukaemia, Acute Lymphocytic; Cancer, Leukaemia, Acute Myelogenous; Cancer, Leukaemia, Chronic Myelogenous; Cancer, Lymphoma, Non-hodgkin's; Myelodysplastic Syndrome	Us	Gamida Cell
Lantidra	Islets Of Langerhans Cell Therapy	2023	Diabetes, Type 1	Us	Celltrans
Amtagvi	Lifileucel	2024	Cancer, Melanoma	Us	Iovance Biotherapeutics

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED GENETICALLY MODIFIED CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Strimvelis	Autologous CD34+ Enriched Cells	2016	Adenosine Deaminase Deficiency	EU, UK, Iceland, Liechtenstein, Norway	Gsk
Kymriah	Tisagenlecleucel-t	2017	Cancer, Leukaemia, Acute Lymphocytic; Cancer, Lymphoma, B-cell, Diffuse Large; Cancer, Lymphoma, Follicular	US, EU, UK, Japan, Australia, Canada, South Korea, Norway, Switzerland, Iceland, Liechtenstein, Brazil	Novartis
Yescarta	Axicabtagene Ciloleucel	2017	Cancer, Lymphoma, B-cell, Diffuse Large; Cancer, Lymphoma, B-cell; Cancer, Lymphoma, Follicular; Cancer, Lymphoma, Non-hodgkin's	Japan, China, Canada, EU, US, UK, Iceland, Liechtenstein, Norway, Brazil	Gilead Sciences
Zynteglo	Betibeglogene Autotemcel	2019	Thalassaemia	Us	Bluebird Bio
Tecartus	Brexucabtagene Autoleucel	2020	Cancer, Lymphoma, Mantle Cell; Cancer, Leukaemia, Acute Lymphocytic	EU, UK, US, Norway, Liechtenstein, Iceland, Brazil	Gilead Sciences
Libmeldy	Atidarsagene Autotemcel	2020	Leukodystrophy, Metachromatic	EU, UK, Iceland, Liechtenstein, Norway, Switzerland	Gsk
Breyanzi	Lisocabtagene Maraleucel	2021	Cancer, Lymphoma, B-cell, Diffuse Large; Cancer, Lymphoma, B-cell; Cancer, Lymphoma, Follicular; Cancer, Leukaemia, Chronic Lymphocytic	EU, US, Japan, Canada, Norway, Iceland, Liechtenstein, Switzerland	Bristol-myers Squibb

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED GENETICALLY MODIFIED CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Abecma	Idecabtagene Vicleucel	2021	Cancer, Myeloma	US, EU, UK, Canada, Japan, Australia, Iceland, Israel, Liechtenstein, Norway, Switzerland	Bluebird Bio
Skysona	Elivaldogene Autotemcel	2021	Adrenoleukodystrophy	Us	Bluebird Bio
Benoda	Relmacabtagene Autoleucel	2021	Cancer, Lymphoma, B-cell, Diffuse Large; Cancer, Lymphoma, Follicular	China	JW Therapeutics
Carvykti	Ciltacabtagene Autoleucel	2022	Cancer, Myeloma	US, EU, UK, Japan, China, Iceland, Liechtenstein, Norway, Brazil	Legend Biotech
Fucaso	Equecabtagene Autoleucel	2023	Cancer, Myeloma	China	Nanjing IASO Biotechnology
Inaticabtagene Autoleucel	Anti-cd19 CAR-T Therapy	2023	Cancer, Leukaemia, Acute Lymphocytic	China	Juventas Cell Therapy
Casgevy	Exagamglogene Autotemcel	2023	Anaemia, Sickle Cell; Thalassaemia	UK, EU, Iceland, Liechtenstein, Norway, US, Bahrain, Saudi Arabia	CRISPR Therapeutics
Lyfgenia	Lovotibeglogene Autotemcel	2023	Anaemia, Sickle Cell	Us	Bluebird Bio
Ct-053	Zevorcabtagene Autoleucel	2024	Cancer, Myeloma	China	Carsgen Therapeutics

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED GENE CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	INN OR DESCRIPTION	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Imlygic	Talimogene Laherparepvec	2015	Melanoma	US, EU, UK, Australia, China, Norway, Iceland, Liechtenstein	Amgen
Luxturna	Voretigene Neparvovec	2017	Leber's Congenital Amaurosis; Retinitis Pigmentosa	US, EU, UK, Australia, Canada, South Korea, Japan, Brazil, Norway, Russian Federation, Iceland, Liechtenstein	Roche
Zolgensma	Onasemnogene Abeparvovec	2019	Spinal Muscular Atrophy	US, EU, UK, Japan, Australia, Canada, Brazil, Israel, Taiwan, South Korea, Norway, Iceland, Liechtenstein,	Regenxbio
Collategene*	Beperminogene Perplasmid	2019	Ischaemia, Limb	Japan	Anges
Delytact	Teserpaturev	2021	Brain Cancer	Japan	Daiichi Sankyo
Upstaza	Eladocagene Exuparvovec	2022	Aromatic L-amino Acid Decarboxylase (AADC) Deficiency	EU, UK, Iceland, Israel, Liechtenstein, Norway	PTC Therapeutics

*In July 2024, AnGes announced it will withdraw application for full approval of Collategene in Japan due to a post-marketing Phase 3 trial failing to reproduce results demonstrated in an earlier domestic trial. AnGes will pull the product from the market and resubmit a new domestic approval application. (Scrip, 2Jul2024)

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

APPROVED GENE CELL PRODUCTS (10-YEAR PERIOD, JANUARY 2014-JUNE 2024)

PRODUCT NAME	GENERIC NAME	YEAR FIRST APPROVED/ADDED	DISEASE(S)	LOCATIONS APPROVED	FIRST LICENSE HOLDER
Roctavian	Valoctocogene Roxaparvovec	2022	Haemophilia A	EU, UK, US, Norway, Iceland, Liechtenstein	Biomarin
Hemgenix	Etranacogene Dezaparvovec	2022	Haemophilia B	US, EU, UK, Canada, Norway, Switzerland, Iceland, Liechtenstein, Norway	Uniqure
Adstiladrin	Nadofaragene Firadenovec	2022	Bladder Cancer	Us	Merck
Vyjuvek	Beremagene Geperpavec	2023	Epidermolysis Bullosa	Us	Krystal Biotech
Elevidys	Delandistrogene Moxeparvovec	2023	Dystrophy, Duchenne's Muscular	Us	Sarepta Therapeutics
Beqvez	Fidanacogene Elaparvovec	2024	Haemophilia B	US, Canada	Roche

