Gene, Cell, + RNA Therapy Landscape Report

Q1 2024 Quarterly Data Report

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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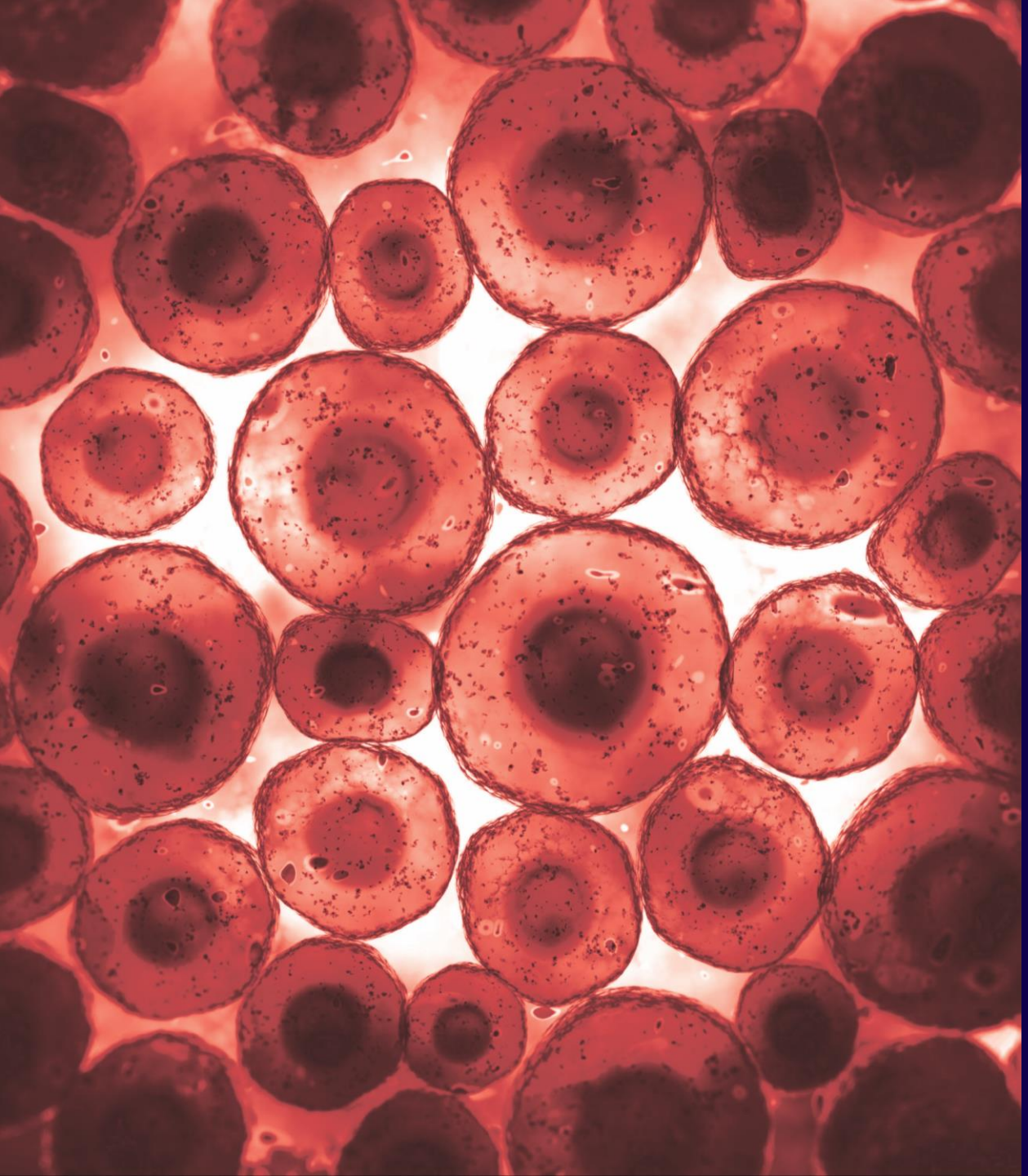

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American Society of Gene + Cell Therapy

Introduction

Following a landmark close to 2023, the cell and gene therapy field has continued its impressive momentum in the first quarter of 2024 with several notable approvals and strong growth in all stages of clinical development.

The field earned the approval of three new therapies—a CAR-T therapy for myeloma in China, an AAV gene therapy for hemophilia B in Canada, and an autologous cell therapy for melanoma in the United States.

Excitingly, there are now more than 4,000 gene, cell, and RNA therapies in development. We also recorded significant increases in the number of therapies across all three phases of development in the clinical pipeline, with notable growth (11 percent) in Phase I programs.

While overall dealmaking rebounded with a 34 percent increase in transactions, the start-up financing landscape continued to face challenges. Both the number and total value of seed and Series A rounds declined in Q1. Nevertheless, the breadth of progress across approvals, clinical development, and the broader ecosystem underscores the progress, promise, and vitality of cell and gene therapy.

David Barrett, JD
CEO, ASGCT

Key takeaways from Q1 2024

Three new approvals headline Q1 2024 in the advanced therapy landscape

- Two new gene therapies were approved: CT-053 (zevorcabtagene autoleucel), a CAR-T therapy developed by CARsgen, was approved for myeloma in China; and Beqvez, an AAV gene therapy developed by Pfizer, was approved for hemophilia B in Canada
- Amtagvi, an autologous cell therapy developed by Iovance Biotherapeutics, was approved for melanoma in the US

The past quarter was one of growth at the clinical development stage (Phase I–III), in particular for gene therapies

- The number of therapies at all three phases of clinical pipeline development has increased since the end of 2023
- Phase I therapy numbers in particular saw their greatest growth (11%) since prior to Q4 2022

Overall dealmaking rebounded for advanced molecular therapy companies, but start-up financing continued to slow

- The sector saw a 34% increase in total deals in Q1 2024, reaching 125 transactions, up from 93 in the previous quarter
- Driving this increase was a substantial jump in total financings; however, start-ups raising seed or Series A funds continued the downward trend seen in previous quarters
- Start-up volume declined by 33% to eight transactions in Q1 2024, and had a nearly 3x decrease in value to $240.1m

Key highlights in Q1 2024

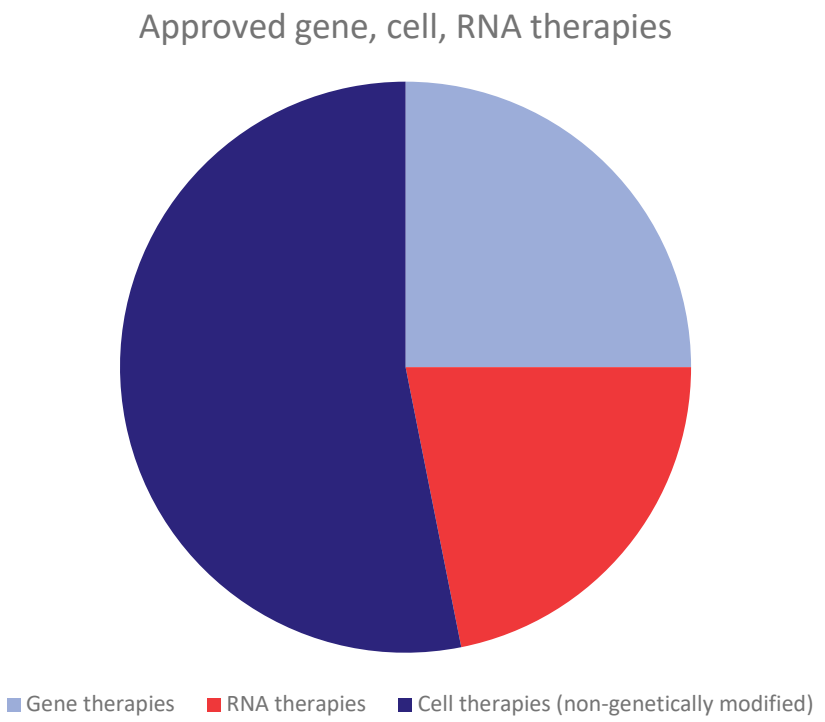
Q1 2024

American Society of Gene + Cell Therapy

Approved gene, cell, and RNA therapies

Globally, for clinical use:

- 32 gene therapies have been approved (including genetically modified cell therapies)
  - In Q1 2024, **CT-053** (CARsgen) was approved for myeloma in China, and **Beqvez** (Pfizer) was approved for hemophilia B in Canada
- 28 RNA therapies have been approved
- 68 non-genetically modified cell therapies have been approved
  - In Q1 2024, **Amtagvi** was approved in the US for the treatment of melanoma



Source: Pharmaprojects | Citeline, April 2024

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Approved gene therapies as of Q1 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)
Collategene	beperminogene perplasmid	2019	Critical limb ischemia	Japan	AnGes
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, April 2024

Text highlighted in yellow represents new approvals during Q1 2024

Approved gene therapies as of Q1 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	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	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; follicular lymphoma	China	JW Therapeutics
Skysona	elivaldogene autotemcel	2021	Early cerebral adrenoleukodystrophy (CALD)	US	bluebird bio
Carvykti	ciltacabtagene autoleucel	2022	Multiple myeloma	US, EU, UK, Japan, Australia, China	Legend Biotech
Upstaza	eladocagene exuparvovec	2022	Aromatic L-amino acid decarboxylase (AADC) deficiency	EU, UK	PTC Therapeutics
Roctavian	valoctocogene roxaparvovec	2022	Hemophilia A	EU, UK, 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

Source: Pharmaprojects | Citeline, April 2024

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Text highlighted in yellow represents new approvals during Q1 2024

Approved gene therapies as of Q1 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	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	Pfizer

Source: Pharmaprojects | Citeline, April 2024

Text highlighted in yellow represents new approvals during Q1 2024

Approved RNA therapies as of Q1 2024 (1/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
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
Moderna COVID-19 vaccine	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

Source: Pharmaprojects | Citeline, April 2024

Text highlighted in yellow represents new approvals during Q1 2024

Approved RNA therapies as of Q1 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	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, April 2024

Text highlighted in yellow represents new approvals during Q1 2024

Approved RNA therapies as of Q1 2024 (3/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Qalsody	tofersen	2023	Amyotrophic lateral sclerosis	US	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	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

*For COVID-19 vaccines, this includes emergency use authorization and full approvals
Note that molnupiravir was previously included in this list; however, it has now been removed as it is no longer considered to fall under the category of RNA therapeutics

Source: Pharmaprojects | Citeline, April 2024

Text highlighted in yellow represents new approvals during Q1 2024

Key highlights in Q1 2024 (1/2)

