Gene, Cell, & RNA Therapy Landscape Report

Q4 2024 Quarterly Data Report

American Society
of Gene + Cell Therapy

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About the authors

The American Society of Gene & Cell Therapy (ASGCT) is the primary professional membership organization for scientists, physicians, patient advocates, and other professionals with interest in gene and cell therapy.

Our members work in a wide range of settings including universities, hospitals, government agencies, foundations, biotechnology, and pharmaceutical companies. ASGCT advances knowledge, awareness, and education leading to the discovery and clinical application of gene and cell therapies to alleviate human disease to benefit patients and society.

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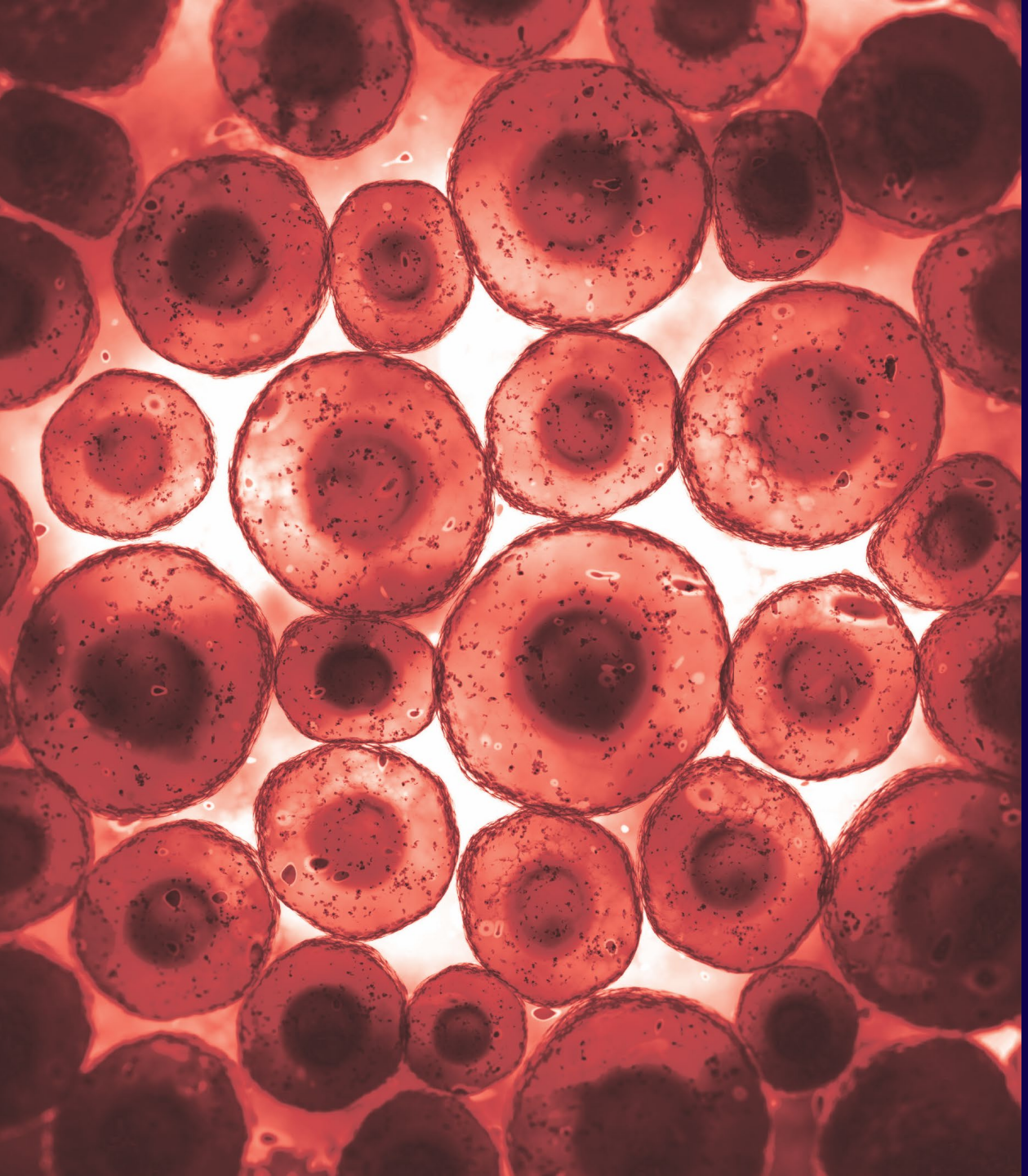
Our global teams of analysts, journalists, and consultants keep their fingers on the pulse of the pharmaceutical, biomedical, and medtech industries, covering it all with expert insights: key diseases, clinical trials, drug R&D and approvals, market forecasts, and more. For more information on one of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



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Introduction

As we wrap up 2024, this report reaffirms the expanding horizons of molecular medicine. While the field has maintained 6-7% growth in the therapeutic pipeline for three years, we're recording remarkable diversification of therapeutic indications. Moreover, Q4 delivered approvals across three modalities: Aucatzyl for acute lymphocytic leukemia, RegeneCyte for blood disorders, and Tryngolza for lipoprotein lipase deficiency. Continuing pipeline dynamics might be the most compelling story.

An 83% surge in pre-registration gene therapy programs—the most in over a year—is another signal that our field is maturing while maintaining robust early-stage innovation. Investment confidence is telling, too; seed and Series A financing reached $609.2 million, up 26% from Q3. Two billion-dollar acquisitions by major pharma companies—Novartis's $1.1B investment in Kate Therapeutics and Roche's $1.5B acquisition of Poseida Therapeutics—underscore the value of next-gen platforms.

The clinical application diversity noted in Q3 is also continuing. RNA therapy trials saw a 53% increase in initiations, with 82% targeting non-oncology indications. Cell therapy trials are similarly expanding beyond cancer, with 58% now focused on non-oncology applications. This broadening therapeutic scope, coupled with steady technological advancement and strong investment flows, suggests we're entering a new phase in the evolution of molecular medicine – one that promises to redefine treatment paradigms across an ever-widening spectrum of diseases.

Thank you,
David Barrett, JD
CEO, ASGCT

Key takeaways from Q4 2024

One new approval seen in each of the gene, cell, and RNA categories in Q4 2024, all in the US

- Aucatzyl, an autologous CD19 chimeric antigen receptor T cell therapy, was approved for acute lymphocytic leukemia; RegeneCyte, an allogeneic hematopoietic stem cell therapy, was approved for patients with blood and immune system disorders; Tryngolza (olezarsen) was approved for lipoprotein lipase deficiency
- In total across 2024, there have been four new gene therapy approvals, two new non-genetically modified cell therapy approvals, and three new RNA approvals

The rate of growth of the gene, cell, and RNA pipeline in 2024 is consistent with the rate seen in the past two years

- Since the start of 2024, the gene, cell, and RNA pipeline landscape has grown by 7%, in line with the annual growth rate seen in 2022 and 2023, which reported growth of 7% and 6%, respectively
- Q4 2024 saw the biggest rise in the number of pre-registration gene therapy programs in over a year, with an increase of 83% since Q3 2024. The average quarter-on-quarter growth at this stage of gene therapy development from the first three quarters of 2024 was 26%

Total dealmaking volume increased across advanced molecular therapy companies

- Continuing the increasing quarterly trend seen since Q2, total dealmaking volume reached 113 and was up by 12% in 2024's final quarter, mainly due to a strong jump in financing transactions
- Big pharma companies notably signed two billion-dollar acquisitions in Q4: Novartis agreed to pay up to $1.1 billion for AAV gene therapy company Kate Therapeutics, and Roche bought allogeneic CAR-T developer Poseida Therapeutics for $1.5 billion
- Dollar volume of seed and Series A financing totaled $609.2 million in Q4, 26% ahead of Q3

Key highlights in Q4 2024

Q4 2024

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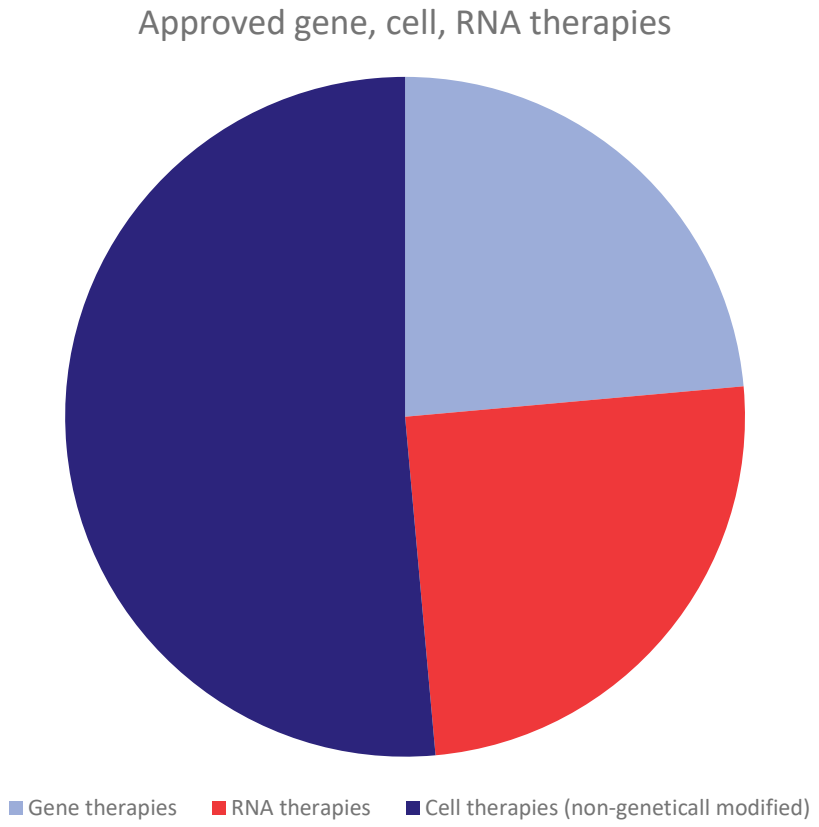
Approved gene, cell, and RNA therapies

Globally, for clinical use:

- 33 gene therapies have been approved (including genetically modified cell therapies)
  - AUCATZYL, Autolus' autologous CD19 chimeric antigen receptor T cell therapy, was approved in the US for the treatment of adults with relapsed or refractory B-cell precursor acute lymphocytic leukemia
- 35 RNA therapies have been approved
  - Ionis Pharmaceuticals' TRYNGOLZA was approved in the US for adults with lipoprotein lipase deficiency
- 72 non-genetically modified cell therapies have been approved
  - StemCyte's REGENECYTE was approved in the US for transplantation in patients with blood and immune system disorders



Source: Pharmaprojects | Citeline, January 2025

Approved gene therapies as of Q4 2024 (1/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved	Originator company
Gendicine	recombinant p53 gene	2004	Head and neck cancer	China	Shenzhen SiBiono GeneTech
Oncorine	E1B/E3 deficient adenovirus	2005	Head and neck cancer; nasopharyngeal cancer	China	Shanghai Sunway Biotech
Rexin-G	mutant cyclin-G1 gene	2006	Solid tumors	Philippines	Epeius Biotechnologies
Neovasculgen	vascular endothelial growth factor gene	2011	Peripheral vascular disease; limb ischemia	Russian Federation, Ukraine	Human Stem Cells Institute
Imlygic	talimogene laherparepvec	2015	Melanoma	US, EU, UK, Australia	Amgen
Strimvelis	autologous CD34+ enriched cells	2016	Adenosine deaminase deficiency	EU, UK	Orchard Therapeutics
Kymriah	tisagenlecleucel-t	2017	Acute lymphocytic leukemia; diffuse large B-cell lymphoma; follicular lymphoma	US, EU, UK, Japan, Australia, Canada, South Korea, Switzerland	Novartis
Luxturna	voretigene neparvovec	2017	Leber's congenital amaurosis; retinitis pigmentosa	US, EU, UK, Australia, Canada, South Korea, Japan	Spark Therapeutics (Roche)
Yescarta	axicabtagene ciloleucel	2017	Diffuse large B-cell lymphoma; non-Hodgkin's lymphoma; follicular lymphoma	US, EU, UK, Japan, Canada, China, Australia	Kite Pharma (Gilead)
Zolgensma	onasemnogene abeparvovec	2019	Spinal muscular atrophy	US, EU, UK, Japan, Australia, Canada, Brazil, Israel, Taiwan, South Korea	Novartis
Zynteglo	betibeglogene autotemcel	2019	Transfusion-dependent beta thalassemia	US	bluebird bio