Source: Pharmaprojects | Citeline, June 2024 *Pharmaprojects is a live database and the data presented in the above table reflects the most current information extracted from the database

PRODUCTS UNDER REGULATORY REVIEW (PRE-REGISTRATION AND PHASE III)

CELL, GENETICALLY-MODIFIED CELL, AND GENE THERAPIES

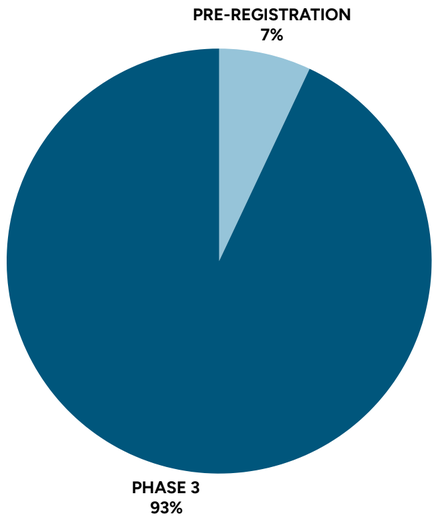
NON-GENETICALLY MODIFIED CELL THERAPIES UNDER REGULATORY REVIEW

46 THERAPIES

46 non-genetically modified cell therapies are under regulatory review (pre-registration or Phase III clinical trials)

- 3 non-genetically modified cell therapies are in pre-registration, accounting for 7% of late-stage non-genetically modified cell therapies
- 43 non-genetically modified cell therapies are in Phase III clinical trials, accounting for 93% of late-stage non-genetically modified cell therapies

% OF NON-GENETICALLY MODIFIED CELL THERAPIES IN LATE-STAGE DEVELOPMENT



DRUG NAME	GENERIC DRUG NAME	CELL TYPE	DISEASE	LICENSE HOLDER	REVIEWER AGENCY
ACE-02	Autologous cultured epidermis with melanocytes	Skin cells	Piebaldism; Vitiligo	Teijin Pharma	MHLW (Japan)
DCVax-Brain	murcidencel	Dendritic cells	Brain cancer	NorthWest Biotherapeutics	MHRA (UK)
SB-623	vandefitemcel	Mesenchymal stem cells (bone marrow)	Traumatic brain injury	SanBio	MHLW (Japan)

Source: Pharmaprojects | Citeline, June 2024

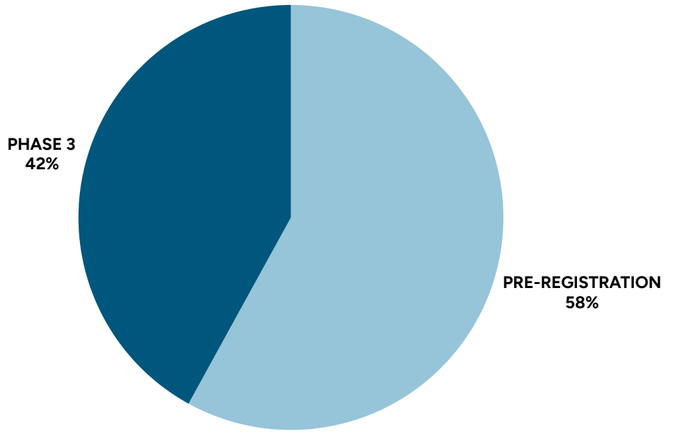
GENETICALLY MODIFIED CELL THERAPIES UNDER REGULATORY REVIEW

12 THERAPIES

12 genetically-modified cell therapies are under regulatory review (pre-registration or Phase III clinical trials)

- 5 genetically-modified cell therapies are in pre-registration, accounting for 42% of late-stage genetically-modified cell therapies
- 7 genetically-modified cell therapies are in Phase III clinical trials, accounting for 58% of late-stage genetically-modified cell therapies

% OF GENETICALLY MODIFIED CELL THERAPIES IN LATE-STAGE DEVELOPMENT



Drug Name	Generic Drug Name	Cell Type	Disease	License Holder	Reviewer Agency
RP-L102	RP-L102	Hematopoietic stem cells	Fanconi's anemia	Rocket Pharmaceuticals	EMA (EU)
ADP-A2M4	afamitresgene autoleucel	T cells	Synovial sarcoma	Adaptimmune	FDA (US)
AUTO-1	obecabtagene autoleucsel	T cells	Cancer, leukaemia, acute lymphocytic	Autolus	FDA (US) EMA (EU)
EB-101	prademagene zamikeracel	Skin cells	Epidermolysis bullosa	Abeona Therapeutics	FDA (US)
Kresladi*	marnetegragene autotemcel	autologous hematopoietic stem cells	Leukocyte adhesion deficiency	Rocket Pharmaceuticals	FDA (US)

*Rocket announced on 28 June 2024 that FDA issued a CRL for Kresladi, requesting limited additional CMC information to complete review

Source: Pharmaprojects | Citeline, June 2024

GENE THERAPIES UNDER REGULATORY REVIEW

27 THERAPIES

27 gene therapies are under regulatory review
(pre-registration or Phase III clinical trials)

- 0 gene therapies are in pre-registration
- 27 gene therapies are in Phase III clinical trials, accounting for 100% of late-stage gene therapies

Source: Pharmaprojects | Citeline, June 2024

SELECT REGULATORY REVIEW
CELL, GENETICALLY-MODIFIED CELL, AND GENE THERAPIES

CASGEVY

First Gene-Editing Therapy U.S. FDA Approved for Sickle Cell Anemia

Casgevy
(exagamglogene autotemcel)

Company:	Vertex Pharmaceuticals Incorporated and CRISPR Therapeutics
Current phase:	Approved
Indication:	Sickle Cell Disease (SCD), Thalassemia
Target:	BCL11A; CRISPR/CRISPR-Cas9
Formulation / dosing:	Intravenous (IV)
Designations:	Fast Track, Orphan, PRIME, Rare Pediatric Disease, RMAT
Upcoming regulatory events:	Regulatory Approval (Canada) from Now – 09/30/24 Regulatory Approval (Switzerland) from Now – 12/31/25