Noteworthy events that happened in Q1 2024

Drug	Event Type	Indication	Molecule	Event Date
DOC1021	Orphan Drug Designation (U.S.)	Brain Cancer (Malignant Glioma; AA and glioblastoma (GBM))	Cellular	02 January 2024
Carteyva	Filing for Approval (China)	Mantle Cell Lymphoma - NHL	Cellular	04 January 2024
CABA-201	Fast Track Status	Systemic Sclerosis	Cellular	08 January 2024
CABA-201	Fast Track Status	Dermatomyositis	Cellular	08 January 2024
Casgevy	Approval (Emerging Markets)	Sickle Cell Anemia	Non-Viral Gene Therapy	09 January 2024
SER-155	Fast Track Status	Graft vs. Host Disease (GVHD) - Treatment	Cellular	09 January 2024
Casgevy	Approval (Emerging Markets)	Thalassemia	Non-Viral Gene Therapy	09 January 2024
SGT-003	Orphan Drug Designation (U.S.)	Duchenne Muscular Dystrophy (DMD)	Viral Gene Therapy	11 January 2024
Hemgenix	Approval (Europe) - Individual Country	Hemophilia B	Viral Gene Therapy	15 January 2024
Casgevy	Approval (U.S.)	Thalassemia	Non-Viral Gene Therapy	16 January 2024
ATSN-101	Rare Pediatric Disease (RPD) Designation	Leber's Congenital Amaurosis (Ophthalmology)	Viral Gene Therapy	16 January 2024
Revascor	Rare Pediatric Disease (RPD) Designation	Chronic Heart Failure - Reduced Ejection Fraction (Chronic HFrEF)	Cellular	18 January 2024
RZ001	Orphan Drug Designation (U.S.)	Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)	Non-Viral Gene Therapy	18 January 2024
KYV-101	Fast Track Status	Multiple Sclerosis (MS)	Cellular	19 January 2024
4D-710	Fast Track Status	Hepatitis B (HBV) Treatment (Antiviral)	Antisense	12 February 2024
FT-002	PRIME Designation (Europe)	Fabry's Disease	Viral Gene Therapy	12 February 2024
Breyanzi	Conditional Marketing Authorisation (Europe)	Thalassemia	Non-Viral Gene Therapy	13 February 2024
Breyanzi	Conditional Marketing Authorisation (Europe)	Sickle Cell Anemia	Non-Viral Gene Therapy	13 February 2024
ACDN-01	Fast Track Status	Lung Cancer - Unspecified	Viral Gene Therapy	13 February 2024
BST02	Orphan Drug Designation (U.S.)	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Antisense	14 February 2024
CABA-201	Orphan Drug Designation (U.S.)	Chronic Heart Failure - Reduced Ejection Fraction (Chronic HFrEF)	Cellular	14 February 2024
Amtagvi	Accelerated/Conditional Approval (U.S.)	Melanoma	Cellular	16 February 2024
Wainua	Rare Pediatric Disease (RPD) Designation	Duchenne Muscular Dystrophy (DMD)	siRNA/RNAi	20 February 2024
GTX-102 (GeneTx)	Fast Track Status	Myotonic Muscular Dystrophy	Oligonucleotide	20 February 2024
Casgevy	Breakthrough Therapy Designation (U.S.)	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Antisense	21 February 2024

Source: Biomedtracker | Citeline, April 2024

Key highlights in Q1 2024 (2/2)

Noteworthy events that happened in Q1 2024

Drug	Event Type	Indication	Molecule	Event Date
KB707	Orphan Drug Designation (Europe)	Hereditary Angioedema (HAE)	Antisense	21 February 2024
Bepirovirsen	Fast Track Status	Polycythemia Vera (PV)	Antisense	21 February 2024
Isaralgagene Civaparvovec	Fast Track Status	Pelizaeus-Merzbacher Disease (PMD)	Antisense	21 February 2024
Revascor	Orphan Drug Designation (Europe)	Cystic Fibrosis (CF)	siRNA/RNAi	22 February 2024
Casgevy	Fast Track Status	Lupus Nephritis	Cellular	22 February 2024
Olezarsen	Orphan Drug Designation (U.S.)	Acute Myelogenous Leukemia (AML)	Cellular	26 February 2024
AOC 1044	Fast Track Status	Non-Hodgkin's Lymphoma (NHL)	Cellular	29 February 2024
PGN-EDODM1	Fast Track Status	Multiple Myeloma (MM)	Cellular	29 February 2024
ION356	Approval (China)	Multiple Myeloma (MM)	Cellular	01 March 2024
IONIS-TMPRSS6-LRx	Orphan Drug Designation (U.S.)	Duchenne Muscular Dystrophy (DMD)	Oligonucleotide	07 March 2024
Donidalorsen	Orphan Drug Designation (U.S.)	Multiple Myeloma (MM)	Cellular	12 March 2024
AlloNK	Regenerative Medicine Advanced Therapy (RMAT) Designation	Osteoarthritis	Viral Gene Therapy	13 March 2024
Olezarsen	Rare Pediatric Disease (RPD) Designation	Duchenne Muscular Dystrophy (DMD)	Oligonucleotide	13 March 2024
LUNAR-CF	Approval (U.S.)	Metachromatic Leukodystrophy	Viral Gene Therapy	18 March 2024
CT053	Orphan Drug Designation (U.S.)	Systemic Sclerosis	Cellular	19 March 2024
IDP-023	Innovative Licensing and Access Pathway (ILAP) (U.K.)	Krabbe Disease (Globoid Cell Leukodystrophy)	Viral Gene Therapy	19 March 2024
IDP-023	NDA/BLA Filing	Neurology - Other	Viral Gene Therapy	19 March 2024
Dilanubicel	Regenerative Medicine Advanced Therapy (RMAT) Designation	Acute Myelogenous Leukemia (AML)	Cellular	19 March 2024

Source: Biomedtracker | Citeline, April 2024

Pipeline overview

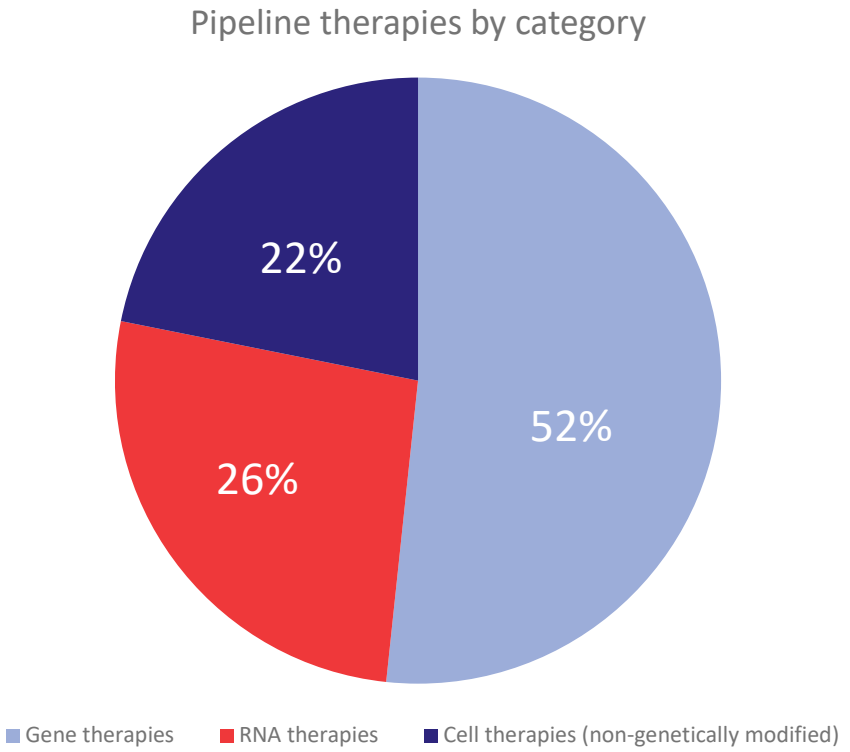
Q1 2024

American Society of Gene + Cell Therapy

Pipeline of gene, cell, and RNA therapies

4,002 therapies are in development, ranging from preclinical through pre-registration

- 2,093 gene therapies (including genetically modified cell therapies such as CAR-T cell therapies) are in development, accounting for 52% of gene, cell, and RNA therapies
- 885 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies



Source: Pharmaprojects | Citeline, April 2024

American Society of Gene + Cell Therapy

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q1 2024

American Society of Gene + Cell Therapy

Gene therapy pipeline: quarterly comparison

- Q1 2024 saw an increase in the number of therapies at each pipeline stage of development except pre-registration
- The number of gene therapies at pre-registration is the lowest it has been since prior to Q4 2022, while Phase I development has seen the largest percentage increase in over a year (11%) between Q4 2023 and Q1 2024
- Therapies currently in pre-registration:
  - In the US
    - RP-L201 (Rocket Pharmaceuticals)
    - EB-101 (Abeona Therapeutics)
    - afami-cel (Adaptimmune Therapeutics)
    - obe-cel (Autolus Therapeutics)

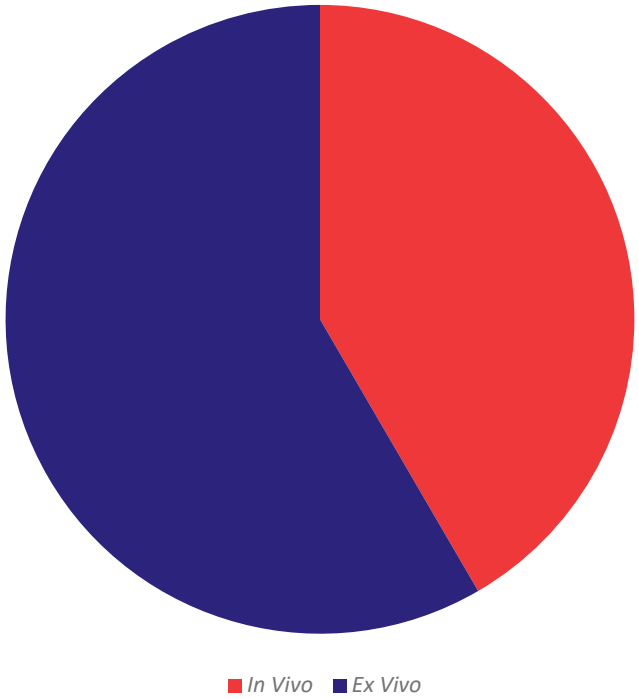
Global Status	Q1 2023	Q2 2023	Q3 2023	Q4 2023	Q1 2024
Preclinical	1,493	1,539	1,522	1,528	1,471
Phase I	245	240	256	270	301
Phase II	247	260	267	274	282
Phase III	30	30	30	33	35
Pre-registration	7	6	7	6	4
Total	**2,022**	**2,075**	**2,082**	**2,111**	**2,093**

Source: Pharmaprojects | Citeline, April 2024

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

- *Ex vivo* genetic modification is more widely used for gene therapies in pipeline development
- In Q1 2024, *in vivo* delivery techniques were used in 42% of gene therapies