Source: Pharmaprojects | Citeline, January 2025

Text highlighted in yellow represents new approvals during Q4 2024

Approved gene therapies as of Q4 2024 (2/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved	Originator company
Tecartus	brexucabtagene autoleucel	2020	Mantle cell lymphoma; acute lymphocytic leukemia	US, EU, UK, Australia, Canada	Kite Pharma (Gilead)
Libmeldy	atidarsagene autotemcel	2020	Metachromatic leukodystrophy	EU, UK, Switzerland, US	Orchard Therapeutics
Breyanzi	lisocabtagene maraleucel	2021	Diffuse large B-cell lymphoma; follicular lymphoma; chronic lymphocytic leukemia; mantle cell lymphoma	US, Japan, EU, Switzerland, UK, Canada	Celgene (Bristol Myers Squibb)
Abecma	idecabtagene vicleucel	2021	Multiple myeloma	US, Canada, EU, UK, Japan, Israel, Switzerland	bluebird bio
Delytact	teserpaturev	2021	Malignant glioma	Japan	Daiichi Sankyo
Relma-cel	relmacabtagene autoleucel	2021	Diffuse large B-cell lymphoma; folli cular lymphoma; mantle cell lymph oma	China	JW Therapeutics
Skysona	elivaldogene autotemcel	2021	Early cerebral adrenoleukodystrophy (CALD)	US	bluebird bio
Carvykti	ciltacabtagene autoleucel	2022	Multiple myeloma	US, EU, UK, Japan, Brazil, Australia, Canada, China	Legend Biotech
Upstaza	eladocagene exuparvovec	2022	Aromatic L-amino acid decarboxyla se (AADC) deficiency	EU, UK, Israel, US	PTC Therapeutics
Roctavian	valoctocogene roxaparvovec	2022	Hemophilia A	EU, US	BioMarin
Hemgenix	etranacogene dezaparvovec	2022	Hemophilia B	US, EU, UK, Canada, Switzerland	uniQure
Adstiladrin	nadofaragene firadenovec	2022	Bladder cancer	US	Merck & Co.
Elevidys	delandistrogene moxeparvovec	2023	Duchenne muscular dystrophy	US	Sarepta Therapeutics
Vyjuvek	beremagene geperpavec	2023	Dystrophic epidermolysis bullosa	US	Krystal Biotech
Fucaso	equecabtagene autoleucel	2023	Multiple myeloma	China	Nanjing IASO Biotechnology

Approved gene therapies as of Q4 2024 (3/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved	Originator company
Casgevy	exagamglogene autotemcel	2023	Sickle cell anemia; thalassemia	US, UK, Bahrain, Saudi Arabia, EU, Canada, Switzerland	CRISPR Therapeutics
inaticabtagene autoleucel	inaticabtagene autoleucel	2023	Acute lymphocytic leukemia	China	Juventas Cell Therapy
Lyfgenia	lovotibeglogene autotemcel	2023	Sickle cell anemia	US	bluebird bio
zevorcabtagene autoleucel	zevorcabtagene autoleucel	2024	Relapsed or refractory multiple myeloma	China	CARsgen Therapeutics
Beqvez	fidanacogene elaparvovec	2024	Hemophilia B	Canada, US, EU	Pfizer
Tecelra	afamitresgene autoleucel	2024	Synovial sarcoma	US	Adaptimmune
Aucatzyl	obecabtagene autoleucel	2024	Acute lymphocytic leukemia	US	Autolus

Source: Pharmaprojects | Citeline, January 2025

Text highlighted in yellow represents new approvals during Q4 2024

Approved RNA therapies as of Q4 2024 (1/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Macugen	pegaptanib octasodium	2004	Wet age-related macular degeneration	US, EU, Canada, Argentina, Brazil, Hong Kong, Japan, Mexico, Pakistan, Peru, Philippines, Singapore, Switzerland, Thailand, Turkey, UK,	Gilead Sciences
Kynamro	mipomersen sodium	2013	Homozygous familial hypercholesterolemia	US, Mexico, Argentina, South Korea	Ionis Pharmaceuticals
Exondys 51	eteplirsen	2016	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Spinraza	nusinersen	2016	Muscular atrophy, spinal	US, EU, UK, Canada, Japan, Brazil, Switzerland, Australia, South Korea, China, Argentina, Colombia, Taiwan, Turkey, Hong Kong, Israel	Ionis Pharmaceuticals
Ampligen	rintatolimod	2016	Chronic fatigue syndrome	Argentina	AIM ImmunoTech
Tegsedi	inotersen	2018	Amyloidosis, transthyretin-related hereditary	EU, UK, Canada, US, Brazil	Ionis Pharmaceuticals
Onpattro	patisiran	2018	Amyloidosis, transthyretin-related hereditary	US, EU, UK, Japan, Canada, Switzerland, Brazil, Taiwan, Israel, Turkey, Australia	Alnylam
Vyondys 53	golodirsen	2019	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Waylivra	volanesorsen	2019	Hypertriglyceridemia; lipoprotein lipase deficiency	EU, UK, Brazil, Canada	Ionis Pharmaceuticals
Comirnaty	tozinameran	2020	Infection, coronavirus, novel coronavirus prophylaxis	UK, Bahrain, Israel, Canada, US, Rwanda, Serbia, United Arab Emirates, Macao, Taiwan, Mexico, Kuwait, Singapore, Saudi Arabia, Chile, Switzerland, EU, Ghana, Colombia, Philippines, Indonesia, Australia, Hong Kong, Peru, South Korea, New Zealand, Japan, Brazil, Sri Lanka, Vietnam, South Africa, Thailand, Oman, Egypt, Malaysia	BioNTech
Spikevax	COVID-19 vaccine, Moderna	2020	Infection, coronavirus, novel coronavirus prophylaxis	US, Canada, Israel, EU, Switzerland, Singapore, Qatar, Vietnam, UK, Philippines, Thailand, Japan, South Korea, Brunei, Paraguay, Taiwan, Botswana, India, Indonesia, Saudi Arabia, Mexico, Australia, Nigeria, Colombia	Moderna Therapeutics

Approved RNA therapies as of Q4 2024 (2/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Givlaari	givosiran	2020	Porphyria	US, EU, UK, Canada, Switzerland, Brazil, Israel, Japan, Australia	Alnylam
Oxlumo	lumasiran	2020	Hyperoxaluria	EU, UK, US, Brazil	Alnylam
Viltepso	viltolarsen	2020	Dystrophy, Duchenne muscular	US, Japan	NS Pharma
Leqvio	inclisiran	2020	Atherosclerosis; heterozygous familial hypercholesterolemia; hypercholesterolemia	EU, UK, Australia, Canada, Israel, US, Saudi Arabia, Japan, China	Alnylam
Amondys 45	casimersen	2021	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Nulibry	fosdenopterin	2021	Molybdenum cofactor deficiency	US, EU, UK, Israel	Orphatec
Gennova COVID-19 vaccine	COVID-19 vaccine, Gennova Biopharmaceuticals	2022	Infection, coronavirus, novel coronavirus prophylaxis	India	Gennova Biopharmaceuticals
Amvuttra	vutrisiran	2022	Amyloidosis, transthyretin-related hereditary	US, EU, UK	Alnylam
Moderna Spikevax Bivalent Original/Omicron vaccine	COVID-19 bivalent original/Omicron vaccine, Moderna	2022	Infection, coronavirus, novel coronavirus prophylaxis	UK, Canada, Taiwan, Switzerland, Japan, EU, Australia, South Korea, Singapore, US	Moderna Therapeutics
ARCoV	COVID-19 vaccine, Suzhou Abogen Biosciences	2022	Infection, coronavirus, novel coronavirus prophylaxis	Indonesia	Suzhou Abogen Biosciences
Pfizer & BioNTech's Omicron BA.4/BA.5-adapted bivalent booster vaccine	Omicron BA.4/BA.5-adapted bivalent booster vaccine	2022	Infection, coronavirus, novel coronavirus prophylaxis	US, UK	BioNTech
CSPC Pharmaceutical COVID-19 vaccine	COVID-19 vaccine, CSPC Pharmaceutical	2023	Infection, coronavirus, novel coronavirus prophylaxis	China	CSPC Pharmaceutical
Sinocelltech COVID-19 vaccine	COVID-19 alpha/beta/delta/Omicron variants S-trimer quadrivalent recombinant protein vaccine	2023	Infection, coronavirus, novel coronavirus prophylaxis	China, UAE, US	Sinocelltech

Source: Pharmaprojects | Citeline, January 2025

Text highlighted in yellow represents new approvals during Q4 2024

Approved RNA therapies as of Q4 2024 (3/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Izervay	avacincaptad pegol sodium	2023	Wet age-related macular degeneration	US	Archemix
Qalsody	tofersen	2023	Amyotrophic lateral sclerosis	US, EU, Japan, China	Ionis Pharmaceuticals
ARCT-154	COVID-19 mRNA vaccine, Arcturus	2023	Infection, coronavirus, novel coronavirus prophylaxis	Japan	Arcturus Therapeutics
Daichirona	COVID-19 vaccine, Daiichi Sankyo	2023	Infection, coronavirus, novel coronavirus prophylaxis	Japan	Daiichi Sankyo
Wainua	eplontersen	2023	Transthyretin-related hereditary amyloidosis	US, Canada	Ionis Pharmaceuticals
Rivfloza	nedosiran	2023	Hyperoxaluria	US	Dicerna Pharmaceuticals
SYS-6006.32	Bivalent COVID-19 mRNA vaccine, CSPC Pharmaceutical	2023	Infection, coronavirus, novel coronavirus prophylaxis	China	CSPC Pharmaceutical
RQ-3033	COVID-19 mRNA vaccine, Walvax Biotechnology	2023	Infection, coronavirus, novel coronavirus prophylaxis	China	Walvax Biotechnology
Rytelo	imetelstat	2024	Myelodysplastic syndrome	US	Geron
mRESVIA	respiratory syncytial virus vaccine, Moderna Therapeutics	2024	Respiratory syncytial virus prophylaxis	US, EU	Moderna Therapeutics
Tryngolza	olezarsen	2024	Lipoprotein lipase deficiency	US	Ionis Pharmaceuticals

*For COVID-19 vaccines, this includes emergency use authorization and full approvals

Source: Pharmaprojects | Citeline, January 2025

Text highlighted in yellow represents new approvals during Q4 2024

Key highlights in Q4 2024

Noteworthy events that happened in Q4 2024

Drug	Event Type	Indication	Molecule	Event Date
Regenecyte	Regenerative Medicine Advanced Therapy (RMAT) Designation	COVID-19 Treatment	Cellular	03 October 2024
Wainua	Approval (UK)	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy	Antisense	14 October 2024
RESTEM	Orphan Drug Designation (US)	Dermatomyositis	Cellular	17 October 2024
VP-001	Orphan Drug Designation (US)	Retinitis Pigmentosa (RP) (Ophthalmology)	Antisense	18 October 2024
MB-108	Orphan Drug Designation (US)	Brain Cancer (Malignant Glioma; AA and glioblastoma (GBM))	Other Nucleic Acid	22 October 2024
Olezarsen	MAA Submission (Europe)	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Antisense	06 November 2024
LION-101	Rare Pediatric Disease (RPD); Orphan Drug Designation (US)	Limb-Girdle Muscular Dystrophy (LGMD)	Other Nucleic Acid	07 November 2024
Aucatzyl	Approval (US)	Acute Lymphoblastic Leukemia (ALL)	Cellular	08 November 2024
Wainua	Filing for Approval (China)	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy	Antisense	12 November 2024
GNSC-001	Fast Track Status	Osteoarthritis	Other Nucleic Acid	12 November 2024
KYV-101	Orphan Drug Designation (Europe)	Myasthenia Gravis (MG)	Other Nucleic Acid	13 November 2024
KEBILIDI	Accelerated/Conditional Approval (US)	Neurology - Other	Viral Gene Therapy	13 November 2024
Plozasiran	NDA/BLA Filing	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Oligonucleotide	18 November 2024
Regenecyte	Approval (US)	Patients with blood and immune system disorders	Cellular	20 November 2024
OCU410ST	Orphan Drug Designation (Europe)	Stargardt Disease (Ophthalmology)	Other Nucleic Acid	20 November 2024
Deramiocel	Orphan Drug Designation (Europe); ATMP Classification	Duchenne Muscular Dystrophy (DMD)	Cellular	20 November 2024
RP-1	NDA/BLA Filing; Breakthrough Therapy Designation (US)	Melanoma	Other Nucleic Acid	21 November 2024
NS-089/NCNP-02	Orphan Drug Designation (Japan)	Duchenne Muscular Dystrophy (DMD)	Antisense	02 December 2024
SC291	Fast Track Status	Systemic Lupus Erythematosus (SLE)	Cellular	02 December 2024
STK-001	Breakthrough Therapy Designation (US)	Dravet Syndrome (Epilepsy)	Antisense	04 December 2024
Revascor	Regenerative Medicine Advanced Therapy (RMAT) Designation	Chronic Heart Failure - Reduced Ejection Fraction (Chronic HFrEF)	Cellular	04 December 2024
AlloNK	Regenerative Medicine Advanced Therapy (RMAT) Designation	Hodgkin's Lymphoma	Cellular	05 December 2024
SER-155	Breakthrough Therapy Designation (US)	Bone Marrow Transplant and Stem Cell Transplant	Cellular	09 December 2024
CAM-101	Fast Track Status	Dry Eye (Ophthalmology)	Cellular	09 December 2024
AAV-AQP1	Regenerative Medicine Advanced Therapy (RMAT) Designation	Xerostomia (Dry Mouth)	Viral Gene Therapy	09 December 2024
Ryoncil	Approval (US)	Graft vs. Host Disease (GVHD) - Treatment	Cellular	18 December 2024
BGC-101	Fast Track Status	Peripheral Arterial Disease (PAD)	Cellular	19 December 2024
UX111	NDA/BLA Filing	Mucopolysaccharidosis IIIA (MPS IIIA; Sanfilippo A Syndrome)	Viral Gene Therapy	19 December 2024
Olezarsen	Approval (US)	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Antisense	19 December 2024
Alhemo	Approval (US)	Hemophilia A and B - General Clotting Products	Cellular	20 December 2024