Pivotal Study	**CLIMB-SCD-121 (Update: 06/14/24)**
Patient inclusion	pts age 12-35y with SCD and a history of ≥2VOCs/y in 2y prior to screening
Study design	Interventional, Single Group Assignment, Open Label, Treatment
Primary focus	Safety and efficacy
Trial efficacy data	Efficacy results are consistent with the reported primary and key secondary endpoints analyses from these exa-cel studies and continue to demonstrate transformative clinical benefit with durable and stable levels of fetal hemoglobin (HbF) and allelic editin
Trial safety data	Safety profile of exa-cel was generally consistent with myeloablative busulfan conditioning and autologous transplantation

Pivotal Study	**CLIMB THAL-111 (Update: 06/14/24)**
Patient inclusion	Pts age 12-35y with Transfusion-Dependent ß-Thalassemia
Study design	Interventional, Single Group Assignment, Open Label, Treatment
Primary focus	Safety and efficacy
Trial efficacy data	Exa-cel treatment resulting in early and sustained increases in Hb and HbF leading to transfusion independence in >90% of pts with TDT and improved QOL
Trial safety data	Safety profile of exa-cel was generally consistent with myeloablative busulfan conditioning and autologous transplantation.

Source: Biomedtracker| Citeline, June 2024

CASGEVY - REGULATORY INSIGHTS

First Gene-Editing Therapy U.S. FDA Approved for Sickle Cell Anemia

REGULATORY OVERVIEW	
EXPECTED EVENT	Regulatory Approval (Canada)
EXPECTED EVENT DATE	Now – 09/30/24
NDS FILING DATE	04/01/24
DESIGNATIONS	Fast Track, Orphan, PRIME, Rare Pediatric Disease, RMAT
PREVIOUS REGULATORY DECISION	Conditional Marketing Authorization (Europe)

SUMMARY OF REGULATORY OUTCOMES

- On February 13, 2024, the European Commission granted conditional marketing authorization to Casgevy for the treatment of SCD or TDT
- On January 16, 2024, the U.S. FDA approved Casgevy for the treatment of TDT
- On January 9, 2024, the SFDA granted Marketing Authorization for Casgevy for the treatment of SCD and TDT
- On December 14, 2023, the EMA's CHMP adopted a positive opinion for the conditional approval of Casgevy for the treatment of SCD or TDT
- On December 8, 2023, the U.S. FDA approved Casgevy for the treatment of SCD
- On December 2, 2023, the National Health Regulatory Authority of Bahrain announced the approval of CASGEVY for the treatment of patients with sickle cell disease and transfusion-dependent beta-thalassemia
- On December 31, 2022, Vertex announced that the Exa-cel submission was completed in the fourth quarter of 2022 in EU and UK for both SCD and TDT

ADDITIONAL NOTES REGULATORY DECISION	COMMENTS
▪ Conditional Marketing Authorization (Europe)	▪ Vertex Pharmaceuticals announced that the European Commission has granted conditional marketing authorization to Casgevy. Casgevy is approved for the treatment of patients who are 12 years of age and older with severe sickle cell disease (SCD) or transfusion-dependent beta thalassemia (TDT), for whom hematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen matched related HSC donor is not available.
▪ U.S. FDA Approval	▪ Vertex Pharmaceuticals announced that the U.S. FDA has approved CASGEVY (exagamglogene autotemcel [exa-cel]), a CRISPR/Cas9 gene-edited cell therapy, for the treatment of transfusion-dependent beta thalassemia (TDT) in patients 12 years and older. ▪ The administration of CASGEVY requires experience in stem cell transplantation; therefore, Vertex is engaging with hospitals to establish a network of authorized treatment centers (ATCs) throughout the U.S. to offer CASGEVY to patients. All nine ATCs activated in the U.S. are able to offer CASGEVY to eligible patients with TDT and SCD.

Source: Biomedtracker| Citeline, June 2024

EBVALLO

First Ever Approval in Europe for an Allogeneic T-Cell Immunotherapy

Ebvallo
(Tabelecleucel)

Company:	Pierre Fabre, Atara Biotherapeutics, and Memorial Sloan Kettering Cancer Center
Current phase:	Approved
Indication:	Post transplant lymphoproliferative disorder
Target:	Epstein Barr Virus (EBV), Immune System, Stem Cells/Other Cell Therapies, T lymphocytes
Formulation / dosing:	Intravenous (IV)
Designations:	Breakthrough, Orphan, PRIME
Upcoming regulatory events:	PDUFA for BLA - First Review – 01/01/2025-03/31/2025

Pivotal Study	**ALLELE (EBV-PTLD after SOT) (Update: 01/31/24)**
Patient inclusion	Eligible patients (of any age) had biopsy-proven EBV-positive post-transplant lymphoproliferative disease, disease that was relapsed or refractory to rituximab after HSCT and rituximab with or without chemotherapy after SOT, and partially HLA-matched and appropriately HLA-restricted tabelecleucel available
Study design	Interventional, Non-Randomized, Parallel Assignment, Open Label, Treatment
Primary focus	Efficacy and safety
Trial efficacy data	Tab-cel provides consistent clinically meaningful outcomes, including improved overall ORR and prolonged DOR and OS
Trial safety data	Tab-cel was well tolerated with no reports of tumor flare reaction, cytokine release syndrome or immune effector cell-associated neurotoxicity syndrome, and no events of graft-versus-host disease or SOT rejection as related to tab-cel

Supporting Clinical Studies	**Phase III – Match (EBV-PTLD after HCT) (Initiation date: 01/2018)**
Patient inclusion	for the treatment of patients with EBV+PTLD following allogeneic hematopoietic cell transplant (HCT) after failure of rituximab
Study design	Interventional
Primary focus	Efficacy and Safety
Study status	Suspended

Source: Biomedtracker| Citeline, June 2024

EBVALLO - REGULATORY INSIGHTS

First Ever Approval in Europe for an Allogeneic T-Cell Immunotherapy

REGULATORY OVERVIEW	
EXPECTED EVENT	PDUFA for BLA - First Review
EXPECTED EVENT DATE	01/01/2025-03/31/2025
BLA FILING DATE	05/20/2024
DESIGNATIONS	Breakthrough, Orphan, PRIME
PREVIOUS REGULATORY DECISION	Swissmedic regulatory approval (Switzerland) MHRA regulatory approval (UK) EC regulatory approval (EU)

SUMMARY OF REGULATORY OUTCOMES

- On May 1, 2024, Swissmedic granted Ebvallo marketing authorization in Switzerland for the treatment of patients with EBV+ PTLD.
- On May 31, 2023, MHRA granted Ebvallo marketing authorization in the UK for the treatment of patients with EBV+ PTLD.
- On December 16, 2022, the EC granted marketing authorization for Ebvallo as a monotherapy for the treatment of adult and pediatric patients two years of age and older with relapsed or refractory Epstein-Barr virus-positive post-transplant lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy.