In vivo vs. *Ex vivo* genetic modification



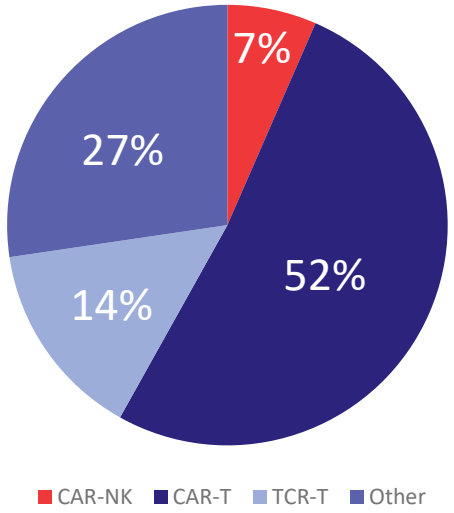
Source: Cell and Gene Therapy dashboard | Citeline, April 2024

American Society of Gene + Cell Therapy

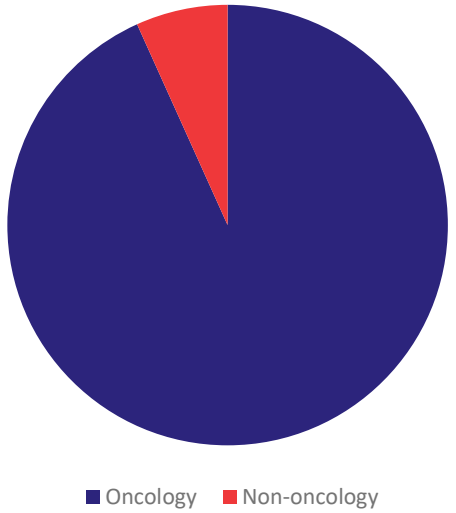
Gene therapy breakdown: CAR-Ts continue to dominate the pipeline

- CAR-T cell therapies remained the most common technology used in the pipeline of genetically modified cell therapies (preclinical through to pre-registration), representing 52%, followed by the “other” category at 27%, 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



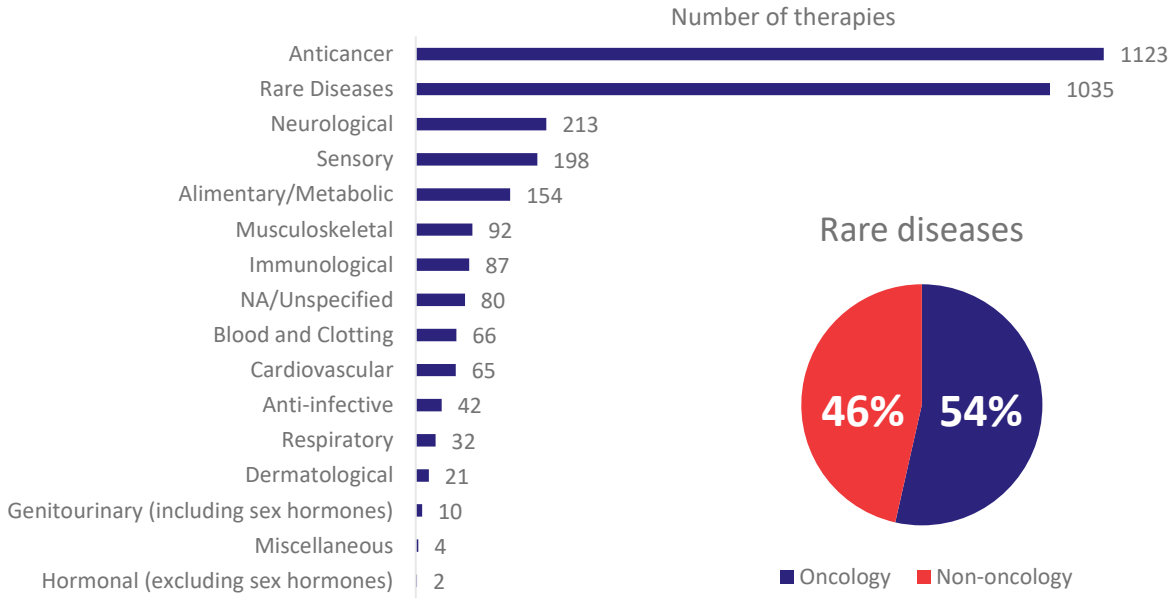
Source: Cell and Gene Therapy dashboard | Citeline, April 2024

American Society of Gene + Cell Therapy

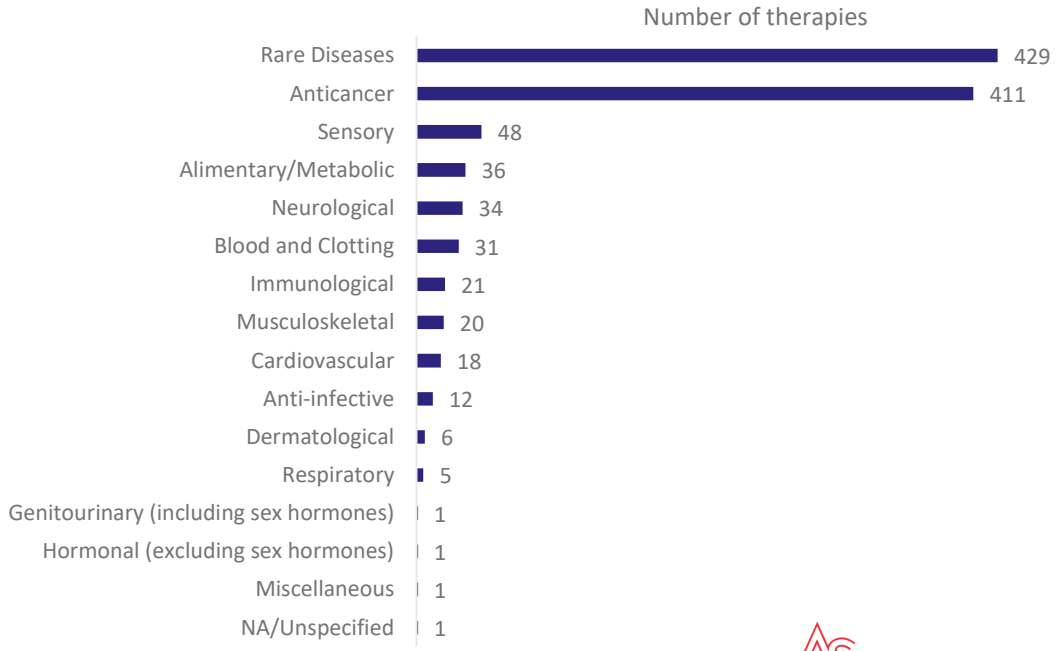
Gene therapy pipeline: most commonly targeted therapeutic areas

- 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 lower than the previous quarter

Number of therapies from preclinical through pre-registration



Therapies in the clinic (excludes preclinical development)



Source: Pharmaprojects | Citeline, April 2024

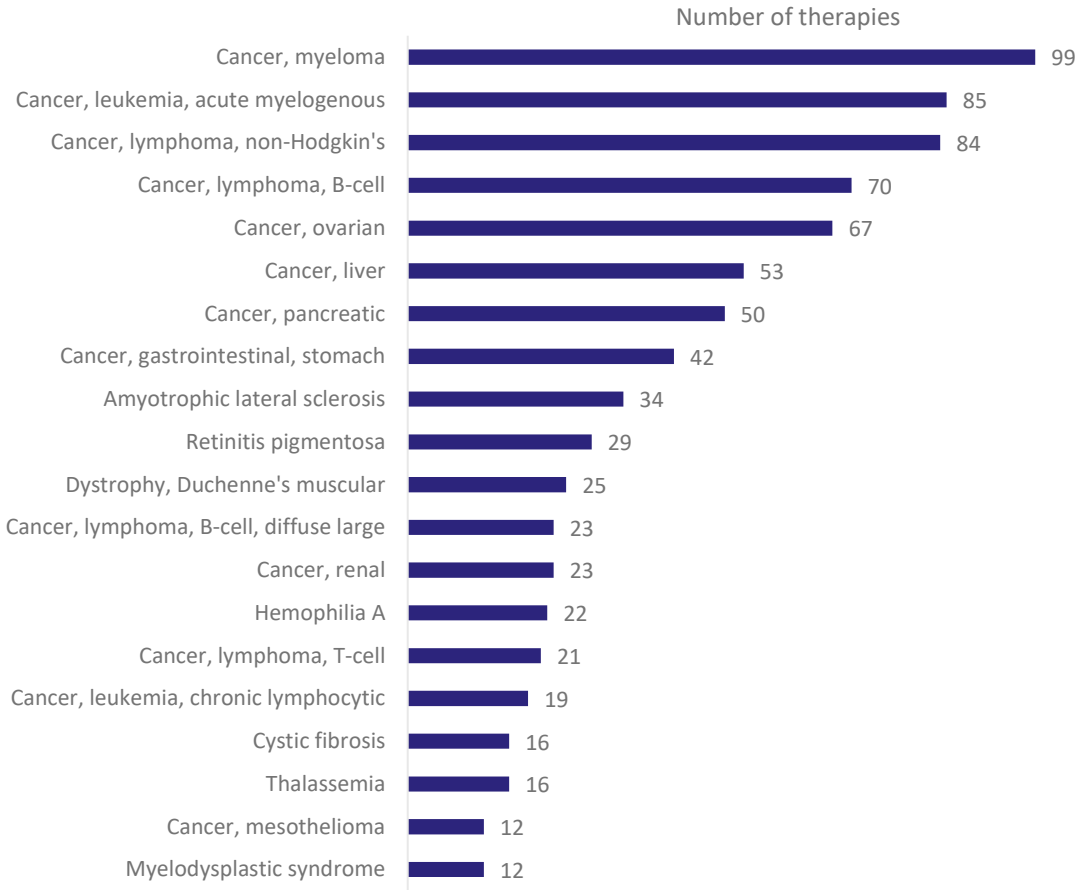
Note: Figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

Gene therapy pipeline: most common rare diseases targeted

- For the 1,035 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 2022 and 2023
- In the same order as the previous quarter, 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, April 2024