Source: Biomedtracker | Citeline, January 2025

Pipeline overview

Q4 2024

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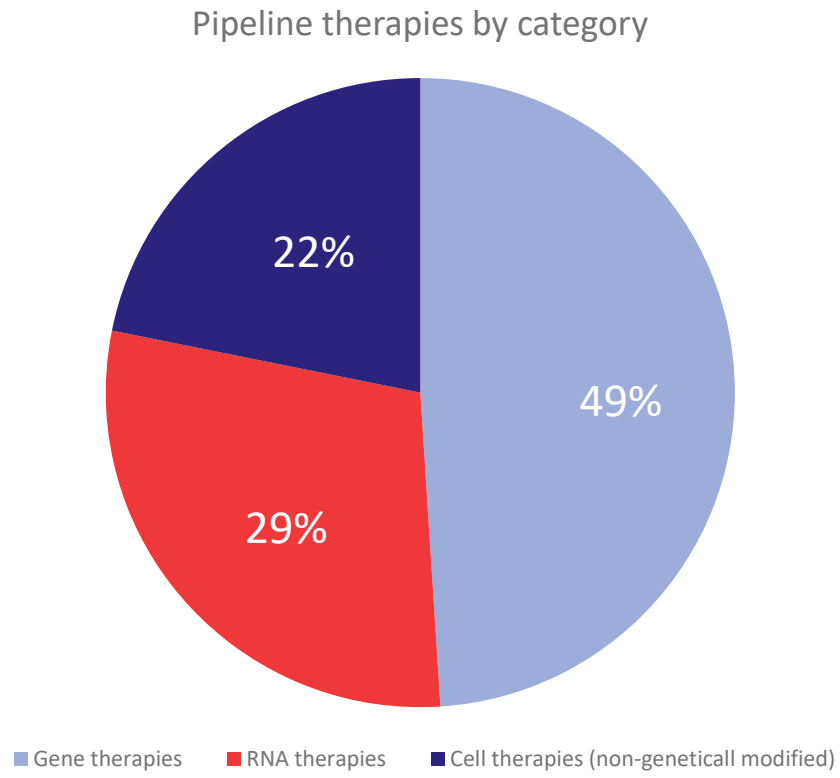
Pipeline of gene, cell, and RNA therapies

4,238 therapies are in development, ranging from preclinical through pre-registration

- 2,117 gene therapies (including genetically modified cell therapies such as CAR-T cell therapies) are in development, accounting for 49% of gene, cell, and RNA therapies
- 944 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies



Source: Pharmaprojects | Citeline, January 2025

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q4 2024

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Gene therapy pipeline: quarterly comparison

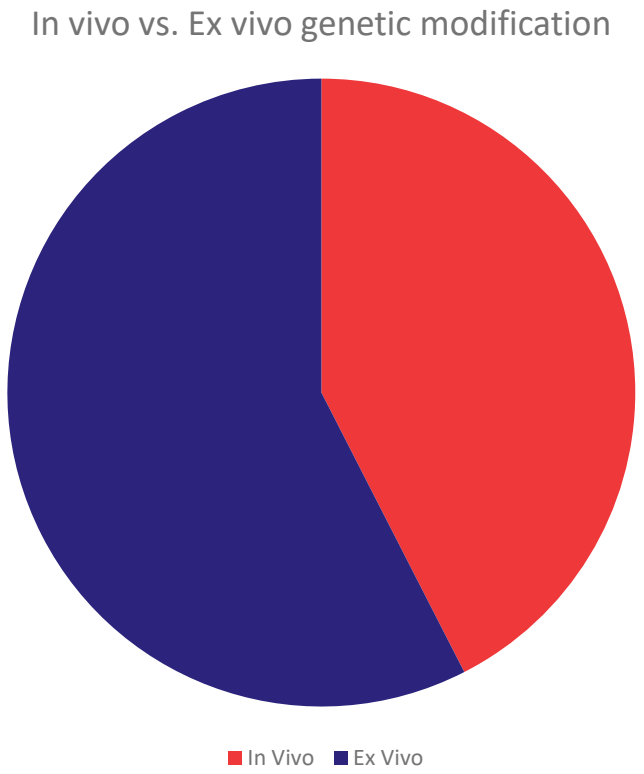
- An increase in the number of gene therapy programs was seen at all stages of pipeline development except for Phase III, which has remained at the same number as seen in the previous quarter
- The number of gene therapies in pre-registration has nearly doubled since Q3 2024; the largest increase seen in over a year for pre-registration therapies
- Therapies currently in pre-registration:
  - In the US
    - RP-L201 (Rocket Pharmaceuticals)
    - Pz-cel (Abeona)
    - NT-501 (Neurotech Pharmaceuticals)
    - UX111 (Ultragenyx)
    - vusolimogene oderparepvec (Replimune)
    - PRGN-2012 (Precigen)
  - In the EU
    - RP-L102 (Rocket Pharmaceuticals)
  - In China
    - BBM-H901 (Belief BioMed)
    - donaperminogene seltoplasmid (Helixmith)
    - pulkilumab (pCAR-19B) cells (Chongqing Precision Biotech)
  - In South Korea
    - Anbal-cel (Curocell)

Global Status	Q4 2023	Q1 2024	Q2 2024	Q3 2024	Q4 2024
Preclinical	1,528	1,471	1,436	1,393	1,424
Phase I	270	301	314	318	341
Phase II	274	282	279	289	306
Phase III	33	35	34	35	35
Pre-registration	6	4	5	6	11
Total	**2,111**	**2,093**	**2,068**	**2,041**	**2,117**

Sources: Pharmaprojects | Citeline, January 2025

Genetic modification: *In vivo* vs. *Ex vivo*

- *Ex vivo* genetic modification is more widely used for gene therapies in pipeline development
- In Q4 2024, *in vivo* delivery techniques were used in 42% of gene therapies

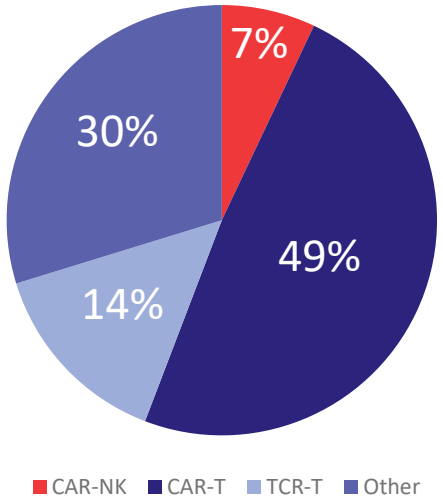


Source: Cell and Gene Therapy dashboard | Citeline, January 2025

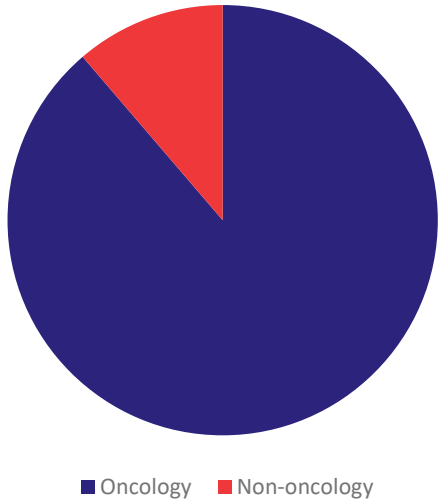
Gene therapy breakdown: CAR-Ts continue to dominate the pipeline

- CAR-T cell therapies remained the most common technology used in the pipeline of genetically modified cell therapies (preclinical through to pre-registration), representing 49%, followed by the "other" category at 30%, which includes a list of less commonly used technologies such as TCR-NK, CAR-M, and TAC-T
- 97% of CAR-T cell therapies were in development for cancer indications. The remaining non-oncology indications included scleroderma, HIV/AIDS, and autoimmune disease (unspecified)

Genetically modified cell therapy breakdown



CAR-T breakdown

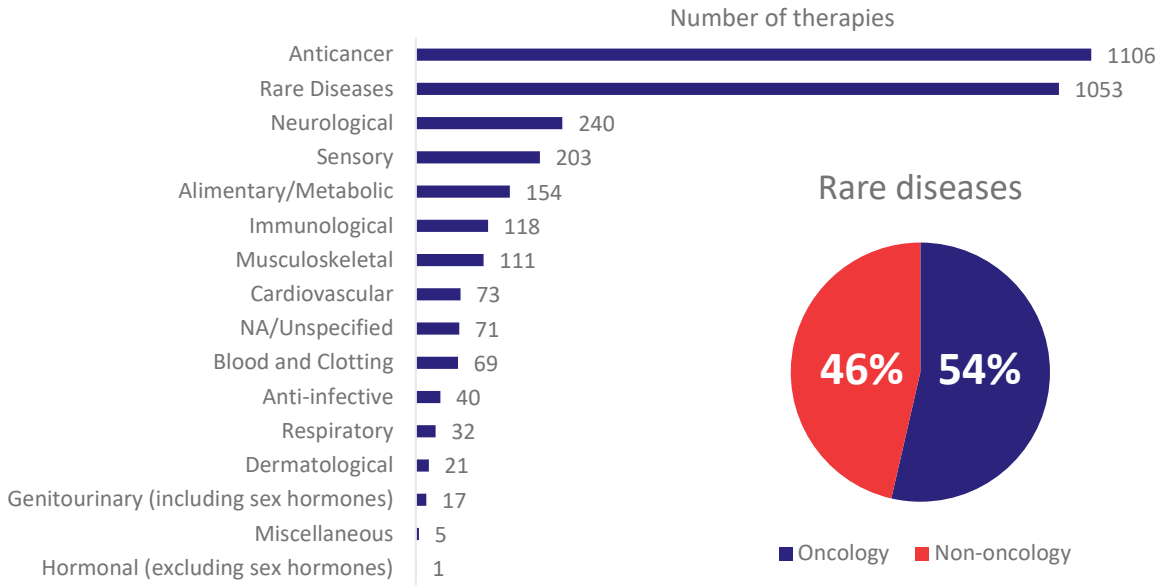


Source: Cell and Gene Therapy dashboard | Citeline, January 2025

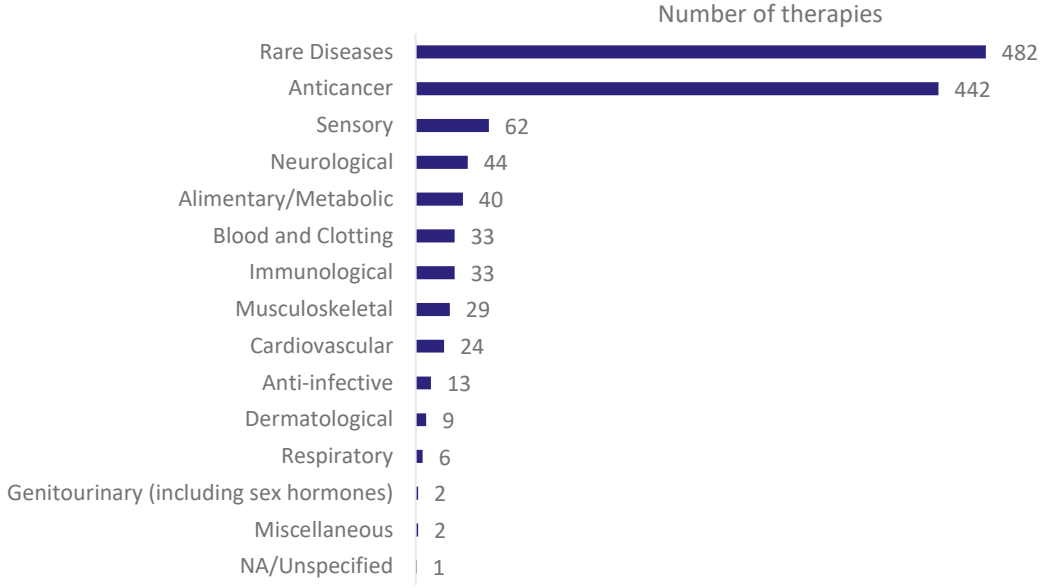
Gene therapy pipeline: most commonly targeted therapeutic areas

- Oncology and rare diseases remained the top areas of gene therapy development in both the overall pipeline (preclinical to pre-registration) and in the clinic (Phase I to pre-registration)
- Development for rare diseases most commonly occurred in oncology, representing a majority of 54% compared to non-oncology rare disease gene therapy pipeline development, one percentage point higher than the previous quarter