ADDITIONAL NOTES REGULATORY DECISION	COMMENTS
▪ Meeting with U.S. FDA	▪ On September 19, 2023, Atara Biotherapeutics reported progress related to the regulatory pathway for tabelecleucel (tab-cel) in the U.S. for patients with EBV+ PTLD. ▪ Following discussions between Atara and the U.S. FDA, the FDA and Atara are now aligned on analytical comparability between manufacturing process versions. This alignment supports Atara's ability to pool the pivotal clinical trial data from different process versions in the Biologics License Application (BLA) submission.

Source: Biomedtracker| Citeline, June 2024

BREYANZI

BMS Expected to Soon Secure an Additional Approval (Follicular Lymphoma)

Breyanzi (lisocabtagene maraleucel)

Company:	Bristol Myers Squibb
Current phase:	Approved
Indication:	Chronic Lymphocytic Leukemia (CLL)/Small Cell Lymphocytic Lymphoma (SLL) – NHL, Diffuse Large B-Cell Lymphoma (DLBCL) – NHL, Follicular Lymphoma (FL), Mantle Cell Lymphoma - NHL
Target:	Autologous Chimeric Antigen Receptor T-cells (CAR-T), Cluster of Differentiation 19 (CD19), Immune System, T lymphocytes
Formulation / dosing:	Intravenous (IV)
Designations:	Orphan
Upcoming regulatory events:	Approval Decision (Japan) – 10/01/2024-4/30/2025

PIVOTAL STUDY	TRANSCEND FL (Update: 12/10/23)
Patient inclusion	Patients 18+y with relapsed or refractory indolent non-Hodgkin lymphoma, including FL, in the second-line and third-line plus setting
Study design	Interventional, Non-Randomized, Single Group Assignment, Open Label, Treatment
Primary focus	Efficacy and safety
Trial efficacy data	The majority of patients with second- or third-line relapsed or refractory FL reported clinically significant improvements in quality of life, disease symptoms, and functioning after being treated with Breyanzi. Those receiving Breyanzi in the second-line setting generally demonstrated greater and faster meaningful improvements in most primary domains, compared to those who received Breyanzi in the third-line setting, including role and cognitive functioning, fatigue, pain, and Functional Assessment of Cancer Therapy Lymphoma scores.
Trial safety data	Breyanzi continued to exhibit a manageable and predictable safety profile with no new safety signals observed and low rates of severe cytokine release syndrome (CRS) and neurologic events (NE)

Source: Biomedtracker| Citeline, June 2024

BREYANZI - REGULATORY INSIGHTS

BMS Expected to Soon Secure an Additional Approval (Follicular Lymphoma)

REGULATORY OVERVIEW	
EXPECTED EVENT	Approval Decision (Japan)
EXPECTED EVENT DATE	10/01/2024-4/30/2025
MHLW FILING DATE	01/30/2024
DESIGNATIONS	Orphan
PREVIOUS REGULATORY DECISION	FDA regulatory approval (US) EC regulatory approval (EU)

SUMMARY OF REGULATORY OUTCOMES

- On May 15, 2024 the U.S. FDA granted accelerated approval for Breyanzi for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received two or more prior lines of systemic therapy.
- On January 30, 2024, Japan's Ministry of Health, Labour and Welfare accepted the supplemental NDA for Breyanzi for the treatment of relapsed or refractory FL.
- On January 30, 2024, the U.S. FDA accepted the company's Biologics License Applications (sBLA) for Breyanzi to expand into new indications to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) and granted Priority Review.

ADDITIONAL NOTES REGULATORY DECISION	COMMENTS
▪ Accelerated/Conditional Approval for sNDA/sBLA (U.S.)	▪ This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). Breyanzi is also included in the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines) for B-cell lymphomas as a Category 2A recommendation for third-line and subsequent therapy for relapsed or refractory FL.

Source: Biomedtracker| Citeline, June 2024

RP-L102

Potential to be First Gene Therapy Approved in the US For Fanconi Anemia

REGULATORY OVERVIEW	
Expected event	CHMP Opinion Approval Decision (Europe)
Expected event date	12/01/2024-06/30/2025 03/02/2025-09/02/2025
EMA filing date	04/02/2024
Designations	Fast Track, Orphan, PRIME, Rare Pediatric Disease, RMAT
Previous regulatory decision	n/a

SUMMARY OF REGULATORY OUTCOMES

- On April 2, 2024, the EMA accepted the Marketing Authorization Application (MAA) for RP-L102, its lentiviral (LV) vector-based investigational gene therapy for Fanconi Anemia (FA), complementation group A.

ADDITIONAL NOTES REGULATORY DECISION	COMMENTS
▪ Meeting with U.S. FDA	▪ Rocket Pharmaceuticals announced the U.S. Phase II clinical development plan for RP-L102, the Company's lentiviral vector (LVV)-based gene therapy for the treatment of Fanconi Anemia (FA). Based on feedback from a recent End-of-Phase I meeting with the U.S. Food and Drug Administration (FDA), Rocket plans to open enrollment for the U.S. Phase II trial of RP-L102 for FA in the fourth quarter of 2019. ▪ One aspect of the agreed upon design is the primary endpoint of resistance to mitomycin-C, a DNA damaging agent, in bone marrow stem cells at a minimum time point of one year. Depending on the totality of available clinical evidence at the time of filing, MMC-resistance may also serve as a surrogate endpoint for an accelerated approval. ▪ Based on the combined feedback from the FDA and the Europe Medicines Agency (EMA), the pivotal study data in support of FA product licensure application is anticipated to be based on the combined U.S. and E.U. Phase II studies. The Center for Definitive and Curative Medicine at Stanford University and Hospital Infantil Universitario Niño Jesús will serve as the lead clinical sites in the U.S. and E.U., respectively. Additional clinical sites may be added in the global Phase II studies.