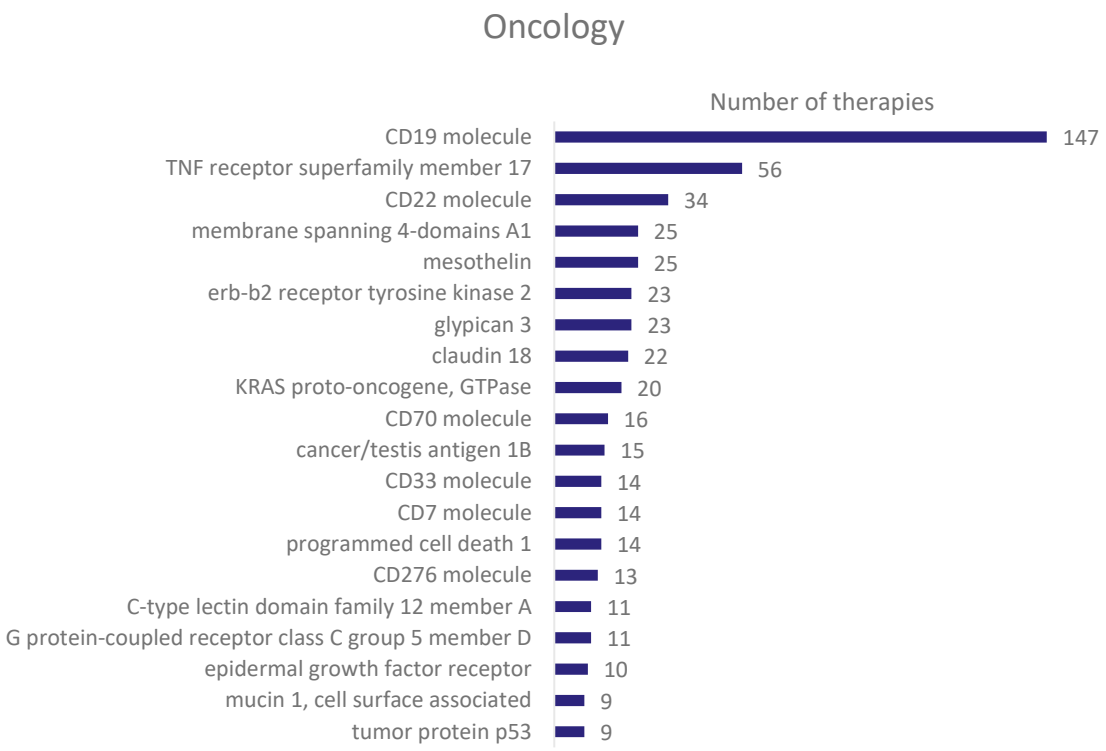
Note: Figures based on indications in pipeline development only for each therapy

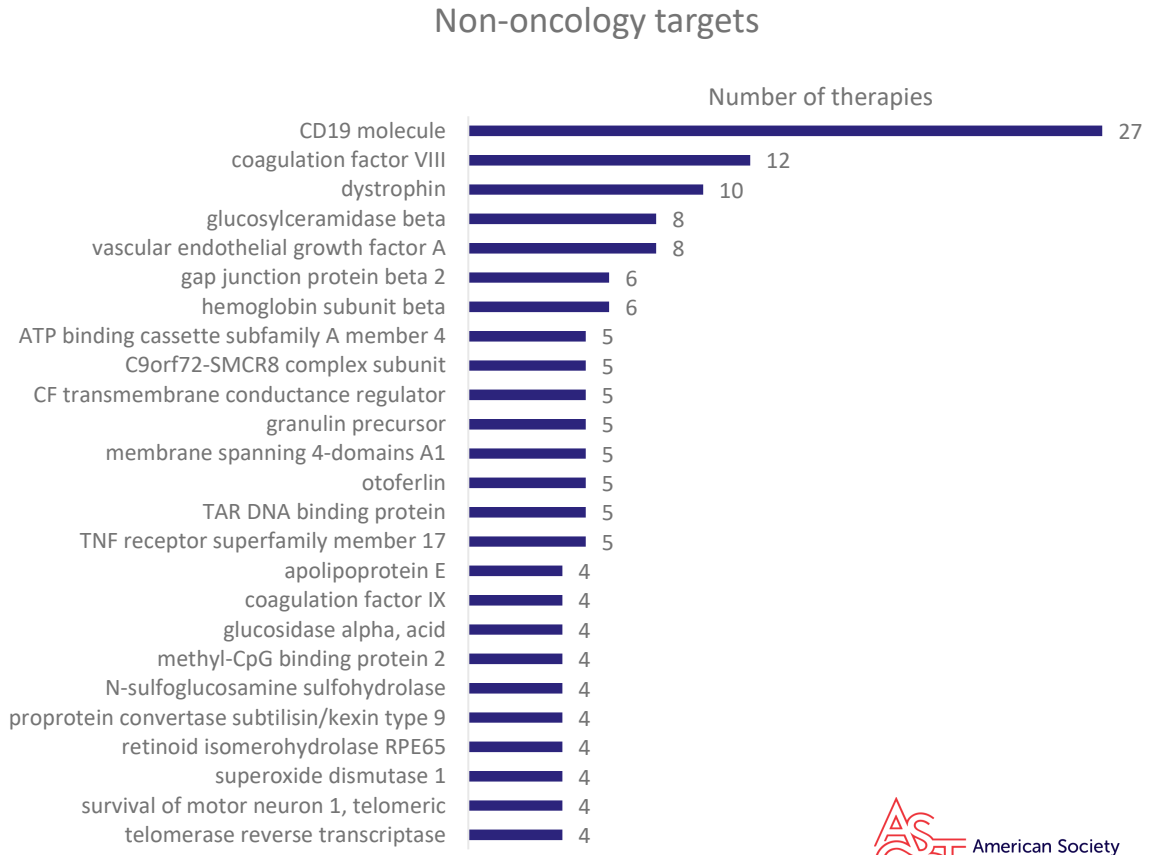
American Society of Gene + Cell Therapy

Gene therapy pipeline: most common targets

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

- CD19, 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 was the most common target for non-oncology indications, while coagulation factor VIII remained the second most common in Q1 2024, as seen in the previous two quarters



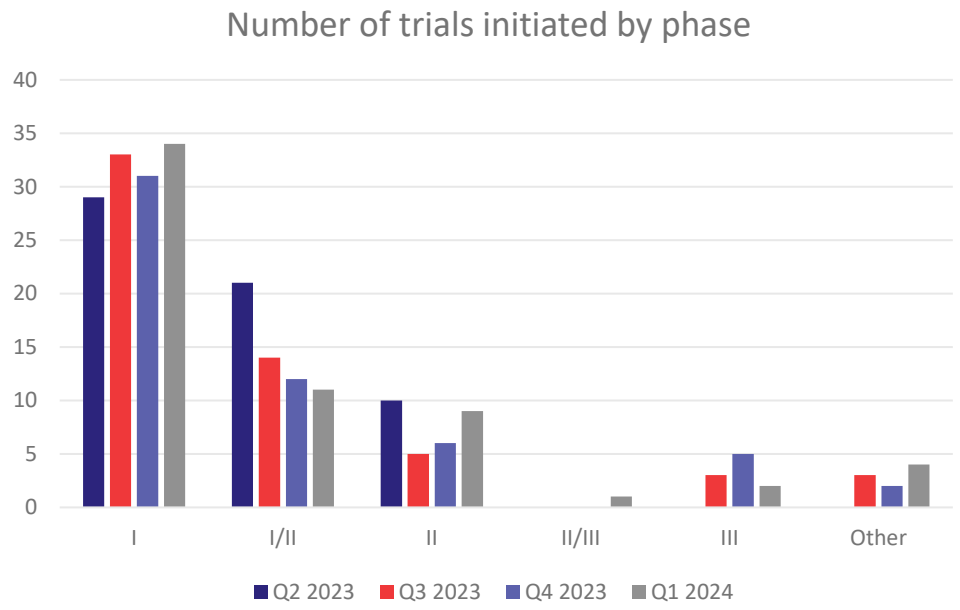


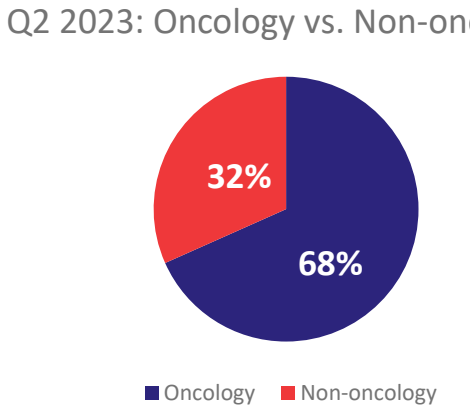
Source: Pharmaprojects | Citeline, April 2024

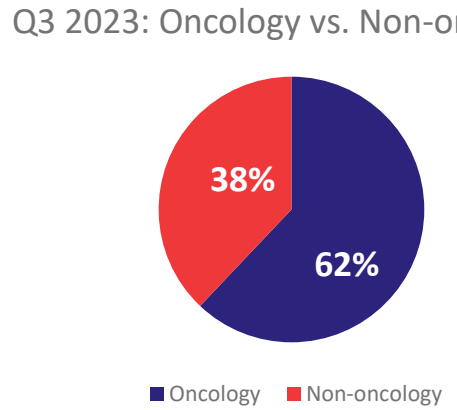
American Society of Gene + Cell Therapy

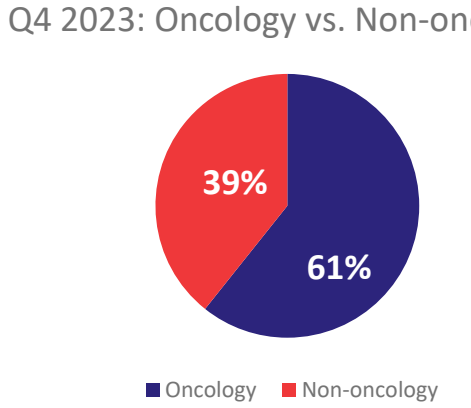
Gene therapy clinical trial activity

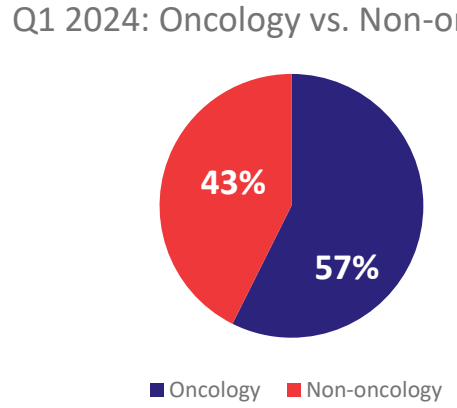
- The proportion of gene therapy trials for non-oncology indications has increased by four percentage points since the previous quarter, to 43%, continuing the trend of an increasing proportion of non-oncology gene therapy trials
- 61 gene therapy trials were initiated in Q1 2024











