Gene, Cell, & RNA Therapy Landscape Report

Q2 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.

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

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

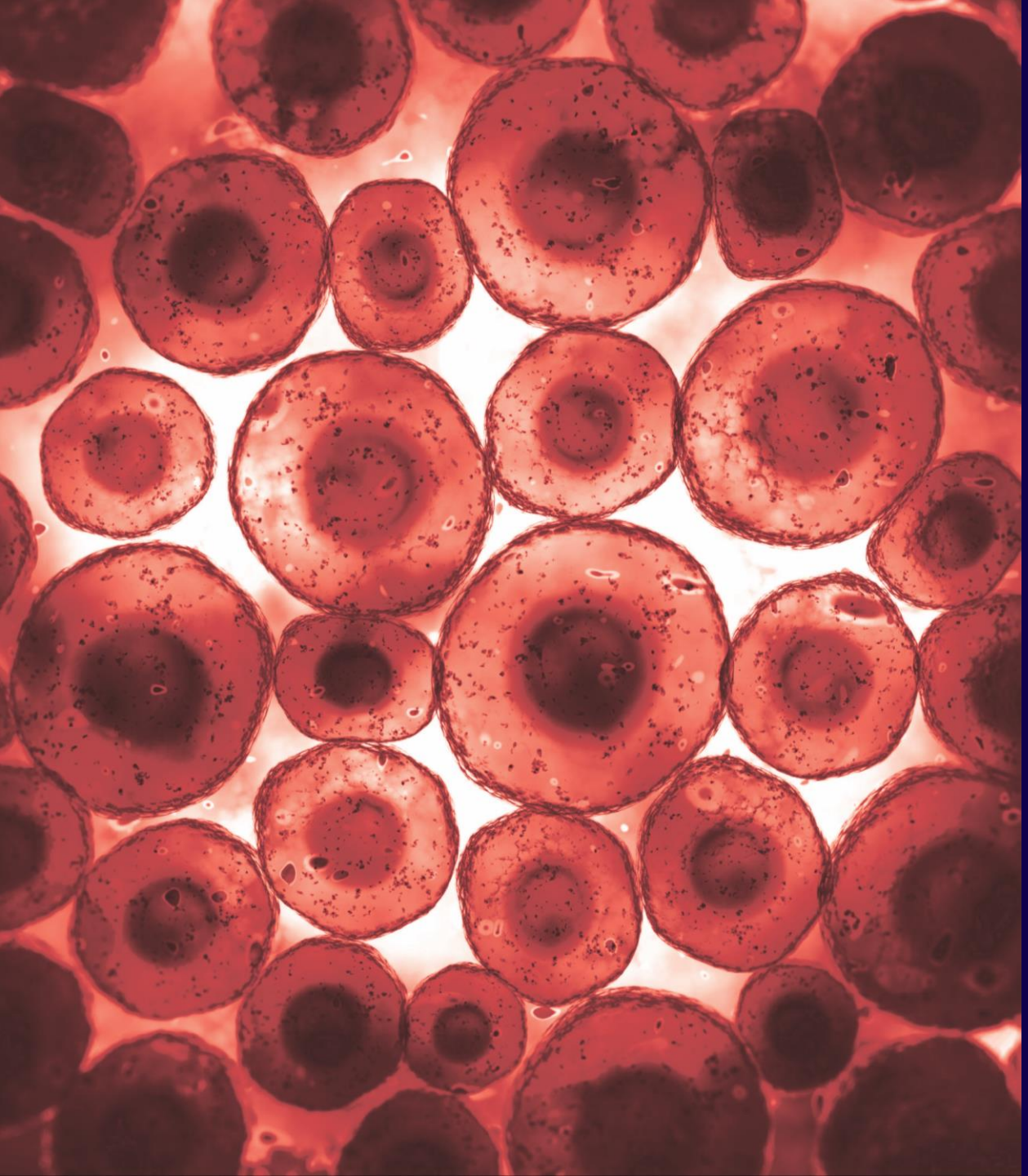


Table of contents

CITELINE
a norstella company

American Society
of Gene + Cell Therapy

Introduction

In the second quarter of 2024, two new RNA therapies were approved in the US; Rytelo was approved for myelodysplastic syndrome and mRESVIA, an mRNA vaccine, was approved for respiratory syncytial virus (RSV) prophylaxis. There were no new gene or cell therapy approvals.