Source: Biomedtracker| Citeline, June 2024

RP-L102

Potential to be First Gene Therapy Approved in the US For Fanconi Anemia

REGULATORY OVERVIEW	
EXPECTED EVENT	CHMP Opinion Approval Decision (Europe)
EXPECTED EVENT DATE	12/01/2024-06/30/2025 03/02/2025-09/02/2025
EMA FILING DATE	04/02/2024
DESIGNATIONS	Fast Track, Orphan, PRIME, Rare Pediatric Disease, RMAT
PREVIOUS REGULATORY DECISION	n/a

SUMMARY OF REGULATORY OUTCOMES

- On April 2, 2024, the EMA accepted the Marketing Authorization Application (MAA) for RP-L102, its lentiviral (LV) vector-based investigational gene therapy for Fanconi Anemia (FA), complementation group A.

ADDITIONAL NOTES REGULATORY DECISION	COMMENTS
▪ Meeting with U.S. FDA	▪ Rocket Pharmaceuticals announced the U.S. Phase II clinical development plan for RP-L102, the Company's lentiviral vector (LVV)-based gene therapy for the treatment of Fanconi Anemia (FA). Based on feedback from a recent End-of-Phase I meeting with the U.S. Food and Drug Administration (FDA), Rocket plans to open enrollment for the U.S. Phase II trial of RP-L102 for FA in the fourth quarter of 2019. ▪ One aspect of the agreed upon design is the primary endpoint of resistance to mitomycin-C, a DNA damaging agent, in bone marrow stem cells at a minimum time point of one year. Depending on the totality of available clinical evidence at the time of filing, MMC-resistance may also serve as a surrogate endpoint for an accelerated approval. ▪ Based on the combined feedback from the FDA and the Europe Medicines Agency (EMA), the pivotal study data in support of FA product licensure application is anticipated to be based on the combined U.S. and E.U. Phase II studies. The Center for Definitive and Curative Medicine at Stanford University and Hospital Infantil Universitario Niño Jesús will serve as the lead clinical sites in the U.S. and E.U., respectively. Additional clinical sites may be added in the global Phase II studies.

Source: Biomedtracker| Citeline, June 2024

HIGHLIGHTS OF REGULATORY EVENTS, KEY GLOBAL LEGISLATIVE/ FRAMEWORK CHANGES, RECENT OR UPCOMING STANDARDS & LATEST APPROVED PRODUCTS

SECTION 2

RECENT & UPCOMING REGULATORY EVENTS

START DATE	END DATE	EVENT DESCRIPTION	TYPE OF EVENT	NAME OF AGENCY
5 August 2024	8 August 2024	Pharmacovigilance Risk Assessment Committee (PRAC)	Meeting	PRAC-EMA
6 August 2024	6 August 2024	Hybrid Public Workshop on Artificial Intelligence in Drug & Biological Product Development	Workshop	FDA-CTTI
13 August 2024	16 August 2024	Committee for Advanced Therapies (CAT) Meeting	Meeting	CAT-EMA
19 August 2024	22 August 2024	Committee for Medicinal Products for Human Use (CHMP)	Meeting	CHMP-EMA
21 August 2024	23 August 2024	WHO-UMC-HSA Inter-Regional Pharmacovigilance Training Workshop 2024	Workshop	WHO-UMC-HSA
3 September 2024	6 September 2024	Paediatric Committee (PDCO) Meeting	Meeting	PDCO-EMA
10 September 2024	11 September 2024	USP-MHLW/PMDA Joint Workshop	Workshop	USP-MHLW/PMDA
11 September 2024	11 September 2024	Clinical Trials Regulation (CTR) Collaborate Stakeholder Meeting	Meeting	EMA
18 September 2024	18 September 2024	Clinical Trials Information System (CTIS): Walk-in clinic on transitioning trials	Live Broadcast	EMA
23 September 2024	26 September 2024	Clinical Trials Information System (CTIS) sponsor end user training programme	Online	EMA
8 October 2024	10 October 2024	PMDA-ATC GMP Inspection Seminar 2024	Seminar	PMDA
19 November 2024	20 November 2024	GMP Forum 2024	Workshop	TGA
TBD	TBD	Frequently Asked Questions - Cell and Gene Therapy Products; Draft Guidance for Industry	Regulatory Consultation	CBER-FDA
TBD	TBD	Accelerated Approval of Human Gene Therapy Products for Rare Diseases; Draft Guidance for Industry	Regulatory Consultation	CBER-FDA

CONCLUDED REGULATORY EVENTS

CONCLUDED REGULATORY EVENTS

TAIWAN FDA

Draft Guidance for CAR-T
[4 October 2023]

Taiwan FDA issued the draft guidance on research and development strategies for CAR-T cell products to reinforce the review process of new drug applications.

CMS

Webinar on Cell and Gene Therapy Access Model
[6 February 2024]

This webinar aims to provide overview of the CGT Access Model.

The slides and webinar recording are available on CMS website.

JOINT US FDA-HEALTH CANADA

ICH Public Meeting
[22 February 2024]

A regional public meeting to provide information to stakeholders and solicit input prior to the next ICH Biannual Assembly meeting.

The meeting agenda and summary of the meeting is available on the FDA website.

COUNCIL OF EU

SoHO Rules Adoption
[27 May 2024]

The Council has adopted new rules aimed at improving the safety and quality of blood, tissues and cells used in healthcare and facilitating cross-border circulation of these substances in the EU.

Next steps: the regulation will now be signed by both the Council and the European Parliament. It will then enter into force following publication in the EU's Official Journal.

Click here to learn more.

CONCLUDED REGULATORY EVENTS

ISCT 2024 GLOBAL REGULATORS SUMMIT

Rare Disease
[28 May 2024]

The ISCT 2024 Global Regulators Summit on Rare Diseases: Overcoming Regulatory Challenges and Optimizing Global Synergies was held in Vancouver, Canada.

Bringing together representatives from 19 regulatory agencies, the summit addressed the global regulatory challenges in the development, manufacture, and access of products to treat rare diseases.

TGA

Webinar: GCP inspection program for clinical trials of medicines, biologicals and devices
[30 May 2024]

This webinar provided an overview of the updates that include clinical trials of medical devices into the GCP inspection program and insights in what to expect and how to prepare for an inspection.