Source: Trialtrove | Citeline, April 2024

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline

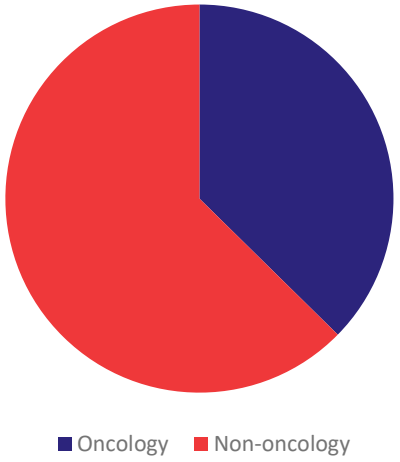
Q1 2024

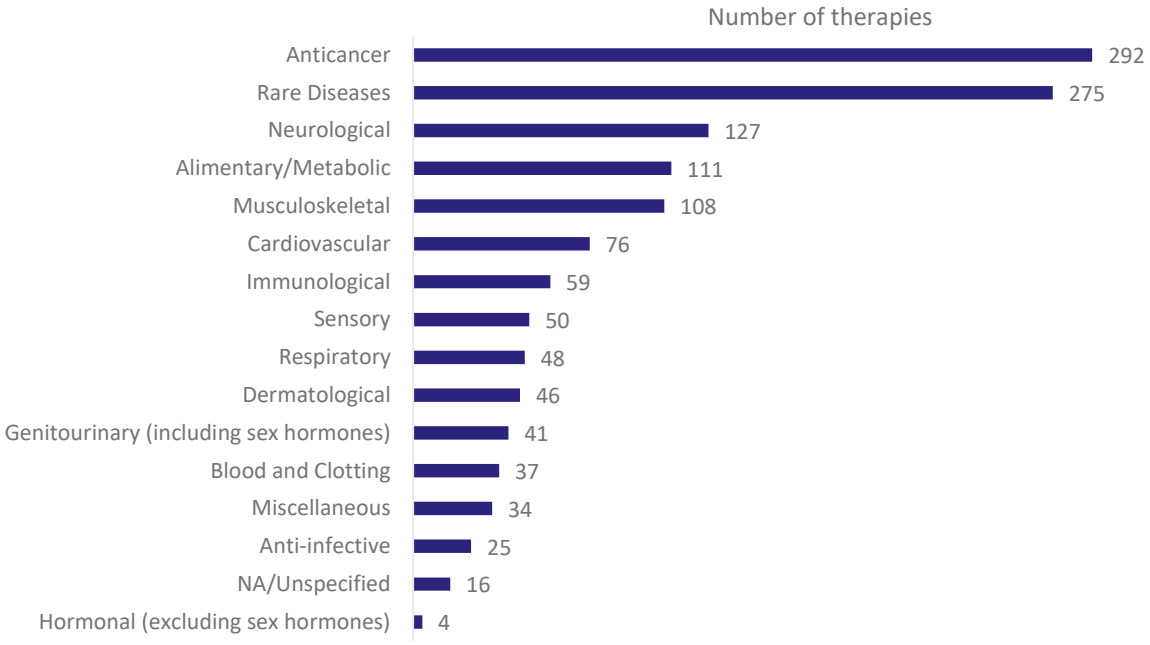
American Society of Gene + Cell Therapy

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, 64% were in development for non-oncology rare diseases, as found in the previous three quarters





Source: Pharmaprojects | Citeline, April 2024

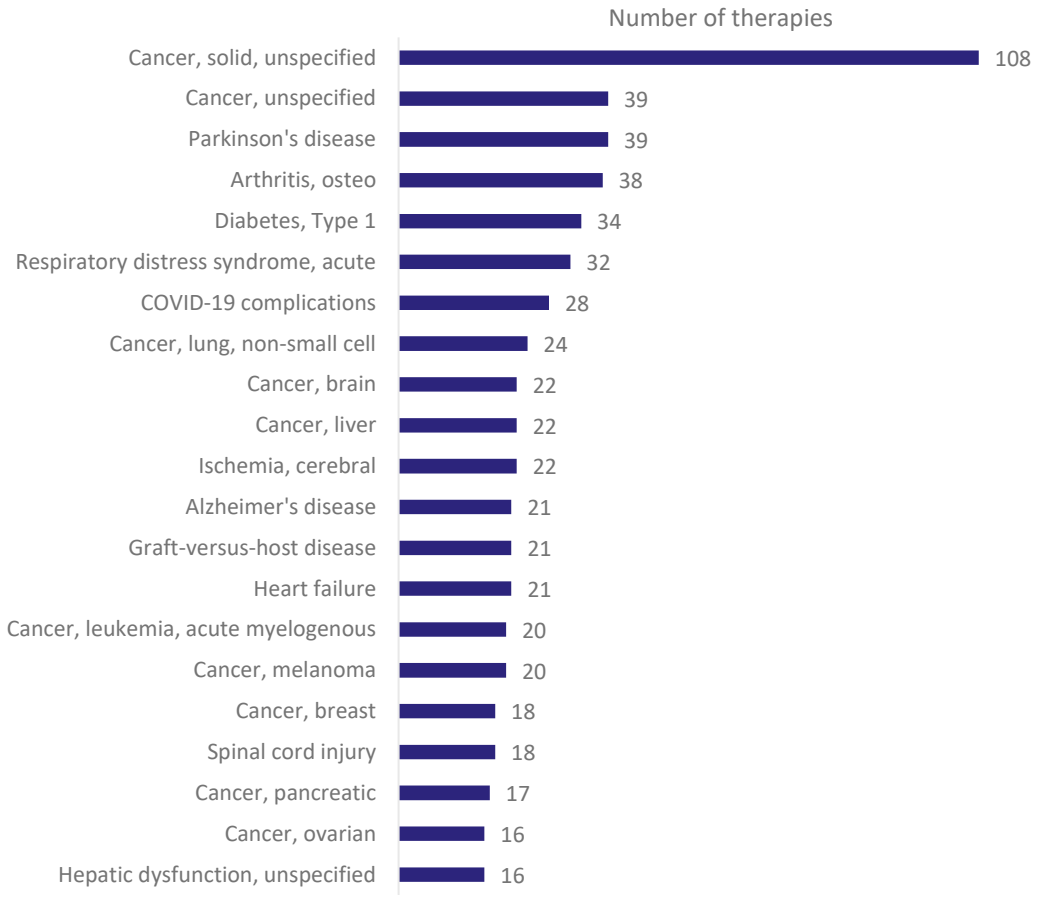
Note: Figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

Of the therapies for which indications are specified, Parkinson’s disease is the most targeted disease, while type 1 diabetes has overtaken acute respiratory distress syndrome to become the third most targeted:

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



Source: Pharmaprojects | Citeline, April 2024

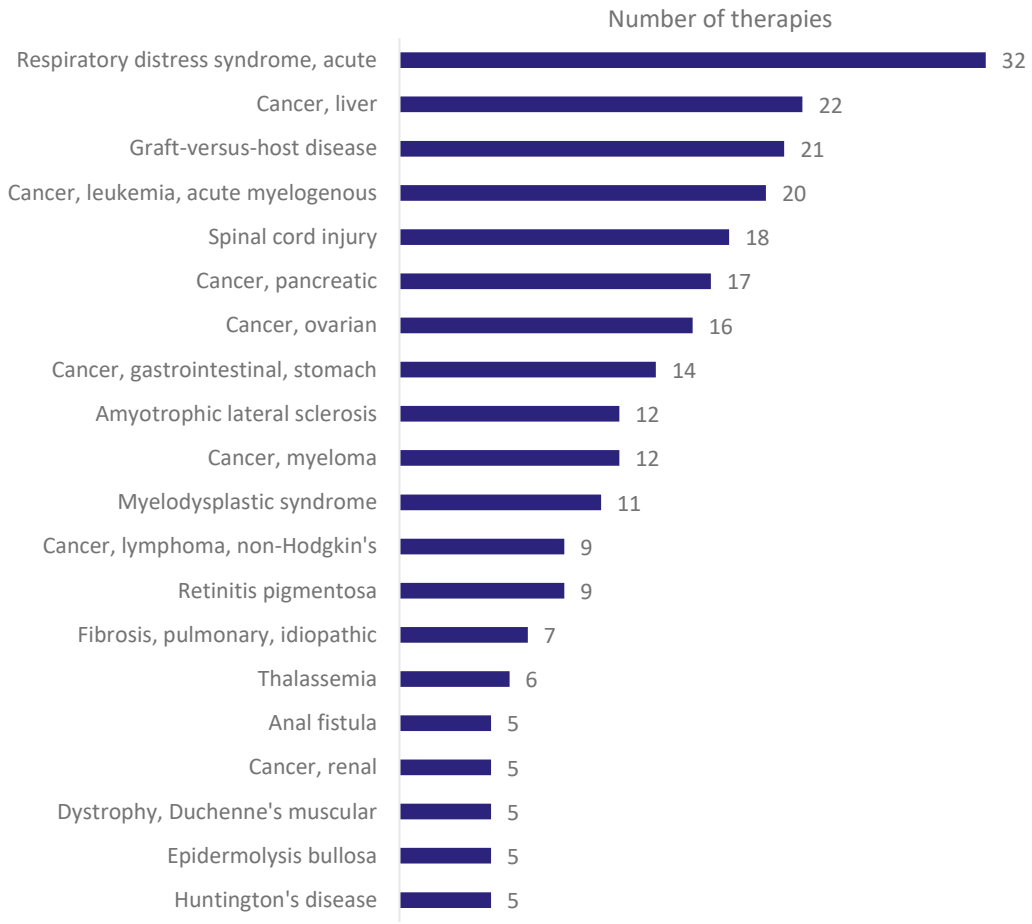
Note: Figures based on indications in pipeline development only for each therapy

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



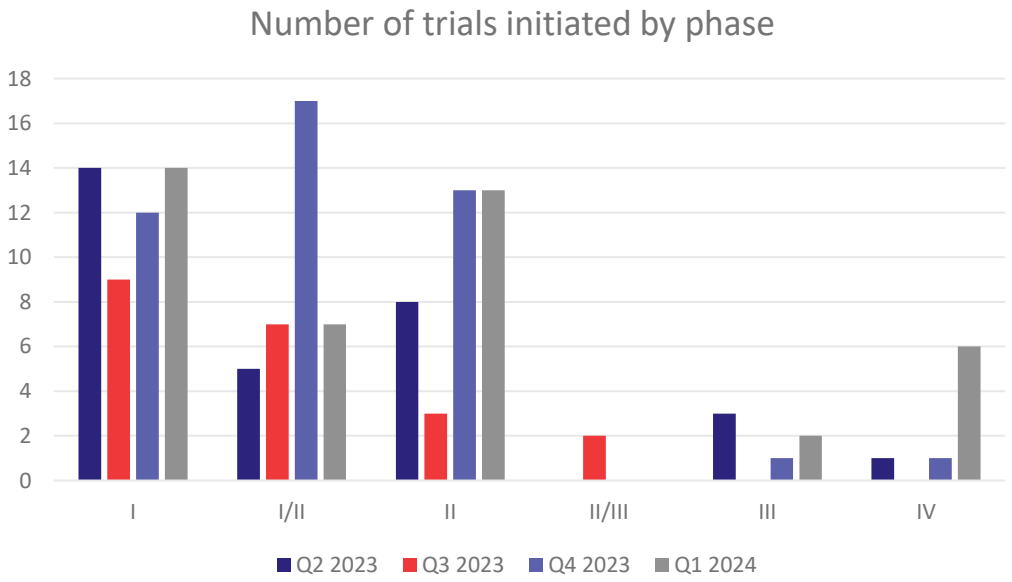
Source: Pharmaprojects | Citeline, April 2024