For the first time in more than a year, the number of Phase II and III clinical trial candidates decreased since the previous quarter while the number of Phase I candidates continues to increase. In the pipeline of 1,023 gene therapies being developed for rare diseases, eight of the top 10 of those rare diseases were oncological. In Q2, 76 gene therapy trials were initiated — a 25% increase since the previous quarter.

Dealmaking dropped 20% from the previous quarter and 15% from the same quarter last year, while alliances and acquisitions increased slightly. There were six transactions completed in Q2, down from eight in Q1. The amount raised in Q2, $266.3 million, is an 11% increase over the previous quarter.

David Barrett, JD
CEO, ASGCT

Key takeaways from Q2 2024

New approvals in Q2 2024 were focused in the RNA landscape

- Two new RNA therapies were approved in the US: Rytelo (imetelstat), an oligonucleotide telomerase inhibitor, was approved for myelodysplastic syndrome; and mRESVIA, an mRNA vaccine, was approved for respiratory syncytial virus (RSV) prophylaxis
- Q2 saw no new gene therapy or cell therapy approvals

Oncology and rare diseases continue to be at the forefront of cell and gene therapy development

- Consistent with previous quarters, the two most targeted indication groups for cell (non-genetically modified) and gene (including genetically modified cell therapies) therapy programs are oncology and rare diseases
- Of the rare diseases, gene therapy development is more focused on oncology rare diseases, while cell therapy rare disease development focuses on non-oncology indications

Driven by a substantial decrease in financing, dealmaking is down for advanced molecular therapy companies

- A total of 100 deals were done in Q2 2024, a 20% decrease from Q1 2024 and down 15% from the same quarter in 2023
- While alliances and acquisitions saw jumps in volume, financings were down 39% to 52 transactions in Q2 2024
- Seed and Series A dollars were up slightly, by 11%, to $266.3 million in Q2 2024, but activity continues to decline, from 8 such financings in Q1 2024 to 6 in Q2 2024