The slides and recording are available on TGA website.

FDA

START Pilot Program
[31 May 2024]

FDA CBER and CDER initiated the program in September 2023 to help further accelerate the development of novel drug and biological products for rare diseases.

On May 29, 2024, FDA notified selected participants of their acceptance into the Program. Click here to learn about the latest update on the program.

JOINT HMA/EMA

Big Data Steering Group workshop on RWE methods
[14 June 2024]

One-day workshop that brought together representatives of regulatory agencies, pharmaceutical companies, patients, healthcare professionals, academia, and health technology assessment bodies.

The event summary and full program agenda are available on the event webpage.

ISCT CONTRIBUTIONS ON GLOBAL REGULATORY GUIDANCE REVIEWS AND CONSULTATIONS

ISCT CONTRIBUTIONS ON GLOBAL REGULATORY GUIDANCE REVIEWS AND CONSULTATIONS

- From potency assurance to clinical research terminologies, ISCT leverages its regulatory expertise to provide guidance and expert opinion to agencies.

- In Q1 2024, with over 12 regulatory consultations open for public comments, ISCT has contributed/commented to 5 key regulatory consultations.

COMMENTED

US FDA -Draft Guidance: Potency Assurance For Cellular
[*Comments were submitted on 27 March 2024*]

US FDA - Draft Guidance: Rwe: Considerations Regarding Non-interventional Studies For Drug And Biological Products
[Comments were submitted on 26 June 2024]

FDA-NIH - Draft Glossary: Resource On Terminology For Clinical Research
[Comments were submitted on 20 June 2024]

US FDA - Draft Guidance: Safety Testing Of Human Allogeneic Cells Expanded For Use In Cell-based Medical Products
[Comments were submitted on July 29]

US FDA - Platform Technology Designation Program For Drug Development
[Comments were submitted on July 29]

REVIEWED BUT NOT COMMENTED

US FDA - Draft Guidance: Advanced Manufacturing Technologies Designation Program

US FDA - Draft Guidance: Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for Fda-Regulated Medical Products

US FDA - Draft Guidance: Use Of Data Monitoring Committees in Clinical Trials

US FDA - Draft Guidance: Early Alzheimer's Disease: Developing Drugs For Treatment

EMA - Draft Scientific Guideline: Quality, Non-clinical And Clinical Requirements for Investigational Advanced Therapy Medicinal Products in Clinical Trials

ICH - Harmonised Guideline: Post-approval Safety Data: Definitions and Standards for Management and Reporting of Individual Case Safety Reports

EMA - Reflection Paper: Use Of Real-World Data in Non-interventional Studies to Generate Real-World Evidence

HIGHLIGHTS OF KEY GLOBAL LEGISLATIVE/FRAMEWORK CHANGES

[US FDA] DRAFT GUIDANCE: POTENCY ASSURANCE FOR CELLULAR AND GENE THERAPY PRODUCTS

SCOPE	The scope of this guidance document is limited to assuring the potency of CGT products that are regulated as biological products under section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262).
PURPOSE	When finalized, this guidance will describe FDA's recommendations for potency assays for CGT products and for a comprehensive approach to potency assurance that is grounded in quality risk management

PUBLIC CONSULTATION PERIOD: 27 DECEMBER 2023 - 27 MARCH 2024

***Source**: US FDA. Draft Guidance for Industry. Potency Assurance for Cellular and Gene Therapy Products. Accessed through https://www.regulations.gov/docket/FDA-2023-D-4299 on 17 June 2024.*

[EMA] DRAFT SCIENTIFIC GUIDELINE: QUALITY, NON-CLINICAL, AND CLINICAL REQUIREMENTS FOR INVESTIGATIONAL ADVANCED THERAPY MEDICINAL PRODUCTS IN CLINICAL TRIALS

SCOPE	The guideline provides guidance on the structure and data requirements for a clinical trial application for investigational ATMPs
PURPOSE	The guideline is multidisciplinary and addresses development, manufacturing, and quality control as well as non-clinical and clinical development of ATMPs.

PUBLIC CONSULTATION PERIOD: 25 MARCH 2024 - 31 MARCH 2024

Source: EMA. Scientific Guideline. Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials. Accessed through https://www.ema.europa.eu/en/guideline-quality-non-clinical-clinical-requirements-investigational-advanced-therapy-medicinal-products-clinical-trials-scientific-guideline on 17 June 2024.

[US FDA] DRAFT GUIDANCE FOR INDUSTRY: CONSIDERATIONS FOR THE USE OF HUMAN AND ANIMAL-DERIVED MATERIALS IN THE MANUFACTURE OF CELLULAR AND GENE THERAPY AND TISSUE-ENGINEERED MEDICAL PRODUCTS

SCOPE	The “materials” covered by this guidance include (1) the reagents, feeder cells and excipients (and other inactive ingredients in the DP) that are in direct contact with the starting material, intermediates, and final products, (2) any materials used to manufacture reagents, feeder cells, and excipients, and (3) materials incorporated in TEMPs.
PURPOSE	This guidance, once finalized, will become a guide to assure the safety, quality, and identity of materials of human and animal origin used in the manufacture of CGT and TEMP products.

PUBLIC CONSULTATION PERIOD: 29 APRIL 2024 - 29 JULY 2024

Source: US FDA. Draft Guidance for Industry. Considerations for the Use of Human-and Animal-Derived Materials and Components in the Manufacture of Cell and Gene Therapy and Tissue-Engineered Medical Products. Accessed through https://www.regulations.gov/docket/FDA-2024-D-1244 on 10 July 2024.

[ICH] HARMONISED GUIDELINE: GENERAL PRINCIPLES ON PLAN, DESIGN AND ANALYSIS OF PHARMACOEPIDEMIOLOGICAL STUDIES THAT UTILIZE REAL-WORLD DATA FOR SAFETY ASSESSMENT OF MEDICINES

SCOPE	The guideline will focus on non-interventional pharmacoepidemiological studies using Real-World Data (RWD) and will include basic principles that may apply to these studies when real-world data elements are included.
PURPOSE	The purpose of this document is to recommend international standards for, and promote harmonization of, the general principles on planning, designing, and analyzing observational (non-interventional) pharmacoepidemiological studies that utilize fit-for-purpose data for safety assessment of medicines (drugs, vaccines, and other biological products).