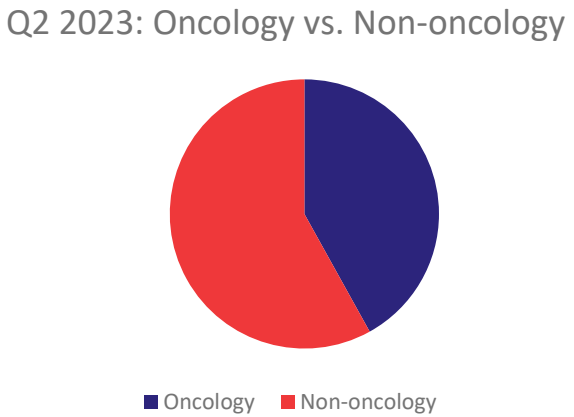
Note: Figures based on indications in pipeline development only for each therapy

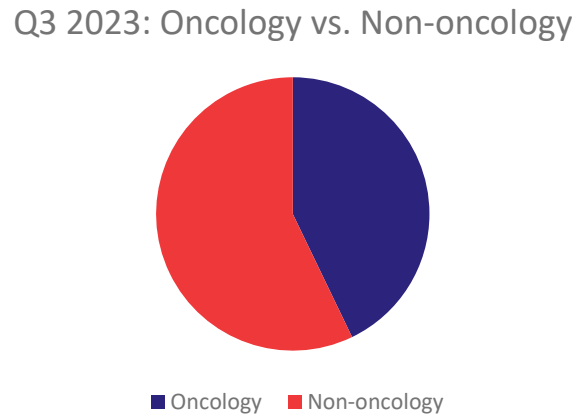
American Society of Gene + Cell Therapy

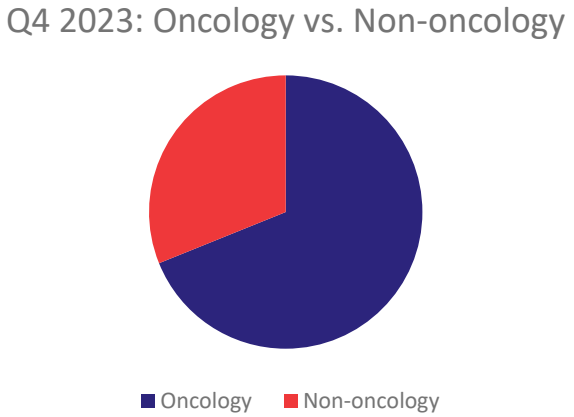
Non-genetically modified cell therapy trial activity

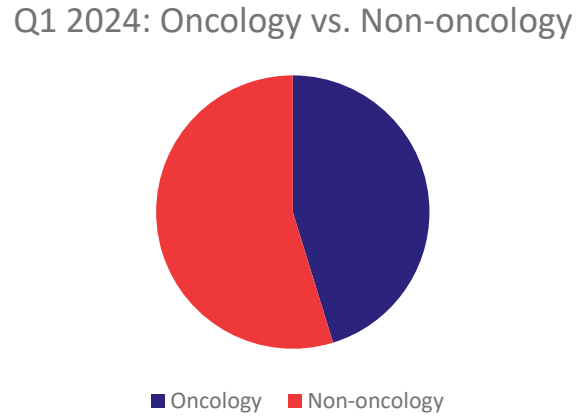
- 42 trials were initiated for non-genetically modified cell therapies in Q1 2024, two fewer than in the previous quarter
- Of these 42, 55% were for non-oncology indications











Source: Trialtrove | Citeline, April 2024

American Society of Gene + Cell Therapy

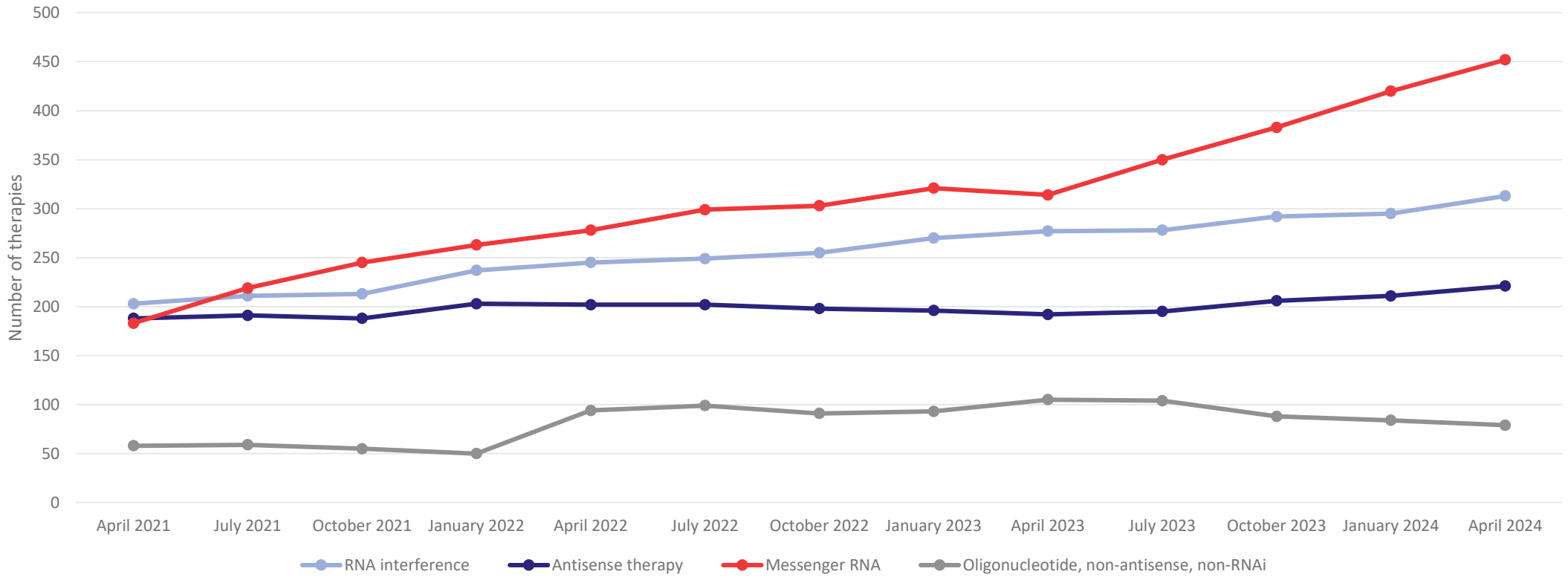
RNA therapy pipeline

Q1 2024

American Society of Gene + Cell Therapy

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

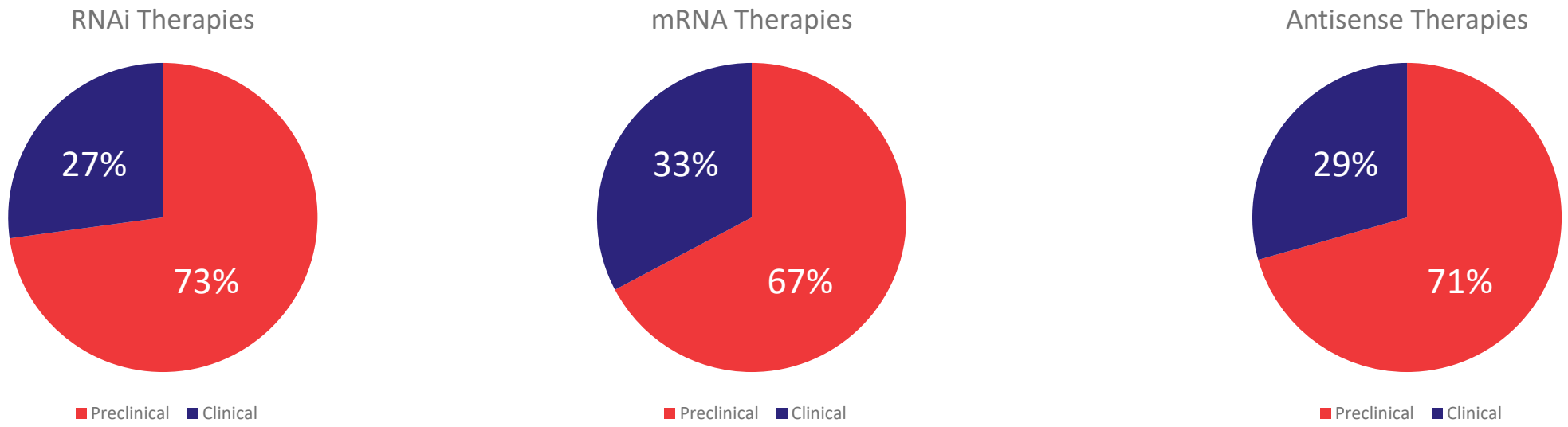


Source: Pharmaprojects | Citeline, April 2024

American Society of Gene + Cell Therapy

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%, 67%, and 71% of their respective pipelines



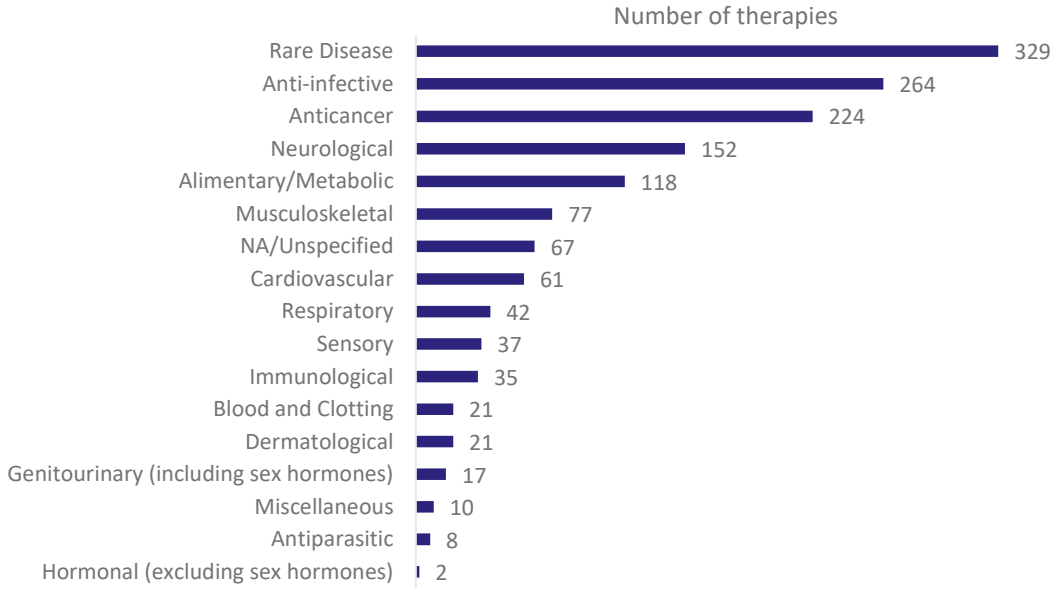
Source: Pharmaprojects | Citeline, April 2024