Number of therapies from preclinical through pre-registration



Therapies in the clinic (excludes preclinical development)



Source: Pharmaprojects | Citeline, January 2025

Note: Figures based on indications in pipeline development only for each therapy

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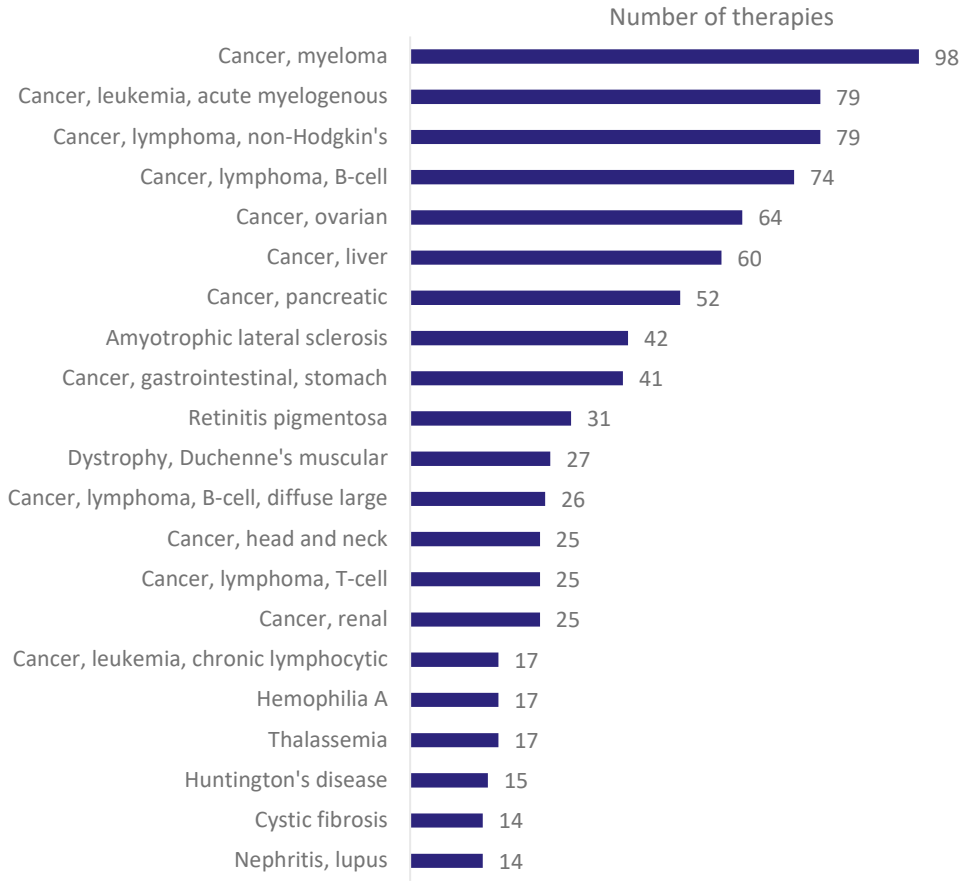
Gene therapy pipeline: most common rare diseases targeted

- For the 1,053 pipeline (preclinical to pre-registration) gene therapies being developed for rare diseases, eight out of the top 10 rare diseases were oncological, a trend seen throughout the past three years
- In the same order as the previous three quarters, the top five rare diseases for which gene therapies are being developed are:

1. Myeloma
2. Acute myelogenous leukemia
3. Non-Hodgkin's lymphoma
4. B-cell lymphoma
5. Ovarian cancer



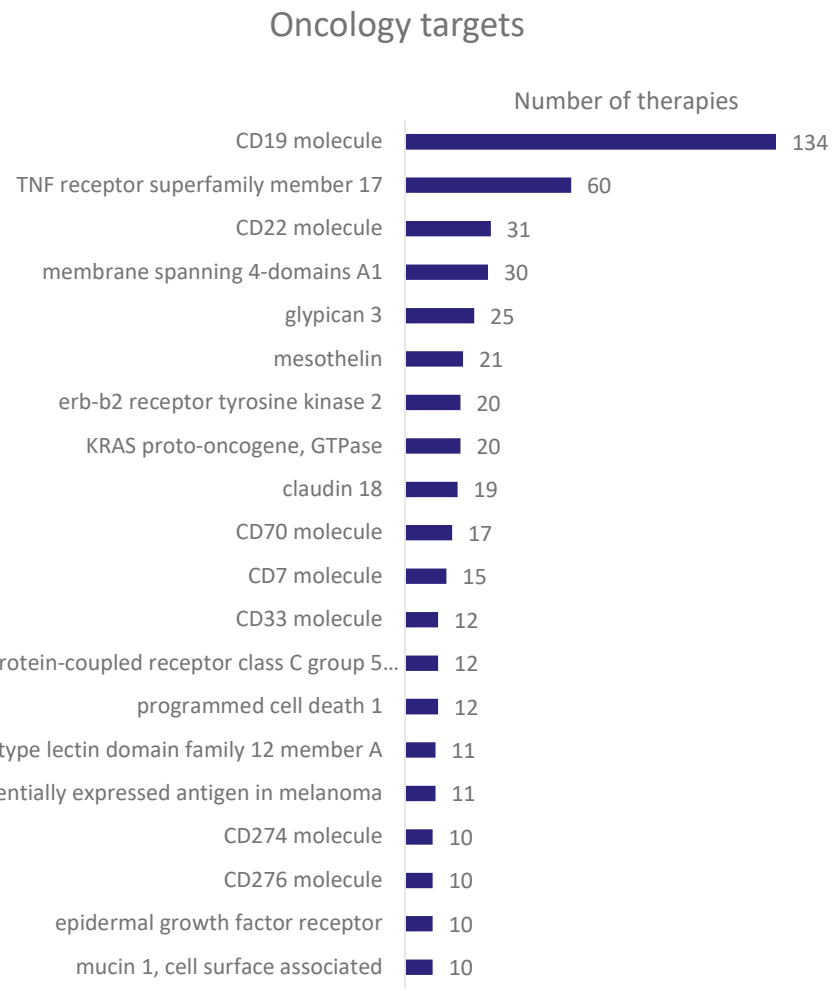
Source: Pharmaprojects | Citeline, January 2025

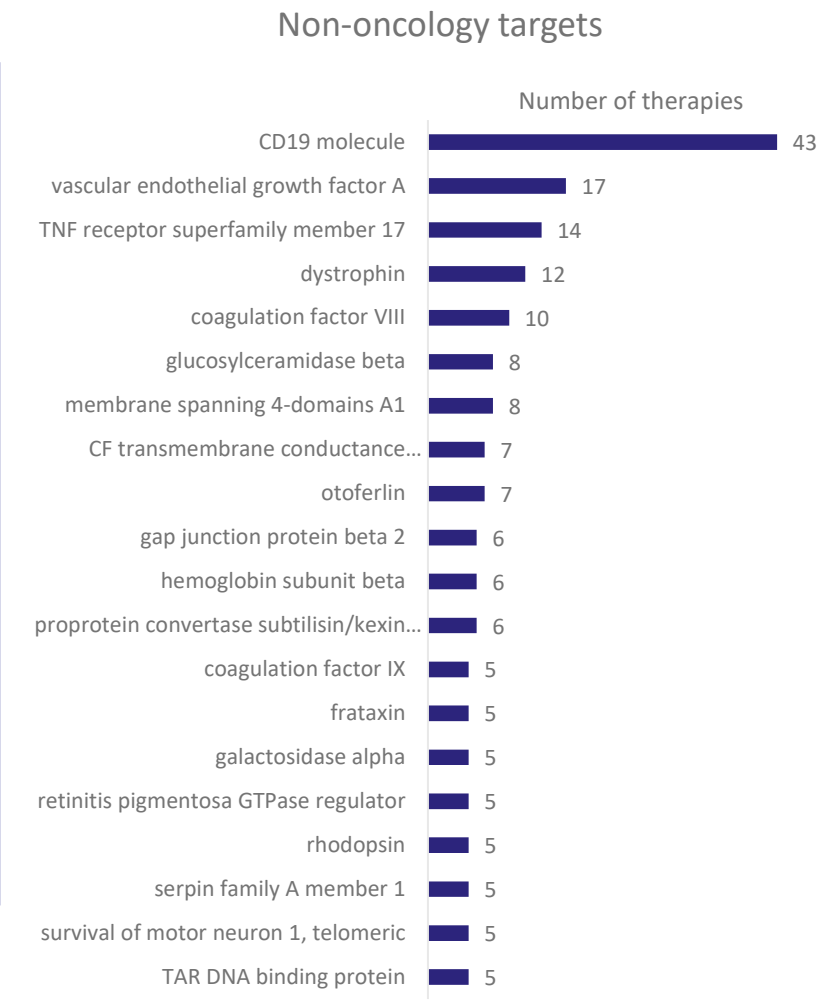
Note: Figures based on indications in pipeline development only for each therapy

Gene therapy pipeline: most common targets

Of the gene therapies in preclinical trials through pre-registration for which targets were disclosed:

- CD19 molecule; B-cell maturation antigen (BCMA), also known as TNF receptor superfamily member 17; and CD22 molecule continued to be the top three most common targets for oncology indications
- CD19 molecule; vascular endothelial growth factor A; and TNF receptor superfamily member 17 continued to be the top three most common targets for non-oncology indications, as found in Q3 2024

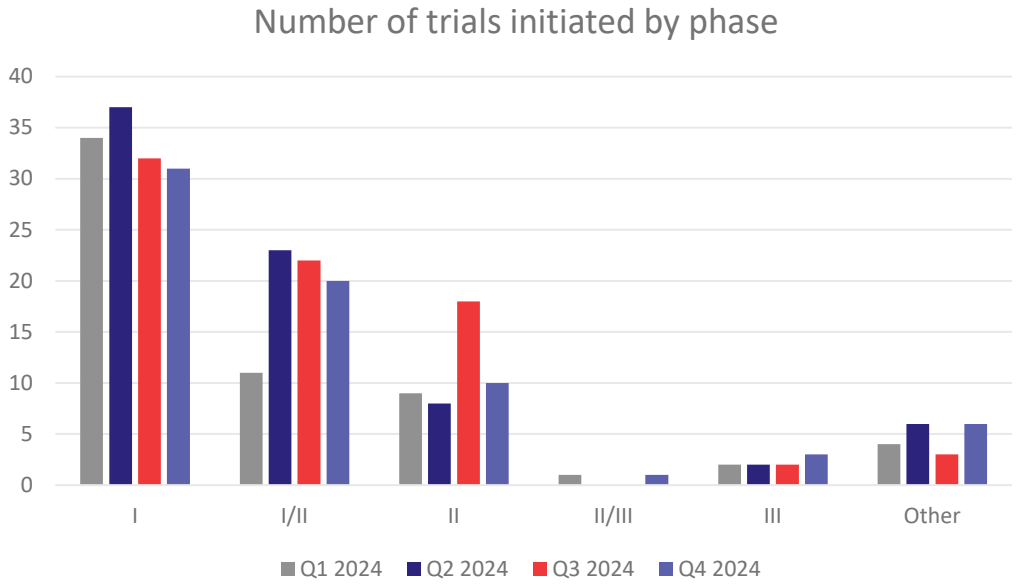


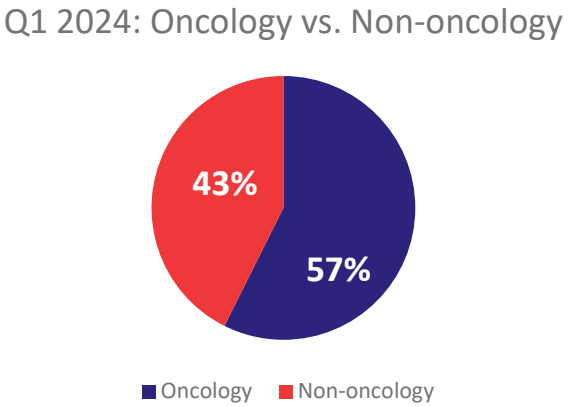


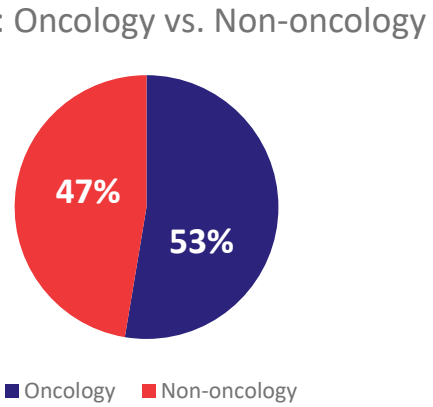
Source: Pharmaprojects | Citeline, January 2025