PUBLIC CONSULTATION PERIOD: 21 MAY 2024 - 30 SEPTEMBER 2024

Source: ICH. Harmonised Guideline. General Principles on Plan, Design and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines. Accessed through https://www.ich.org/page/public-consultations on 17 June 2024.

ISCT

[US FDA] DRAFT GUIDANCE: SAFETY TESTING OF HUMAN ALLOGENEIC CELLS EXPANDED FOR USE IN CELL-BASED MEDICAL PRODUCTS

SCOPE	This guidance applies to allogeneic cell-based products that are regulated by the Office of Therapeutic Products of the Center for Biologics Evaluation and Research (CBER) under section 351 of the Public Health Service Act (42 U.S.C. 262).
PURPOSE	The purpose of this document is to provide guidance on safety testing to assist manufacturers in addressing the requirements of 21 CFR 610.18(c)(1), 21 CFR 312.23(a)(7), and other relevant regulations, as applicable, with respect to human allogeneic cells expanded for use in cell-based medical products.

PUBLIC CONSULTATION PERIOD: 29 APRIL 2024 - 29 JULY 2024

Source: US FDA. Draft Guidance for Industry. Safety Testing of Human Allogeneic Cells Expanded for Use in Cell-Based Medical Products. Accessed through https://www.regulations.gov/docket/FDA-2024-D-1243 on 17 June 2024.

[EMA] REFLECTION PAPER: USE OF REAL-WORLD DATA IN NON-INTERVENTIONAL STUDIES TO GENERATE REAL-WORLD EVIDENCE

SCOPE	The scope of this reflection paper is the design, conduct and analysis of NIS using RWD to generate RWE for regulatory purposes.
PURPOSE	This reflection paper discusses methodological aspects of non-interventional studies (NIS) using real-world data (RWD) in order to generate real-world evidence (RWE) for regulatory purpose. This reflection paper is therefore relevant to all stakeholders involved in the planning, conduct and analysis of NIS using RWD to generate RWE for regulatory purposes, including Marketing Authorisation Holders (MAHs) and Applicants, regulatory authorities, HTA bodies, payers, academia, RWD holders and healthcare professionals' and patients' associations.

PUBLIC CONSULTATION PERIOD: 3 MAY 2024 - 31 AUGUST 2024

Source: EMA. Reflection paper on use of real-world data in non-interventional studies to generate real-world evidence. Accessed through https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-real-world-data-non-interventional-studies-generate-real-world-evidence_en.pdf on 3 July 2024.

[US FDA] DRAFT GUIDANCE FOR INDUSTRY: PLATFORM TECHNOLOGY DESIGNATION PROGRAM FOR DRUG DEVELOPMENT

SCOPE	This guidance provides details about the implementation of the platform technology designation program established by section 506K of the Federal Food, Drug, and Cosmetic Act (FD&C Act).
PURPOSE	This program is intended to result in efficiencies in drug development, manufacturing, and review processes for drug product applications that incorporate designated platform technologies.

PUBLIC CONSULTATION PERIOD: 28 MAY 2024 - 29 JULY 2024

Source: US FDA. Draft Guidance for Industry: Platform Technology Designation Program. Accessed through https://www.regulations.gov/docket/FDA-2024-D-1829 on 3 July 2024.

[BRITISH PHARMACOPOEIA] ATMP GUIDANCE ON T CELL AND NK CELL CHARACTERISATION ASSAYS

SCOPE	This guidance concentrates on potency assays for T cell and NK cell CGT products
PURPOSE	This guidance is intended to be helpful for several reasons including standardised approaches to T cell and NK cell characterization and provide a framework of considerations for validation of T cell and NK cell assays.

PUBLISHED DATE: 8 APRIL

Source: British Pharmacopoeia. Guidance. T cell and NK cell characterization assays. Accessed through https://www.pharmacopoeia.com/content/html/246 on 17 June 2024.

LATEST APPROVED PRODUCTS

LATEST APPROVALS* (H1 2024)

BEQVEZ/DURVEQTIX	Gene Therapy for Adults with Hemophilia B • HEALTH CANADA-Approval [27 Dec 2023]; **US FDA-BLA Approval [25 Apr 2024]**; **EMA-Conditional MA [30 May 2024]**
CASGEVY	The first gene therapy to cure Sickle Cell Disease (SCD) and Transfusion-Dependent b-Thalassemia (TDT) utilizes the genome editing technology (CRISPR/Cas9) • MHRA-Approval [15 Nov 2023]; NHRA-Approval [5 Dec 2023]; US FDA- BLA Approval, SCD Indication [8 Dec 2023]; EMA-Marketing Authorization, SCD & TDT Indication [15 Dec 2023]; **US FDA-BLA Approval, TDT Indication [16 Jan 2024]**
AMTAGVI	First Cellular Therapy to treat Patients with Unresectable or Metastatic Melanoma • **US FDA-BLA Approval [16 Feb 2024]**
LIBMELDY/LENMELDY	First Gene Therapy for Children with Metachromatic Leukodystrophy (MLD) • EMA-Marketing Authorization [17 Dec 2020]; SWISSMEDIC-Marketing Authorization [7 Dec 2023]; **US FDA-BLA Approval [18 Mar 2024]**
ZEVORCABTAGENE AUTOLEUCEL	CAR-T Therapy for Relapsed or Refractory Multiple Myeloma • **NMPA-Approval [1 Mar 2024]**

*This includes the initial/first, secondary, and modifications/updates to existing approvals

ISCT REGULATORY WATCHDOG

REGULATORY WATCHDOG

- An initiative under the ISCT Legal and Regulatory Affairs Committee providing relevant regulatory news updates to our members.