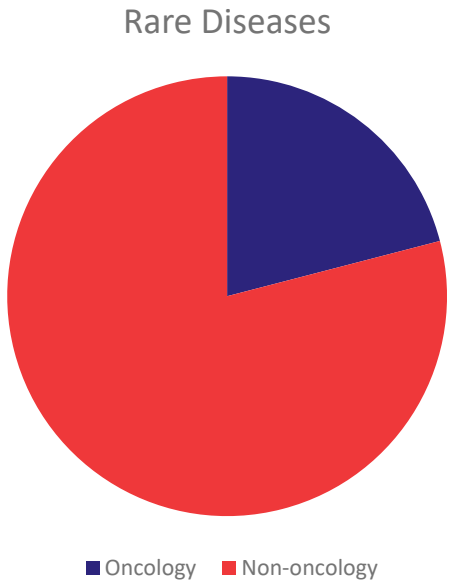
American Society of Gene + Cell Therapy

RNA therapies: most commonly targeted therapeutic areas

Of the 1,072 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 remained the second most commonly targeted, above oncology indications
- Non-oncology indications continued to be the most targeted rare diseases by RNA therapies, representing a majority of 80%





Source: Pharmaprojects | Citeline, April 2024

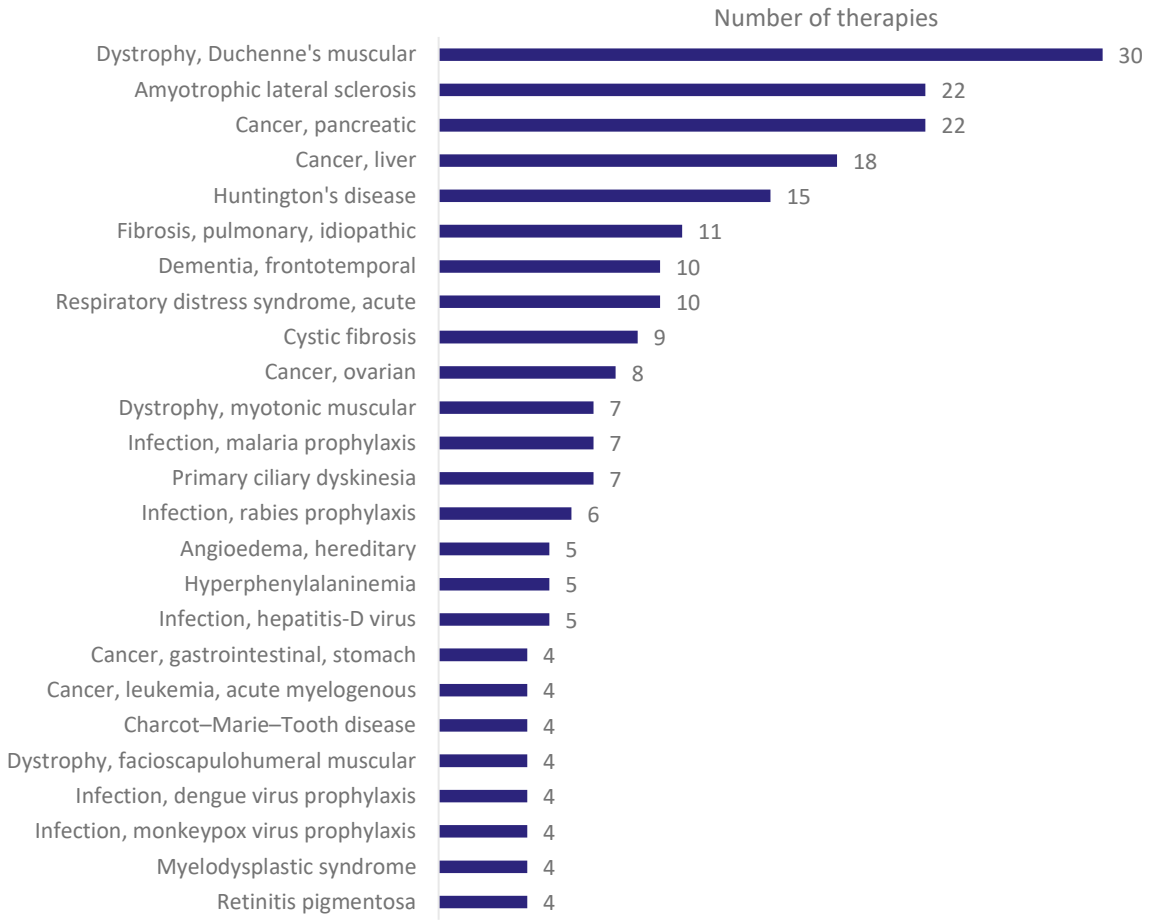
Note: Figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

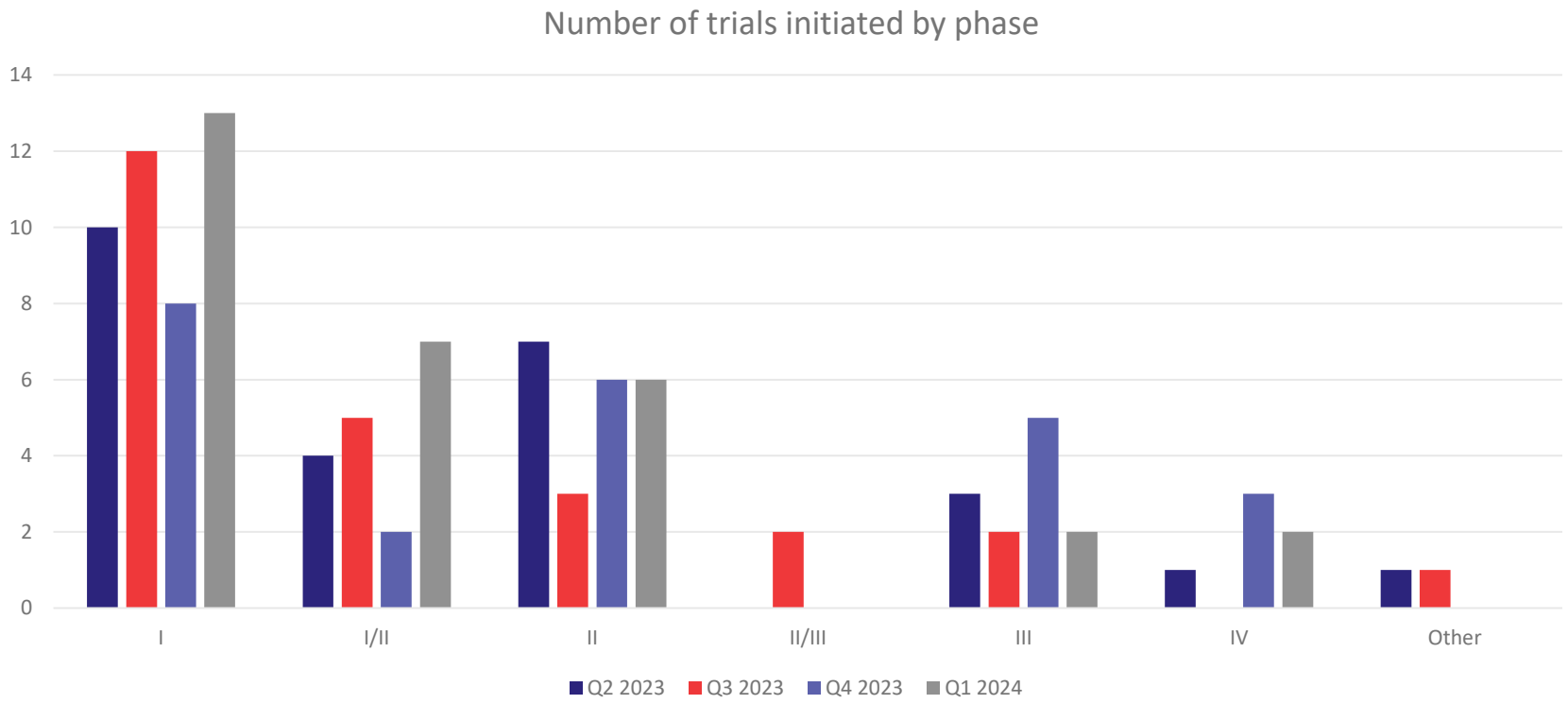


Source: Pharmaprojects | Citeline, April 2024

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

RNA therapy pipeline: clinical trial activity

- 30 RNA trials were initiated in Q1 2024, compared to 24 in Q4 2023, 90% of which were for non-oncology indications



Source: Trialtrove | Citeline, April 2024

American Society of Gene + Cell Therapy

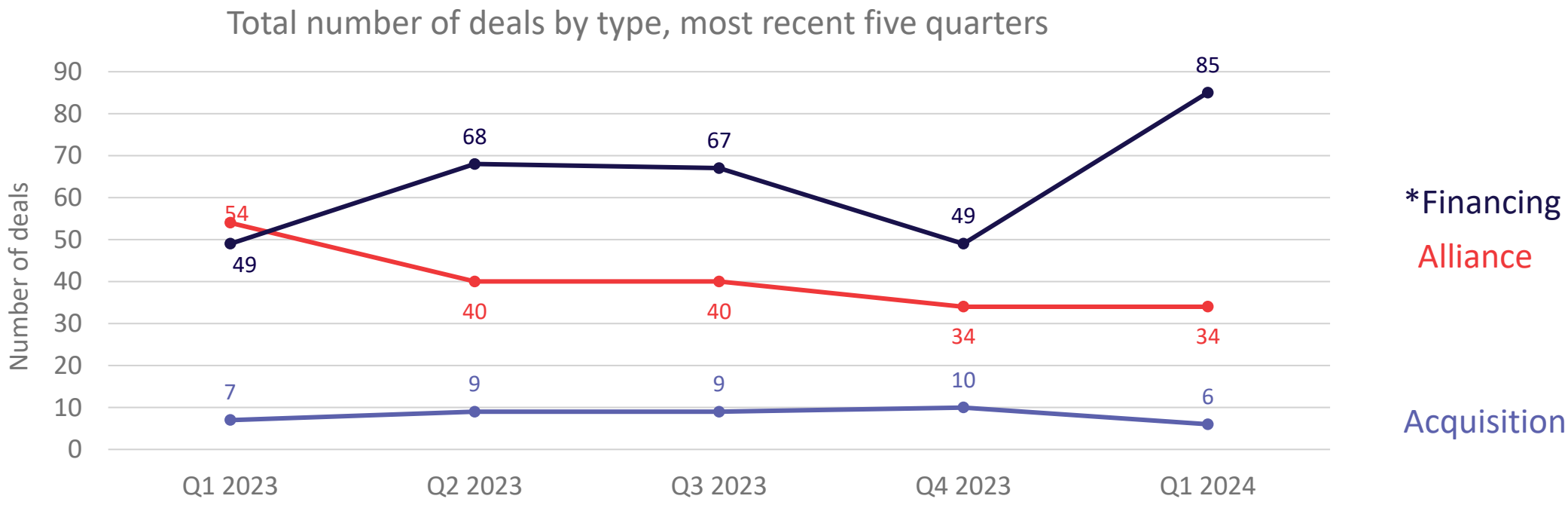
Overview of dealmaking for gene, cell, and RNA therapy companies