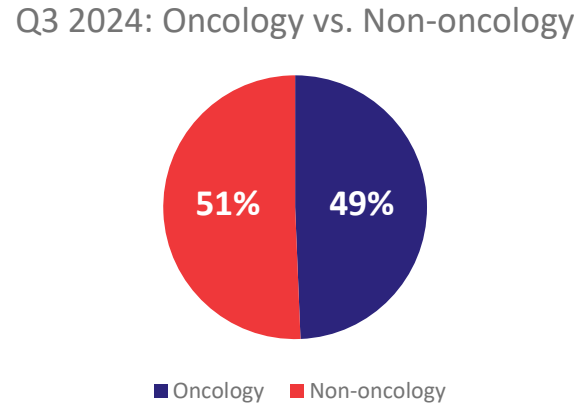
Gene therapy clinical trial activity

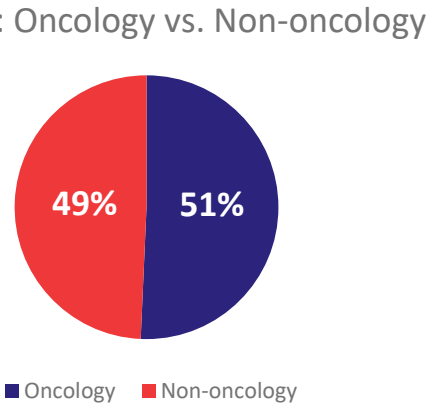
- The proportion of gene therapy trials for non-oncology indications decreased for the first time in over a year to 49%, breaking the trend of growth in the proportion of non-oncology gene therapy trials
- 71 gene therapy trials were initiated in Q4 2024, six fewer than the previous quarter











Source: Trialtrove | Citeline, January 2025

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Non-genetically modified cell therapy pipeline

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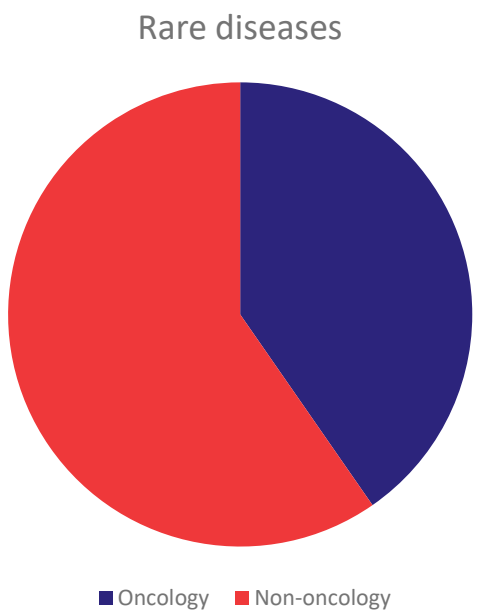
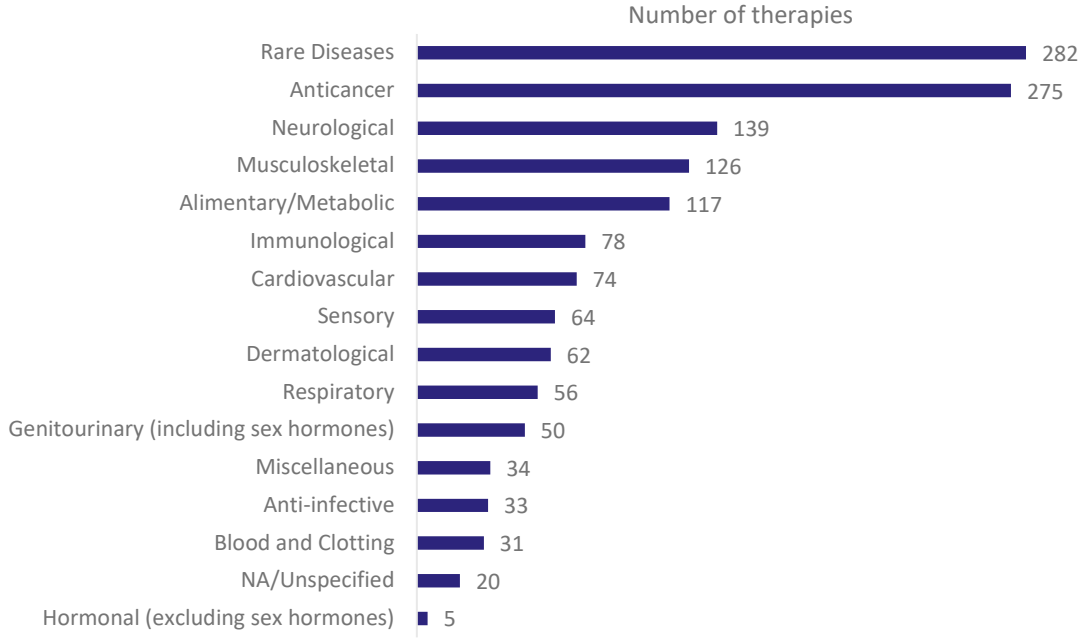
Non-genetically modified cell therapy pipeline: most commonly targeted therapeutic areas

Of the cell therapies in development (preclinical through pre-registration):

- Oncology and rare diseases remained the top areas of non-genetically modified cell therapy development
- Of the non-genetically modified cell therapies in preclinical to pre-registration stages for rare diseases, 61% were in development for non-oncology rare diseases, as found in the previous quarter





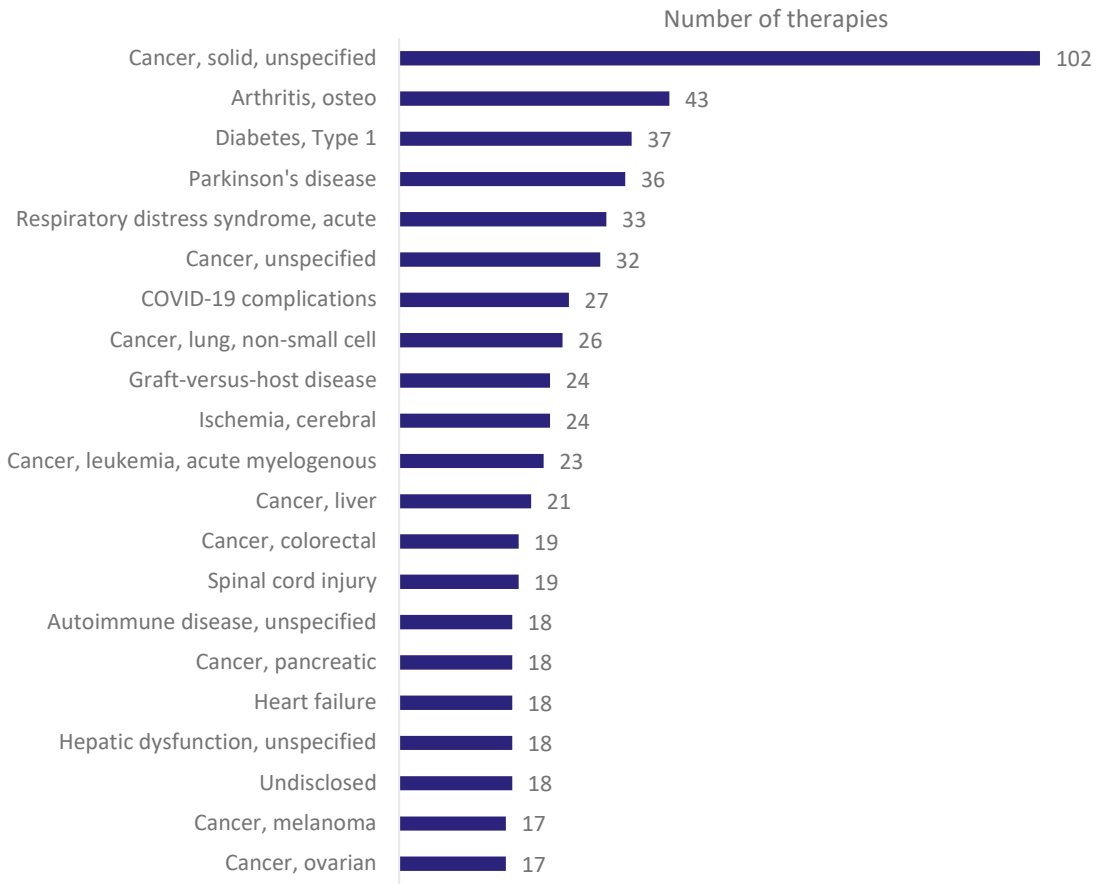
Source: Pharmaprojects | Citeline, January 2025

Note: Figures based on indications in pipeline development only for each therapy

Non-genetically modified cell therapy pipeline: most common diseases targeted

Of the therapies for which indications are specified, in the same order as found in the previous quarter, the most targeted indications in Q4 2024 were:

1. Osteoarthritis
2. Type 1 diabetes
3. Parkinson's disease



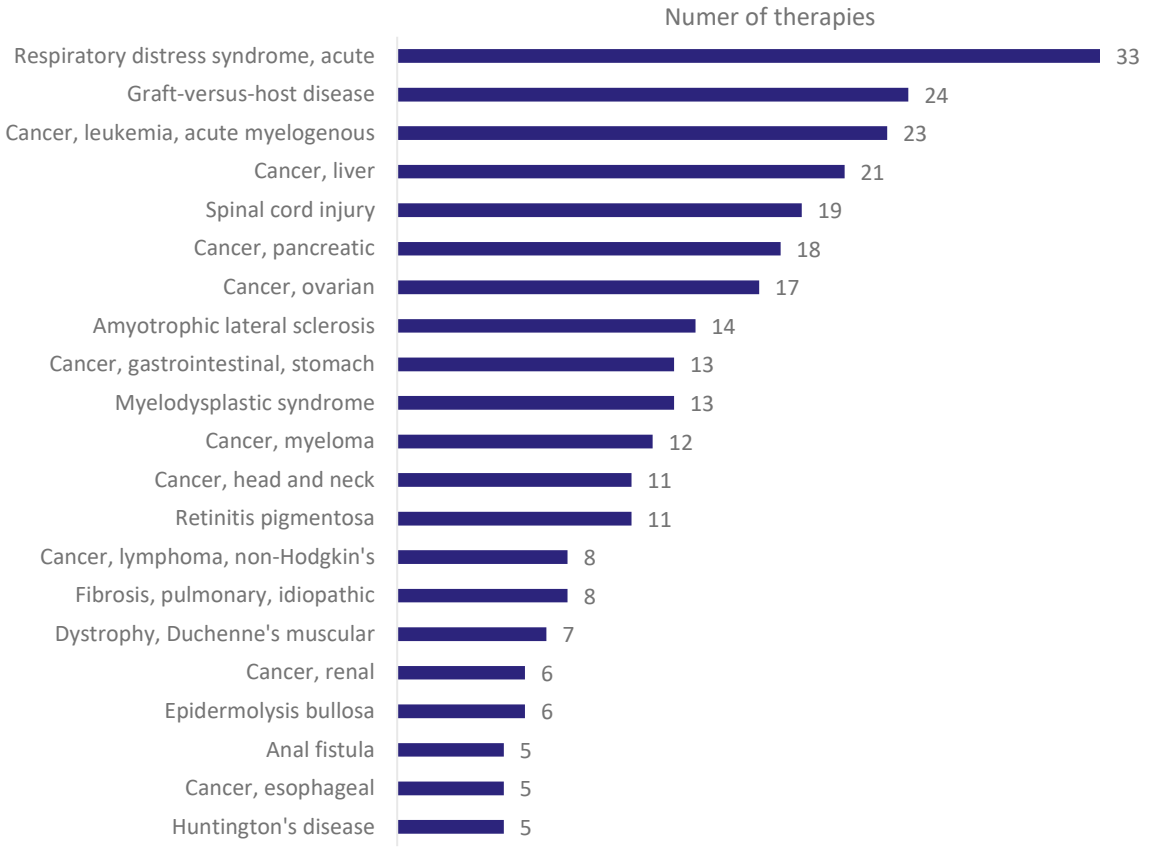
Source: Pharmaprojects | Citeline, January 2025

Note: Figures based on indications in pipeline development only for each therapy

Non-genetically modified cell therapy pipeline: most common rare diseases targeted

Of the therapies in development (preclinical through pre-registration) for rare diseases:

- The top three oncology indications were acute myelogenous leukemia, liver cancer, and pancreatic cancer
- The top three non-oncology indications were acute respiratory distress syndrome, graft-versus-host disease, and spinal cord injury