- Featured bi-monthly in the Telegraft, a hub to provide updates from our global community, Regulatory Watchdog provides regulatory updates from the following regions:

REGULATORY WATCHDOG
AUSTRALIA & NEW ZEALAND

REGULATORY WATCHDOG
EUROPE

REGULATORY WATCHDOG
NORTH AMERICA

REGULATORY WATCH DOG
SOUTH & CENTRAL AMERICA

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REFERENCES, METHODOLOGY, GLOSSARY OF KEY TERMS

METHODOLOGY: SOURCES AND SCOPE OF THERAPIES

- Sources for all data come from Citeline (formerly Pharma Intelligence)

- **Pipeline and Trial Data**
  - Data derived from Pharmaprojects and Trialtrove
  - Therapeutic classes included in report categorizations:
  - Gene therapies:
  - Genetically-modified cell therapies:
  - Non-genetically modified cell therapies:

- **Event Data**
  - Data derived from Biomedtracker

GLOSSARY OF KEY TERMS

THERAPY TYPE DEFINITIONS

Gene therapy is the use of genetic material to treat or prevent disease. For the purpose of this report, the following terms shall mean the following:

Gene Therapy	Drugs containing an active ingredient synthesised following vector-mediated introduction of a genetic sequence into target cells in or ex-vivo. Used to replace defective or missing genes (as in cystic fibrosis) as well as to introduce broadly acting genetic sequences for the treatment of multifactorial diseases (e.g. cancer). Direct administration of oligonucleotides without using vectors is covered separately in the Antisense Therapy class, RNA Interference class or Oligonucleotide, Non-Antisense, Non-RNAi class. Platform technologies for gene delivery are covered separately in the Gene Delivery Vector class.

*The key terms and definitions used in this report are referring to the method the data is pulled, organized, and presented.

GLOSSARY OF KEY TERMS

GENETICALLY-MODIFIED CELL THERAPY INCLUDES THE FOLLOWING:

Cellular Therapy, Chimeric Antigen Receptor	Cellular therapy consisting of cells that have been modified to express a chimaeric antigen receptor (CAR). This CAR receptor that gives CAR cells the cells the ability to bind to a specific protein on target cells.
Cellular Therapy, Other	Cellular therapies that do not fall under "Cellular therapy, stem cell", "Cellular therapy, CAR", "Cellular therapy, TIL", or "Cellular therapy, TCR" categories or the specific cellular therapy is unspecified.
Cellular Therapy, Stem Cell	Regenerative therapy which promotes the repair response of injured tissue using stem cells (cells from which all other specialised cells would originate).
Cellular Therapy, T Cell Receptor	Cellular therapies whereby natural T-cells collected for the patient, are engineered to express artificial receptors (usually through viral transfections) that would target specific intracellular antigens (as peptides bound to proteins encoded by the major histocompatibility complex, MHC).

*The key terms and definitions used in this report are referring to the method the data is pulled, organized, and presented.

GLOSSARY OF KEY TERMS

GENETICALLY-MODIFIED CELL THERAPY INCLUDES THE FOLLOWING:

Cellular Therapy, Tumour Infiltrating Lymphocyte	Adoptive cellular transfer of tumour resident T cells from tumour material, their expansion ex vivo and transfer back into the same patient after a lymphodepleting preparative regimen.
Gene Therapy	Drugs containing an active ingredient synthesised following vector-mediated introduction of a genetic sequence into target cells in or ex-vivo. Used to replace defective or missing genes (as in cystic fibrosis) as well as to introduce broadly acting genetic sequences for the treatment of multifactorial diseases (e.g. cancer). Direct administration of oligonucleotides without using vectors is covered separately in the Antisense Therapy class, RNA Interference class or Oligonucleotide, Non-Antisense, Non-RNAi class. Platform technologies for gene delivery are covered separately in the Gene Delivery Vector class.

*The key terms and definitions used in this report are referring to the method the data is pulled, organized, and presented.

GLOSSARY OF KEY TERMS

NON-GENETICALLY-MODIFIED CELL THERAPY INCLUDES THE FOLLOWING:

Cellular Therapy, Chimeric Antigen Receptor	Cellular therapy consisting of cells that have been modified to express a chimaeric antigen receptor (CAR). This CAR receptor that gives CAR cells the cells the ability to bind to a specific protein on target cells.
Cellular Therapy, Other	Cellular therapies that do not fall under "Cellular therapy, stem cell", "Cellular therapy, CAR", "Cellular therapy, TIL", or "Cellular therapy, TCR" categories or the specific cellular therapy is unspecified.
Cellular Therapy, Stem Cell	Regenerative therapy which promotes the repair response of injured tissue using stem cells (cells from which all other specialised cells would originate).
Cellular Therapy, T Cell Receptor	Cellular therapies whereby natural T-cells collected for the patient, are engineered to express artificial receptors (usually through viral transfections) that would target specific intracellular antigens (as peptides bound to proteins encoded by the major histocompatibility complex, MHC).
Cellular Therapy, Tumour Infiltrating Lymphocyte	Adoptive cellular transfer of tumour resident T cells from tumour material, their expansion ex vivo and transfer back into the same patient after a lymphodepleting preparative regimen.

*The key terms and definitions used in this report are referring to the method the data is pulled, organized, and presented.

GLOSSARY OF KEY TERMS

GENETICALLY-MODIFIED CELL THERAPY INCLUDES THE FOLLOWING:

Cellular Therapy, Other	Cellular therapies that do not fall under "Cellular therapy, stem cell", "Cellular therapy, CAR", "Cellular therapy, TIL", or "Cellular therapy, TCR" categories or the specific cellular therapy is unspecified.
Cellular Therapy, Stem Cell	Regenerative therapy which promotes the repair response of injured tissue using stem cells (cells from which all other specialised cells would originate).
Cellular Therapy, T Cell Receptor	Cellular therapies whereby natural T-cells collected for the patient, are engineered to express artificial receptors (usually through viral transfections) that would target specific intracellular antigens (as peptides bound to proteins encoded by the major histocompatibility complex, MHC).
Cellular Therapy, Tumour Infiltrating Lymphocyte	Adoptive cellular transfer of tumour resident T cells from tumour material, their expansion ex vivo and transfer back into the same patient after a lymphodepleting preparative regimen.

GLOSSARY OF KEY TERMS

DEVELOPMENT STATUS DEFINITIONS

Pipeline	Drugs that are in active development
Preclinical	Not yet tested in humans
Phase I	Early trials, usually in volunteers, safety, PK, PD
Phase II	First efficacy trials in small numbers of patients
Phase III	Large-scale trials for registrational data
Pre-registration	Filing for approval made to regulatory authorities
Approved	Approval from relevant regulatory authorities for human use

UNSPECIFIED INDICATIONS

Cancer, unspecified	Indications for which the specific tumor type is not specified
Cancer, hematological, unspecified	Indications for which the specific hematological cancer is not specified
Cancer, solid, unspecified	Indications for which the specific solid tumor is not specified

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