Q1 2024

American Society of Gene + Cell Therapy

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

- Advanced molecular companies signed a total of 125 deals in Q1 2024, a 34% increase over the previous quarter's aggregate of 93
- Q1 2024's total was not only 14% ahead of the 110 deals seen during the same quarter of 2023, but also represents a single-quarter high within the last year
- Driving the increase in 2024's opening quarter was financing volume, which rose by 74% from 49 to 85 transactions



Source: Biomedtracker | Citeline, BioSciDB | Evaluate, April 2024

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

American Society of Gene + Cell Therapy

Q1 2024 acquisitions in gene, cell, and RNA therapy

- Acquisition volume continues to trend downward quarter by quarter; Q1 2024's six total deals was down from Q4 2023's total of 10, and is also the lowest quarterly volume seen in the last year
- In Q1 2024's largest deal, Novo Nordisk is paying up to €1bn ($1.1bn) up front plus earn-outs for Cardior, which targets non-coding RNAs in cardiac diseases, focusing on a lead candidate in heart failure patients with reduced ejection fraction
- Regeneron created a new entity called Regeneron Cell Medicines by acquiring 2seventy bio's immune cell therapy pipeline for $5m

Deal date	Deal title	Potential deal value (USD $)
2 January 2024	Tome Biosciences Acquires Replace Therapeutics	185,000,000
23 January 2024	NAYA Biosciences to Acquire Florida Biotechnologies	25,000,000
30 January 2024	Regeneron to Acquire 2seventy bio's Platforms and Clinical Programs	5,000,000
28 February 2024	Ginkgo Bioworks Acquires Patch Biosciences	Undisclosed
29 February 2024	StemCell Technologies Acquires SQZ Biotechnologies Company	11,800,000
25 March 2024	Novo Nordisk to Acquire Cardior Pharmaceuticals for €1B	1,107,697,000

Source: Biomedtracker | Citeline, BioSciDB | Evaluate, April 2024

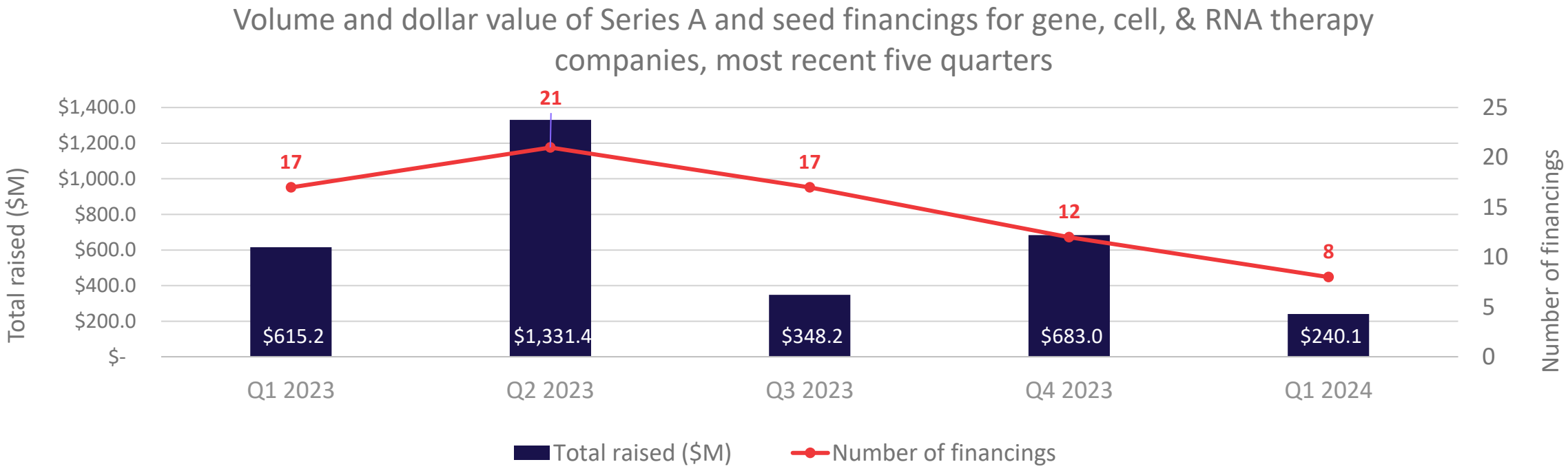
Start-up funding for gene, cell, and RNA therapy companies

Q1 2024

American Society of Gene + Cell Therapy

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

- The volume of start-up financing continues to decrease, with eight seed and Series A financings completed in Q1 2024, a 33% decline from Q4 2023's 12 transactions
- Total value from seed and Series A financings was also down in Q1 2024, totaling $240.1m, a nearly 3x decrease from the previous quarter
- Q1 2024's figures also represent declines compared with the opening quarter of 2023



Source: Biomedtracker | Citeline, Evaluate, April 2024

American Society of Gene + Cell Therapy

Q1 2024 start-up financing for gene, cell, and RNA therapy companies

Deal date	Deal title	Modality type	Company location	Academic source	Potential deal value ($M)
4 January 2024	Resalis Therapeutics Raises €10M Series A to Complete First Clinical Trial for RES-010 in Obesity	Antisense oligonucleotides	Italy / Torino	Aalborg University; Harvard Medical School	10.9
17 January 2024	Bolden Therapeutics Closes $1.5M Pre-Seed Financing	Exon-skipping antisense oligonucleotides	United States / Massachusetts / Boston	Brown University	1.5
17 January 2024	Tr1x Raises $75M in Series A Round	Allogeneic cell therapy	United States / California / San Diego	Stanford University	75.0
23 January 2024	GenEdit Brings in $24M in Series A1 Round	Non-viral genetic delivery	United States / California / San Francisco	UC Berkeley	24.0
20 February 2024	MIP Discovery Raises £7M Series A Round	Reagents for downstream bioprocessing	United Kingdom / Bedfordshire	Newcastle University	8.8
29 February 2024	Kenai Therapeutics Raises $82M in Series A Round	Allogeneic cell therapy	United States / California / San Diego	n/a – established by Cure Parkinson's	82.0
14 March 2024	Asgard Therapeutics Closes $32.8M Series A Round	In vivo cell reprogramming	Sweden / Lund	University of Coimbra; Lund University	32.8
19 March 2024	Portal Biotechnologies Gets $5M in Pre-Seed Round	Intracellular delivery in gene editing and gene expression modulation	United States / Massachusetts / Watertown	n/a – established by former leadership of SQZ Biotechnologies	5.0

Source: Biomedtracker | Citeline, Evaluate, April 2024

Notable Q1 2024 start-up gene, cell, and RNA therapy companies

Company details	Academic source	Financing type/ amount raised	Lead investor(s)	Therapy areas of interest
Off-the-shelf dopamine neuron replacement therapies using induced pluripotent stem cell technology	n/a - established by Cure Parkinson's	Series A/$82M	Alaska Permanent Fund Corporation; Cure Ventures; The Column Group	Parkinson's disease (moderate-to-severe, mild-to-severe rapid progressing, and young onset forms)
Type 1 regulatory T-cell therapies	Stanford University	Series A/$75M	The Column Group	Autoimmune and inflammatory diseases including IBD, GvHD, and multiple B-cell mediated AID
Gene therapies for in vivo reprogramming of cancer cells into antigen-presenting dendritic cells	University of Coimbra; Lund University	Series A/$32.8M	RV Invest; Johnson & Johnson Innovation – JJDC, Inc.	Oncology

Source: Biomedtracker | Citeline, Evaluate, April 2024

Upcoming catalysts

Q1 2024

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward-looking events) expected in Q2 2024

Therapy	Generic name	Disease	Catalyst	Catalyst date
mRNA-1345	n/a	Respiratory Syncytial Virus (RSV) Prevention	PDUFA/Approval Decision (U.S.)	10 May 2024 - 10 May 2024
Breyanzi	lisocabtagene maraleucel	Follicular Lymphoma (FL)	PDUFA for sNDA/sBLA	23 May 2024 - 23 May 2024
EB-101	n/a	Epidermolysis Bullosa	PDUFA/Approval Decision (U.S.)	25 May 2024 - 25 May 2024
HPC-cord blood therapy	n/a	Ischemic Stroke	PDUFA/Approval Decision (U.S.)	19 Mar 2024 - 31 May 2024
Breyanzi	lisocabtagene maraleucel	Mantle Cell Lymphoma - NHL	PDUFA for sNDA/sBLA	31 May 2024 - 31 May 2024
Rytelo	imetelstat	Myelodysplastic Syndrome (MDS)	PDUFA/Approval Decision (U.S.)	14 Jun 2024 - 14 Jun 2024
Beqvez	fidanacogene elaparvovec	Hemophilia B	PDUFA/Approval Decision (U.S.)	01 Apr 2024 - 30 Jun 2024
Kresladi	leukocyte adhesion deficiency-1 gene therapy	Autoimmune Disorders	PDUFA/Approval Decision (U.S.)	30 Jun 2024 - 30 Jun 2024
Beqvez	fidanacogene elaparvovec	Hemophilia B	CHMP (European Panel) Results	01 Mar 2024 - 30 Sep 2024
Izervay	avacincaptad pegol	Dry Age-Related Macular Degeneration (Dry AMD)/Geographic Atrophy (Ophthalmology)	CHMP (European Panel) Results	01 May 2024 - 30 Nov 2024
Beqvez	fidanacogene elaparvovec	Hemophilia B	Approval Decision (Europe)	01 May 2024 - 30 Nov 2024
QALSODY	tofersen	Amyotrophic Lateral Sclerosis (ALS)	Approval Decision (Europe)	08 Jan 2024 - 31 Dec 2024
Rytelo	imetelstat	Myelodysplastic Syndrome (MDS)	CHMP (European Panel) Results	01 Jun 2024 - 31 Dec 2024
mRNA-1345	n/a	Respiratory Syncytial Virus (RSV) Prevention	Approval Decision (Europe)	01 Jun 2024 - 31 Dec 2024
Wainua	eplontersen	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)	Approval Decision (Europe)	08 Jan 2024 - 31 Dec 2024
Breyanzi	lisocabtagene maraleucel	Indolent Non-Hodgkin's Lymphoma - iNHL	PDUFA for sNDA/sBLA	01 Jan 2024 - 31 Dec 2024
Oxlumo	lumasiran	Hyperoxaluria	Supplemental Approval (Europe)	29 Jan 2024 - 31 Jan 2025

Source: Biomedtracker | Citeline, April 2024

Appendix

Methodology, sources, and glossary of key terms

Q1 2024

American Society of Gene + Cell Therapy

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	Buy-out, divestiture, spin-out, full acquisition, partial acquisition, reverse acquisition

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American Society of Gene + Cell Therapy

Usage Guidelines

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