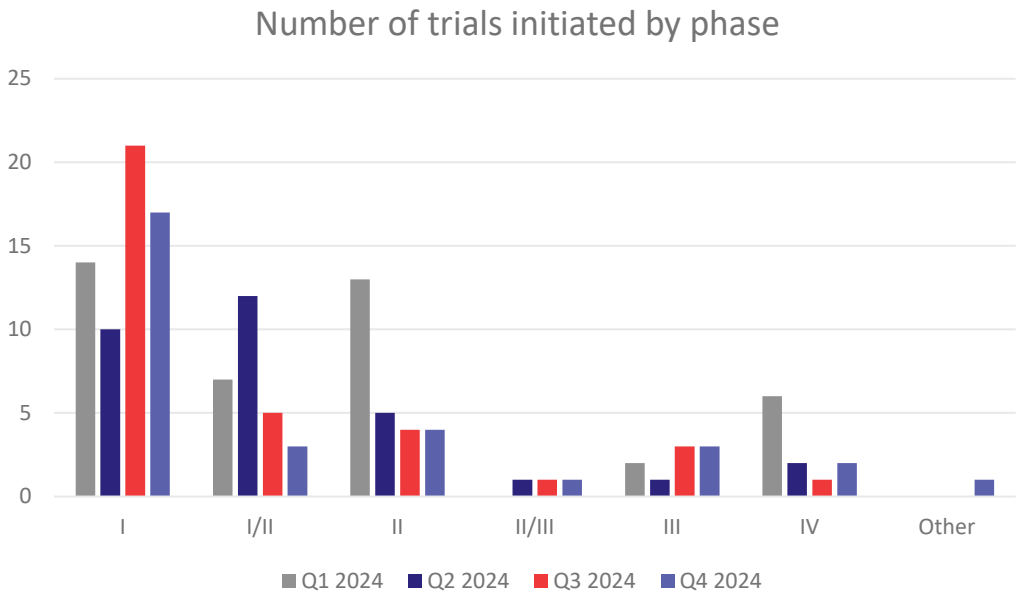


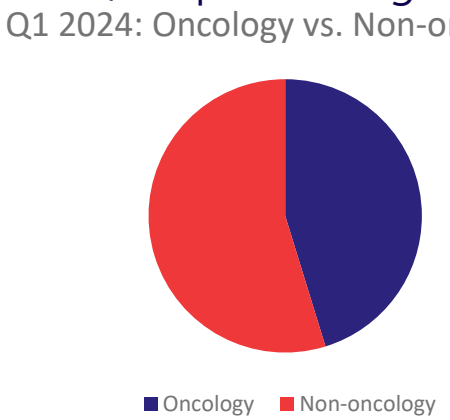
Source: Pharmaprojects | Citeline, January 2025

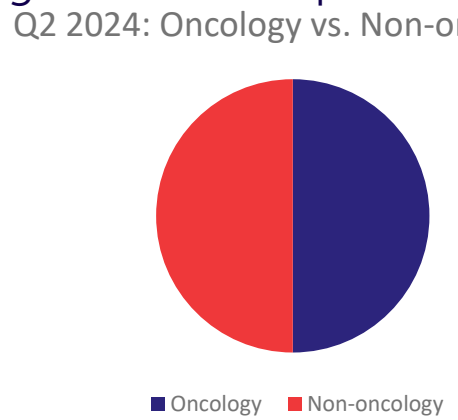
Note: Figures based on indications in pipeline development only for each therapy

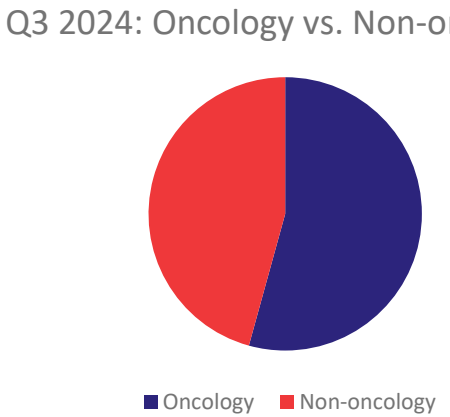
Non-genetically modified cell therapy trial activity

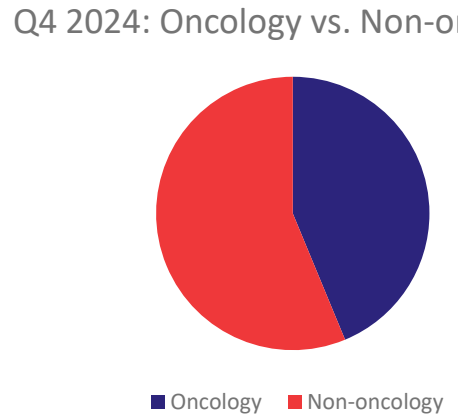
- 31 trials were initiated for non-genetically modified cell therapies in Q4 2024, four fewer than in Q3 2024
- Of these 31, 58% were for non-oncology indications, 12 percentage points higher than the previous quarter











Source: Trialtrove | Citeline, January 2025

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RNA therapy pipeline

Q4 2024

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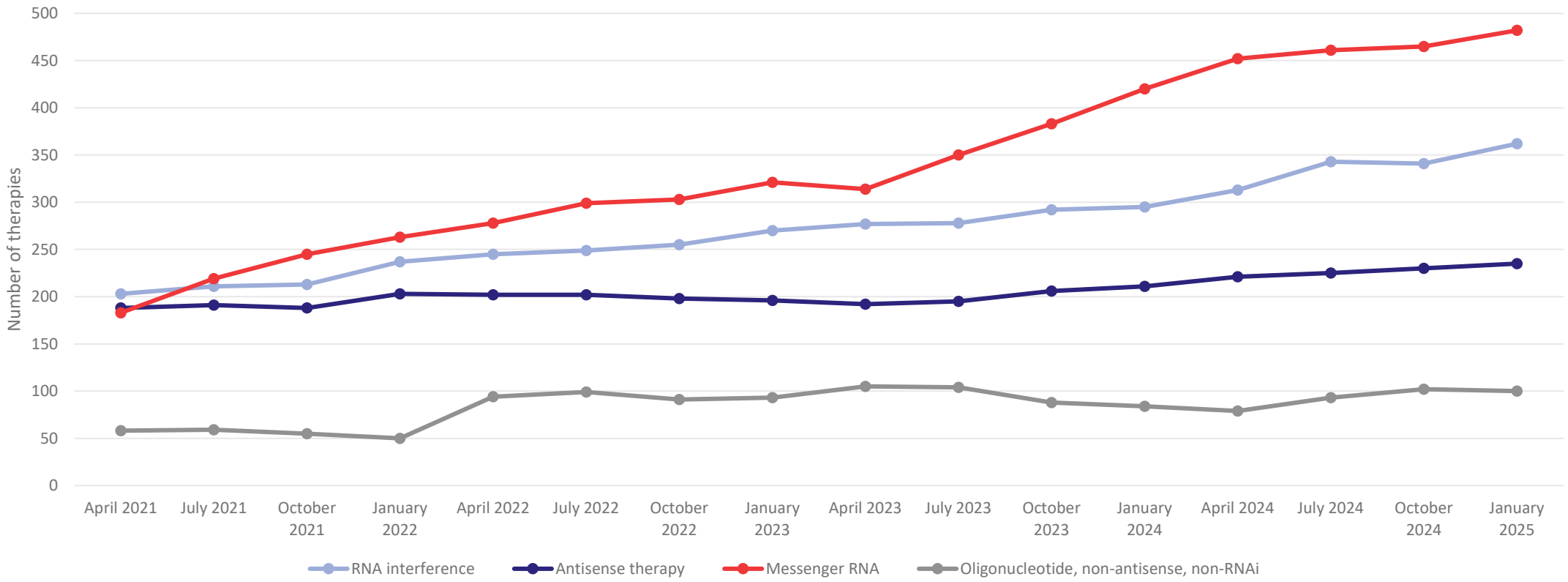
RNA therapy pipeline: most common modalities

- Of RNA therapies in the pipeline, messenger RNA (mRNA) and RNA interference (RNAi) continued to be the preferred RNA modalities for research



Source: Pharmaprojects | Citeline, January 2025

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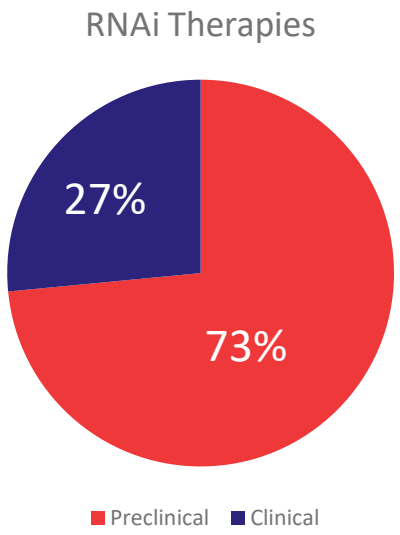
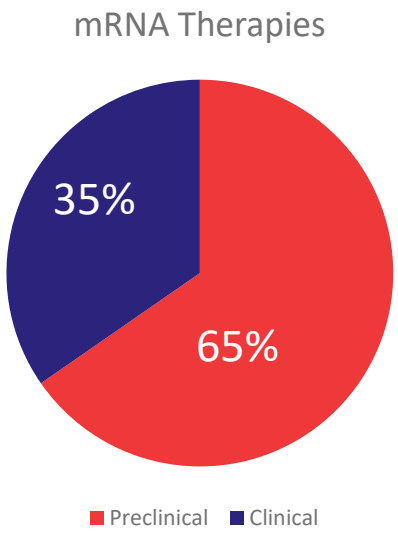
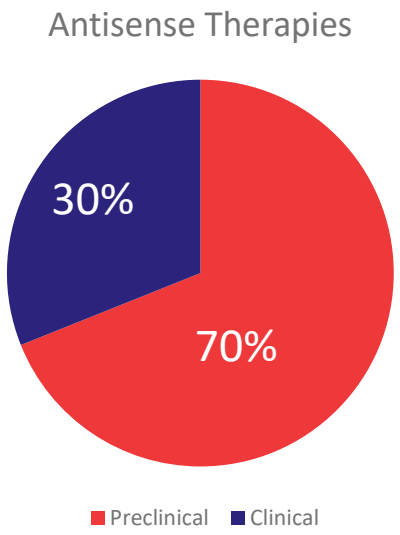
RNAi, mRNA, and antisense oligonucleotides: preclinical vs. clinical

- The majority of RNAi, mRNA, and antisense therapies in development were in the preclinical stage, representing 73%, 65%, and 70% of their respective pipelines





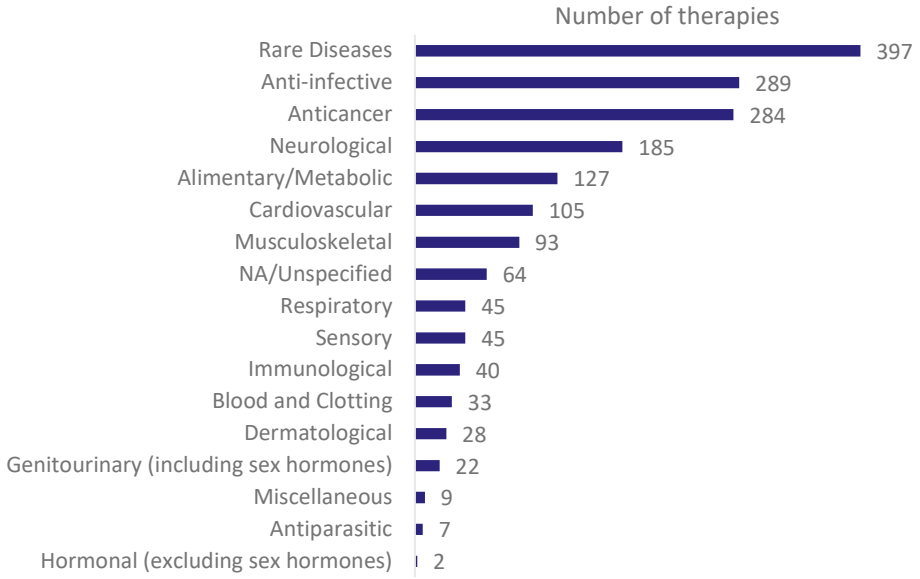


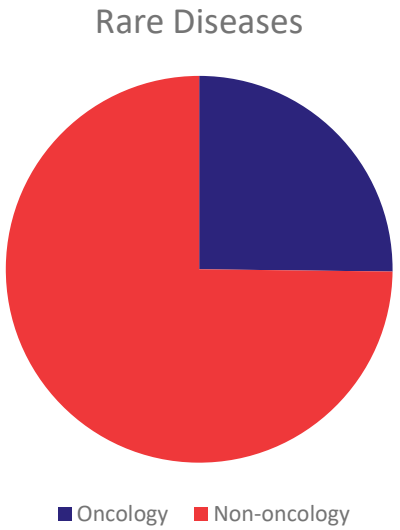
Source: Pharmaprojects | Citeline, January 2025

RNA therapies: most commonly targeted therapeutic areas

Of the 1,261 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Rare diseases remained the top targeted therapeutic area by RNA therapies, while anti-infective indications have regained position as the second most commonly targeted
- Non-oncology indications continued to be the most targeted rare diseases by RNA therapies, representing a majority of 76%





Source: Pharmaprojects | Citeline, January 2025

Note: Figures based on indications in pipeline development only for each therapy

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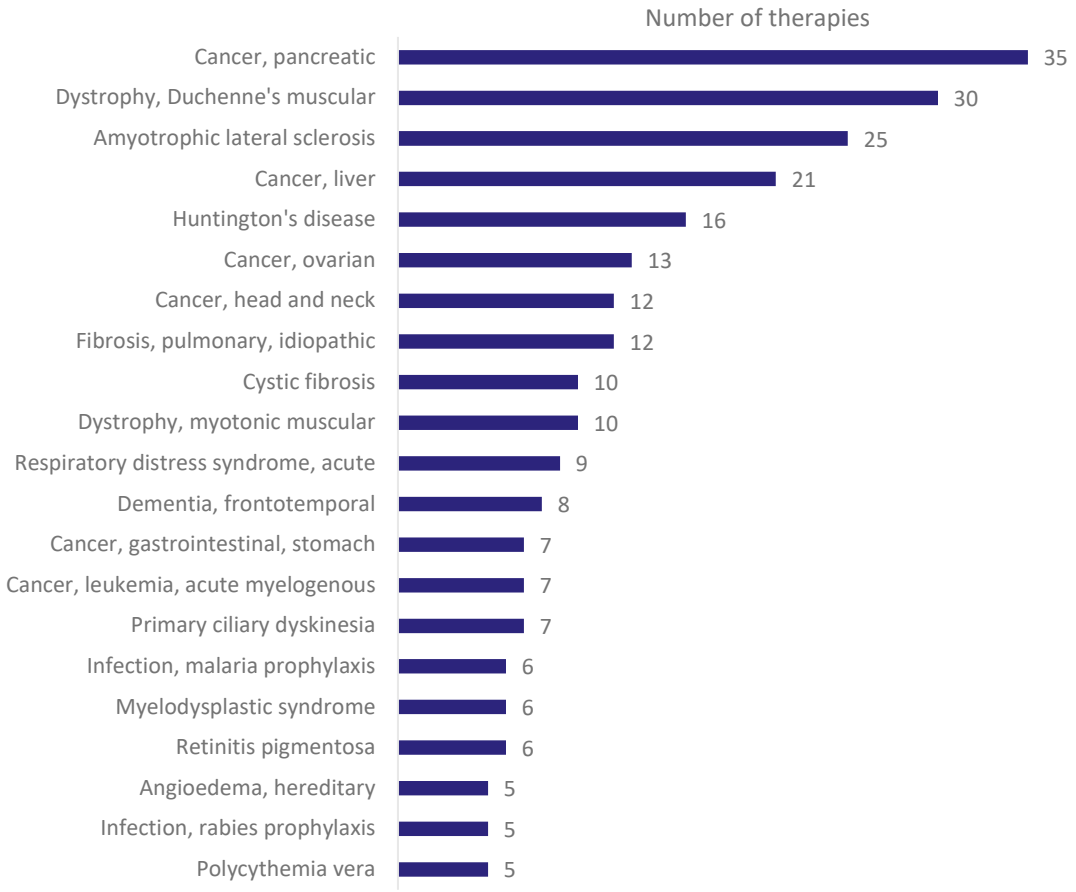
RNA therapies: most common rare diseases targeted

Of the RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Top specified rare oncology indications were pancreatic, liver, and ovarian cancer
- For non-oncology rare diseases, Duchenne muscular dystrophy, amyotrophic lateral sclerosis, and Huntington's disease were the most targeted indications



Source: Pharmaprojects | Citeline, January 2025

Note: Figures based on indications in pipeline development only for each therapy

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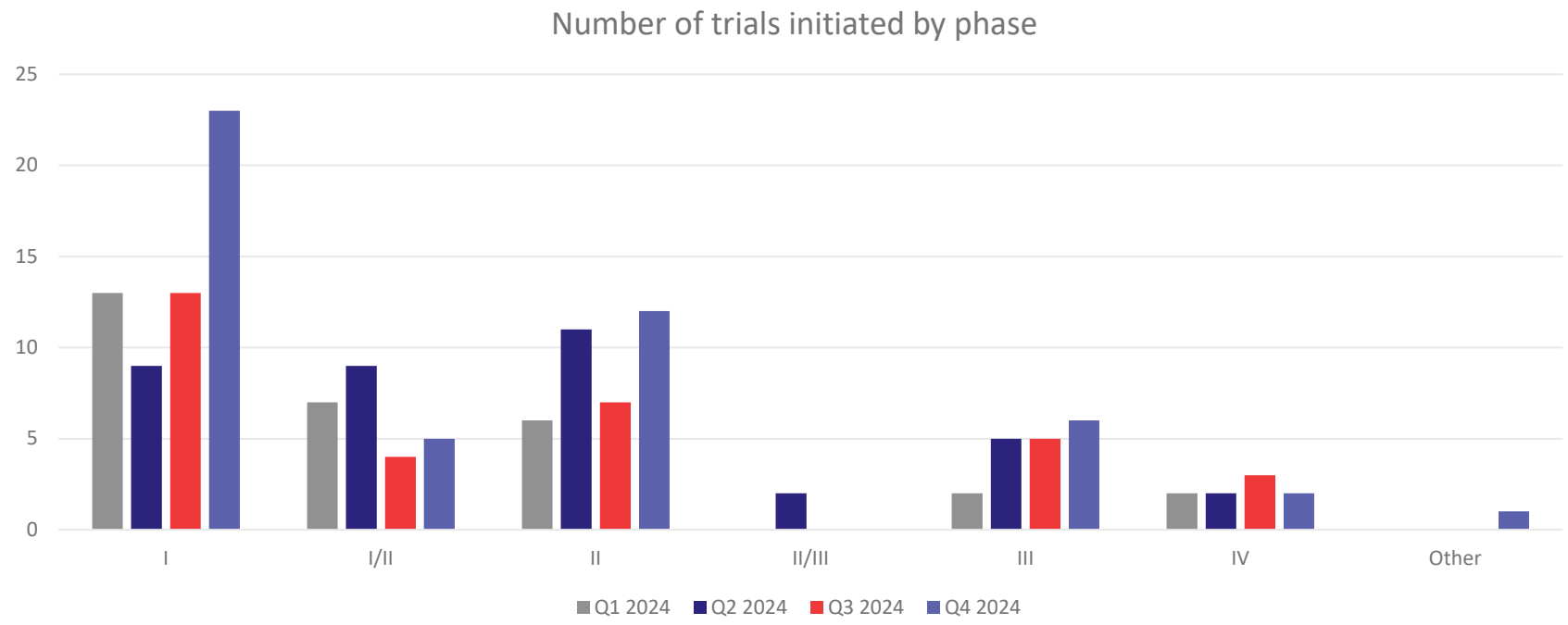
RNA therapy pipeline: clinical trial activity

- 49 RNA trials were initiated in Q4 2024, compared to 32 in Q3 2024, 82% of which were for non-oncology indications



Source: Trialtrove | Citeline, January 2025

Overview of dealmaking for gene, cell, and RNA therapy companies

Q4 2024

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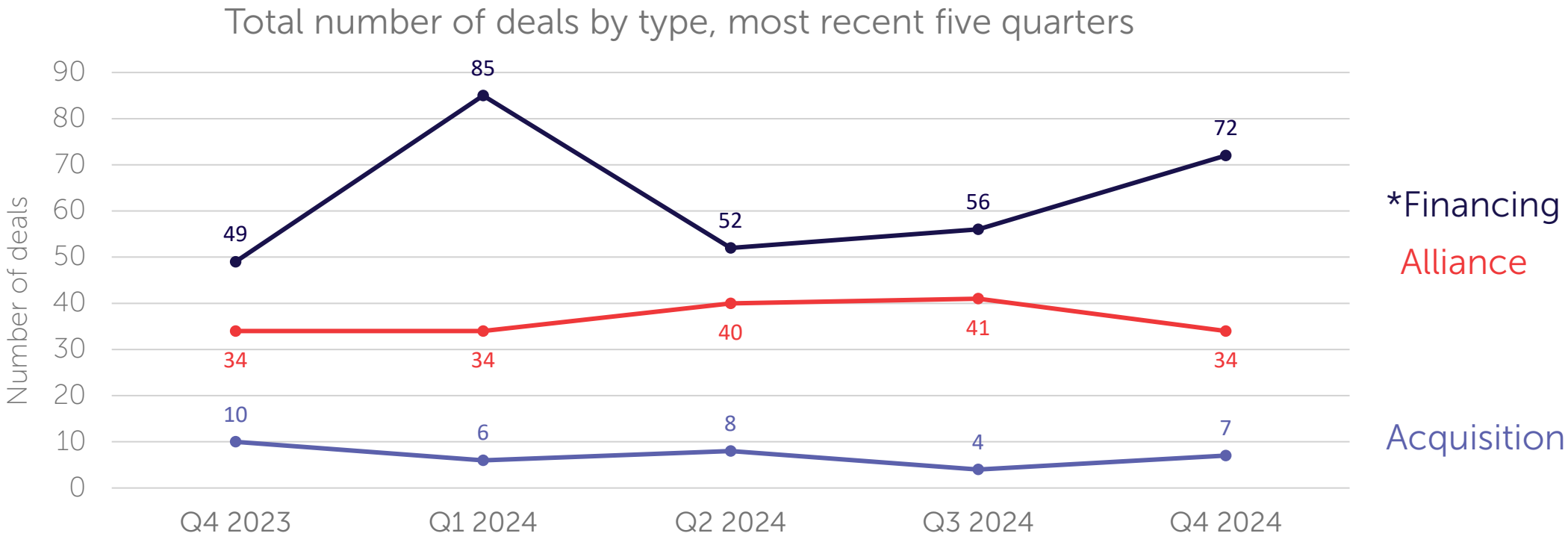
Alliance, acquisition, and financing in gene, cell, and RNA therapy

- Q4 2024 featured a total of 113 deals, a 12% increase over the previous quarter's 101 amount, and also up 22% from the 93 deals in the final quarter of 2023
- The increase in Q4 2024 was mainly due to financing transactions, which jumped from 56 in Q3 to 72 in Q4, plus a small jump in acquisitions
- Alliance volume, at 34 partnerships, was down 17% compared with 41 in Q3



Source: Biomedtracker | Citeline, BioSciDB | Evaluate, January 2025

*Financings include public financings (IPOs and follow-ons) plus privately raised funding through venture rounds, debt offerings, or private investment in public equity

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Q4 2024 acquisitions in gene, cell, and RNA therapy

- A total 7 advanced molecular therapy acquisitions took place in Q4 2024, up from 4 in the previous quarter, but still down from the high of 10 deals seen in 2023's closing quarter
- Big pharma companies completed two billion-dollar acquisitions: Novartis will pay up to $1.1 billion in up-front and milestone payments for Kate Therapeutics and its DELIVER (Directed Evolution of AAV Capsid Leveraging In Vivo Expression of Transgene RNA) engineering platform; and Roche bought allogeneic CAR-T developer Poseida Therapeutics for $1.5 billion

Deal date	Deal title	Potential deal value (USD $)
18 October 2024	REGiMMUNE and Kiji Therapeutics to Merge	Undisclosed
22 October 2024	Ocuphire Pharma Acquires Opus Genetics	Undisclosed
24 October 2024	Lyell Immunopharma to Acquire ImmPACT Bio; Acquisition Completed	30,000,000
21 November 2024	Novartis Acquires Kate Therapeutics for up to $1.1B to Enhance Gene Therapy Efforts	1,100,000,000
26 November 2024	Roche to Acquire Poseida Therapeutics, Including Cell Therapy Candidates and Related Platform Technologies	1,500,000,000
02 December 2024	NKGen Selected as Stalking Horse Bidder to Acquire NKMax	18,000,000
17 December 2024	Ultimovacs Enters Agreement to Combine Its Business With Zelluna Immunotherapy	Undisclosed

Source: Biomedtracker | Citeline, BioSciDB | Evaluate, January 2025

Start-up funding for gene, cell, and RNA therapy companies

Q4 2024

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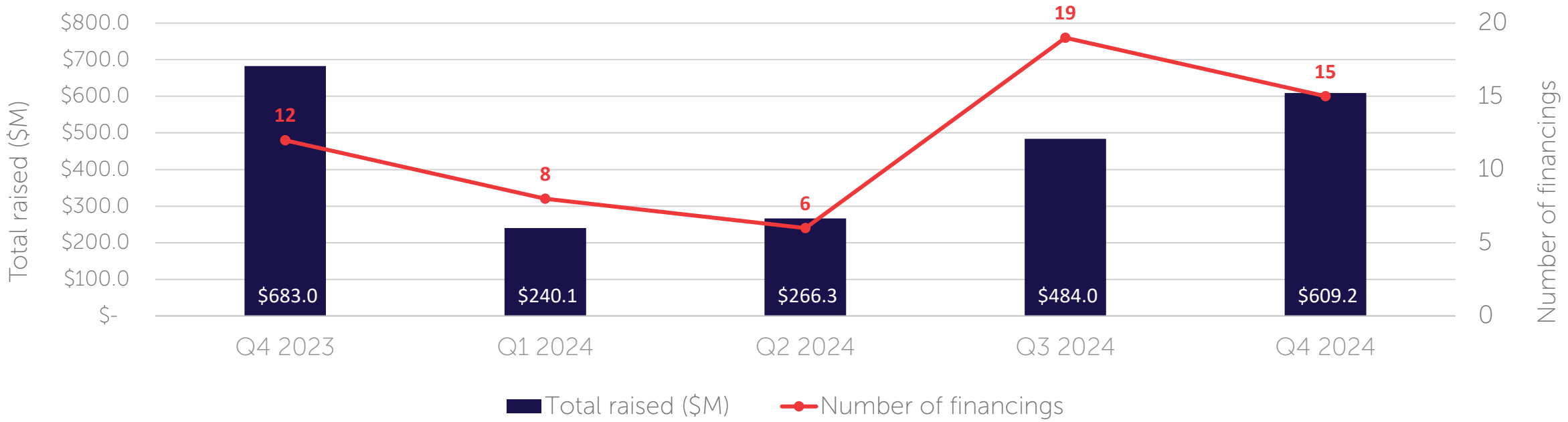
Start-up financing for gene, cell, and RNA therapy companies

- Seed and Series A financings for advanced molecular therapy companies strengthened, with a total of $609.2 million raised in Q4 2024, 26% ahead of Q3's $484 million
- At 15 transactions, start-up financing volume was down 21% from the previous quarter, but ahead of the total 12 from the same quarter in 2023

Volume and dollar value of Series A and seed financings for gene, cell, & RNA therapy companies, most recent five quarters



Source: Biomedtracker | Citeline, Evaluate, January 2025

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Q4 2024 start-up financing for gene, cell, and RNA therapy companies (1/2)

Deal date	Deal title	Modality type	Company location	Academic source	Potential deal value ($M)
07 October 2024	Judo Bio Launches With $100M	RNAi	United States / Massachusetts / Cambridge	Undisclosed (incubated by Atlas Venture and The Column Group)	100
08 October 2024	City Therapeutics Launches with $135M Series A Financing	RNAi	United States / Massachusetts / Cambridge	Ohio State University; University of Tokyo's Institute of Molecular and Cellular Biosciences; University of Massachusetts Chan Medical School's RNA Therapeutics Institute	135
09 October 2024	Clock.bio Gets $5.3M in Seed Round	iPSC therapy	United Kingdom / Cambridge	University of Cambridge's Milner Therapeutics Institute	5
11 October 2024	Somagenetix Raises CHF10M in Series A Round	Gene therapy	Switzerland / Zurich	University of Zurich	12
15 October 2024	invIOs Raises €8.2M in Series A Financing	Individualized immune cell therapy	Austria / Vienna	n/a; spun off from Apieron, which was acquired by Ligand Pharmaceuticals	9
15 October 2024	Shift Bioscience Completes $16M Seed Financing	Gene-based interventions for rejuvenating cells	United Kingdom / Cambridge	University of Cambridge	16
23 October 2024	March Biosciences Raises $28.4M in Oversubscribed Series A Round	CAR-T	United States / Texas / Houston	Center for Cell and Gene Therapy (Baylor College of Medicine, Houston Methodist Hospital, Texas Children's Hospital)	28

Q4 2024 start-up financing for gene, cell, and RNA therapy companies (2/2)

Deal date	Deal title	Modality type	Company location	Academic source	Potential deal value ($M)
30 October 2024	Leal Therapeutics Closes $45M Financing Round	Antisense oligonucleotides	United States / Massachusetts / Worcester	n/a; founded by former CEO of Prevail Therapeutics, which was acquired by Eli Lilly	45
12 November 2024	Trace Neuroscience Launches with $101M Series A Financing	Antisense oligonucleotides	United States / California / South San Francisco	Stanford University; Francis Crick Institute; National Institute of Neurological Disorders and Stroke	101
28 November 2024	Celosia Secures $16.75M Funding for ALS Gene Therapy	Gene therapy	Australia / Sydney	Macquarie University	17
25 November 2024	Kanglin Biotechnology Raises $20M in Series A Round	Genetically modified cell therapy	China / Hangzhou	Undisclosed	20
17 December 2024	Akamis Bio Raises $60M in Series A Prime Financing	Gene therapy	United Kingdom / Abingdon	n/a; formerly PsiOxus Therapeutics	60
19 December 2024	Portal Biotechnologies Gets $7M in Seed Financing	Intracellular delivery in gene editing and gene expression modulation	United States / Massachusetts / Watertown	n/a; established by former leadership of SQZ Biotechnologies	7
19 December 2024	Tolerance Bio Raises $20.2M in Seed Funding Round	iPSC therapy	United States / Pennsylvania / Philadelphia	University of Colorado; University of Florida	20
23 December 2024	GEMMABio Secures $34M in Seed Funding	Gene therapy	United States / Pennsylvania / Philadelphia	University of Pennsylvania	34

Notable Q4 2024 start-up gene, cell, and RNA therapy companies

Company details	Academic source	Financing type/ amount raised	Lead investor(s)	Therapy areas of interest
Trigger molecule engineering to develop siRNA therapies with improved potency and delivery	Ohio State University; University of Tokyo's Institute of Molecular and Cellular Biosciences; University of Massachusetts Chan Medical School's RNA Therapeutics Institute	Series A/$135M	ARCH Venture Partners	Undisclosed prevalent diseases
Antisense oligonucleotide that corrects splicing of UNC13A, a protein critical in neuronal communication	Stanford University; Francis Crick Institute; National Institute of Neurological Disorders and Stroke	Series A/$101M	Third Rock Ventures	Neurology (ALS)
STRIKE (Selectively Targeting RNA Into KidnEy) platform to produce ligand-siRNA conjugates for gene silencing in specific kidney cells	Undisclosed (incubated by Atlas Venture and The Column Group)	Seed and Series A/$100M	Atlas Venture; The Column Group; Droia Ventures	Systemic and renal diseases

Upcoming catalysts

Q4 2024

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Upcoming Catalysts

Below are noteworthy catalysts (forward-looking events) expected in Q1 2025

Therapy	Generic name	Disease	Catalyst	Catalyst date
UM171	dorocubicel	Myelodysplastic Syndrome (MDS)	Approval Decision (Europe)	25 February 2025 - 25 April 2025
Pz-cel	prademagene zamikeracel	Epidermolysis Bullosa	PDUFA/Approval Decision (US)	29 April 2025 - 29 April 2025
Breyanzi	lisocabtagene maraleucel	Follicular Lymphoma (FL)	CHMP (European Panel) Supplemental Filing Results	01 January 2025 - 30 June 2025
RP-L102	n/a	Fanconi Anemia	CHMP (European Panel) Results	01 December 2024 - 30 June 2025
Aucatzyl	obecabtagene autoleucel	Acute Lymphoblastic Leukemia (ALL)	CHMP (European Panel) Results	01 January 2025 - 31 July 2025
Breyanzi	lisocabtagene maraleucel	Follicular Lymphoma (FL)	Supplemental Approval (Europe)	19 March 2025 - 19 August 2025
Elevidys	delandistrogene moxeparvovec	Duchenne Muscular Dystrophy (DMD)	CHMP (European Panel) Results; Approval Decision (Japan)	01 February 2025 - 31 August 2025
Amvuttra	vutrisiran	Transthyretin Amyloid Cardiomyopathy (ATTR-CM, Wild Type Or Hereditary)	CHMP (European Panel) Supplemental Filing Results	01 March 2025 - 31 August 2025
RP-L102	n/a	Fanconi Anemia	Approval Decision (Europe)	02 March 2025 - 02 September 2025
Amtagvi	lifileucel	Melanoma	CHMP (European Panel) Results	01 March 2025 - 30 September 2025
Aucatzyl	obecabtagene autoleucel	Acute Lymphoblastic Leukemia (ALL)	Approval Decision (Europe)	01 March 2025 - 30 September 2025
Beqvez	fidanacogene elaparvovec	Hemophilia B	Approval Decision (Japan)	01 March 2025 - 30 September 2025
Elevidys	delandistrogene moxeparvovec	Duchenne Muscular Dystrophy (DMD)	Approval Decision (Europe)	01 April 2025 - 31 October 2025
Amvuttra	vutrisiran	Transthyretin Amyloid Cardiomyopathy (ATTR-CM, Wild Type Or Hereditary)	Supplemental Approval (Europe)	01 May 2025 - 31 October 2025
Plozasiran	n/a	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	PDUFA/Approval Decision (US)	18 November 2024 - 18 November 2025
Amtagvi	lifileucel	Melanoma	Approval Decision (Europe)	01 May 2025 - 30 November 2025

Source: Biomedtracker | Citeline, January 2025

Appendix

Methodology, sources, and glossary of key terms

Q4 2024

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Methodology: sources and scope of therapies

Sources for all data come from Citeline

Pipeline and trial data

- Data derived from **Pharmaprojects** and **Trialtrove**
- Therapeutic classes included in report categorizations:
  - Gene therapies: gene therapy; cellular therapy, chimeric antigen receptor; cellular therapy, T cell receptor; lytic virus
  - Cell therapies: cellular therapy, other; cellular therapy, stem cell; cellular therapy, tumor-infiltrating lymphocyte
  - RNA therapies: messenger RNA; oligonucleotide, non-antisense, non-RNAi; RNA interference; antisense therapy

Deal, financing, and catalyst data

- Data derived from **Biomedtracker**. The following industry categorizations of deals are included: gene therapy, cell therapy; antisense, oligonucleotides
- Additional alliance and acquisition deals data from **BioSciDB**, part of **Evaluate Ltd.** The following industry categorizations of deals are included: cell therapy – stem cells/factors, oligonucleotides, antisense/triple helix, gene therapy, RNAi

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	Therapies containing an active ingredient synthesized 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
Cellular therapy, chimeric antigen receptor *(falls under gene therapy in this report)*	Cellular therapy consisting of T cells that have been modified to express a chimeric antigen receptor (CAR) – this is a cell surface receptor that gives the T cells the ability to target a specific protein and fight the targeted cells
Cellular therapy, T cell receptor *(falls under gene therapy in this report)*	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)
Lytic virus *(falls under gene therapy in this report)*	Therapies that have a replication-competent virus, that lyse pathogenic cells directly. These are normally genetically modified to render them harmless to normal tissues. Examples include oncolytic viruses that specifically attack cancer cells

Glossary of Key Terms

Therapy type definitions, cont.

Cell therapy includes the following therapeutic classes:

Cellular therapy, stem cell	Regenerative therapy which promotes the repair response of injured tissue using stem cells (cells from which all other specialized cells would originate)
Cellular therapy, tumor-infiltrating lymphocyte	Adoptive cellular transfer of tumor-resident T cells from tumor material, their expansion *ex vivo,* and transfer back into the same patient after a lymphodepleting preparative regimen
Cellular therapy, other	Cellular therapies that do not fall under the categories of cellular therapy, stem cell; cellular therapy, CAR; cellular therapy, TIL; cellular therapy, TCR; or the specific cellular therapy are unspecified

Glossary of Key Terms

Therapy type definitions, cont.

RNA therapy includes the following therapeutic classes:

Messenger RNA	Therapies that carry the desired mRNA code to overcome genetic mutations. The mRNA sequence will replace the defective mRNA in a patient and start producing the desired protein
Oligonucleotide, non-antisense, non-RNAi	Synthetic therapeutic oligonucleotides which operate by a mechanism other than antisense or RNA interference (RNAi). This includes ribozymes, aptamers, decoys, CpGs, and mismatched and immunostimulant oligonucleotides. Sequences delivered using vectors (gene therapy) are covered separately in "gene therapy." Antisense and RNAi oligonucleotides are covered separately in "antisense therapy" and "RNA interference," respectively
RNA interference	Includes products which act therapeutically via an RNA interference (RNAi) mechanism, including small interfering RNAs (siRNAs). These may be synthetic oligonucleotides, or RNAi sequences may be expressed from a vector as a form of gene therapy (see "gene therapy" therapeutic class). *In vivo*, these sequences block the expression of a specific protein by forming an RNA-induced silencing complex, which then specifically binds to and degrades a complementary mRNA encoding the target protein. The use of RNAi purely as a drug discovery tool (e.g., in transgenic animal model production or in target validation) is not covered in this section
Antisense therapy	Antisense compounds under development as potential therapeutics. These may be synthetic oligonucleotides, or antisense RNA may be expressed from a vector as a form of gene therapy. They may prevent the expression of a specific protein *in vivo* by binding to and inhibiting the action of mRNA, since they have a specific oligonucleotide sequence which is complementary to the DNA or RNA sequence that codes for the protein

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

Deal type categories

Alliances	Co-marketing, co-promotion, disease management, joint venture, manufacturing or supply, marketing-licensing, product or technology swap, product purchase, R&D and marketing-licensing, reverse licensing, trial collaborations
Financing	Convertible debt, FOPO, IPO, nonconvertible debt, financing/other, private investment in public equity, private placement, royalty sale, special-purpose financing vehicle, spin-off
Acquisitions	Buyout, divestiture, spin-out, full acquisition, partial acquisition, reverse acquisition

Report Contributors

David Barrett, JD
CEO
American Society of Gene + Cell Therapy

Shardha Yeeles
Senior Consultant
Citeline

Alex Wendland, MSJ
Director of Communications
American Society of Gene + Cell Therapy

Amanda Micklus, MSc
Senior Manager, Consulting & Analytics
Citeline

Devin Rose
Communications Manager
American Society of Gene + Cell Therapy

CITELINE a norstella company

American Society of Gene + Cell Therapy

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Contact: David Barrett, JD
at info@asgct.org

Contact:
clientservices@citeline.com