Key highlights in Q2 2024

Q2 2024

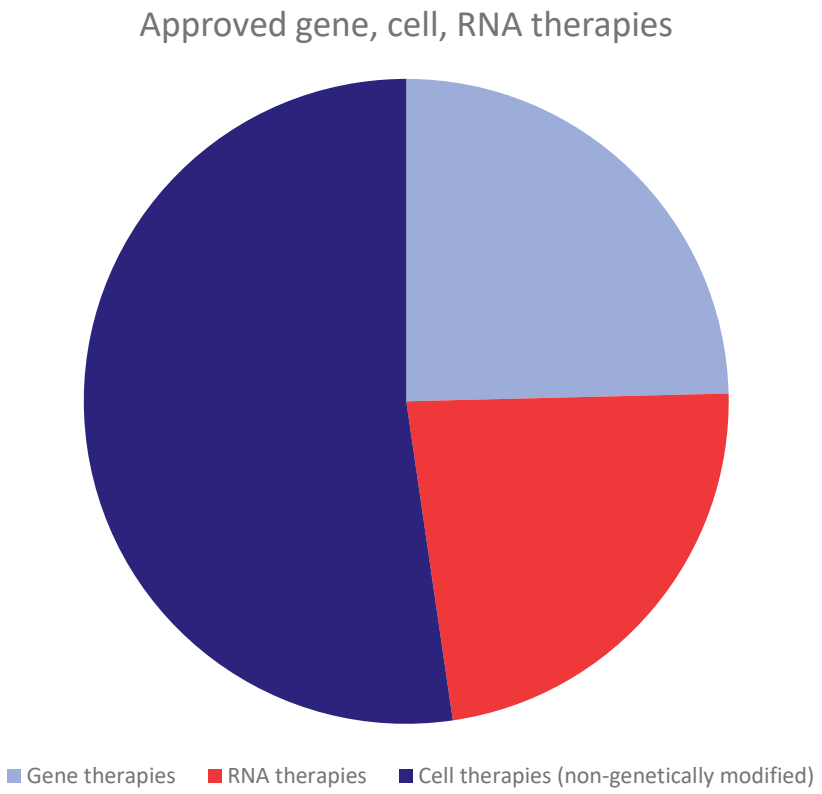
CITELINE
a norstella company

American Society of Gene + Cell Therapy

Approved gene, cell, and RNA therapies

Globally, for clinical use:

- 31 gene therapies have been approved (including genetically modified cell therapies)
- 30 RNA therapies have been approved
  - Rytelo, an oligonucleotide telomerase inhibitor developed by Geron, was approved in myelodysplastic syndrome in the US
  - mRESVIA, an mRNA respiratory syncytial virus (RSV) vaccine developed by Moderna, was approved in the US
- 68 non-genetically modified cell therapies have been approved



Source: Pharmaprojects | Citeline, July 2024

Approved gene therapies as of Q2 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

*AnGes have withdrawn the application, filed in May 2023, for full approval in Japan for Collategene for use in patients with severe peripheral vascular disease

Source: Pharmaprojects | Citeline, July 2024; Press release, AnGes, 24 Jun 2024, link

Text highlighted in yellow represents new approvals during Q2 2024

Approved gene therapies as of Q2 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; 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, Canada	Legend Biotech
Upstaza	eladocagene exuparvovec	2022	Aromatic L-amino acid decarboxylase (AADC) deficiency	EU, UK	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

Source: Pharmaprojects | Citeline, July 2024

Text highlighted in yellow represents new approvals during Q2 2024

Approved gene therapies as of Q2 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, US	Pfizer

Source: Pharmaprojects | Citeline, July 2024

Text highlighted in yellow represents new approvals during Q2 2024

Approved RNA therapies as of Q2 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, July 2024

Text highlighted in yellow represents new approvals during Q2 2024

Approved RNA therapies as of Q2 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, July 2024

Text highlighted in yellow represents new approvals during Q2 2024

Approved RNA therapies as of Q2 2024 (3/3)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Qalsody	tofersen	2023	Amyotrophic lateral sclerosis	US, EU	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
Rytelo	imetelstat	2024	Myelodysplastic syndrome	US	Geron
mRESVIA	respiratory syncytial virus vaccine, Moderna Therapeutics	2024	Respiratory syncytial virus prophylaxis	US	Moderna Therapeutics

*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, July 2024

Text highlighted in yellow represents new approvals during Q2 2024

Key highlights in Q2 2024 (1/2)

Noteworthy events that happened in Q2 2024

Drug	Event Type	Indication	Molecule	Event Date
RP-L102	European Filing Accepted	Fanconi Anemia	Viral Gene Therapy	02 April 2024
LX2006	Fast Track Status	Friedreich's Ataxia	Viral Gene Therapy	16 April 2024
AB-1002	Fast Track Status	Chronic Heart Failure - Reduced Ejection Fraction (Chronic HFrEF)	Viral Gene Therapy	18 April 2024
EB-101	Complete Response Letter (CRL)	Epidermolysis Bullosa	Viral Gene Therapy	22 April 2024
DVX101	Fast Track Status	Acute Myelogenous Leukemia (AML)	Cellular	24 April 2024
ACDN-01	Rare Pediatric Disease (RPD) Designation	Stargardt Disease (Ophthalmology)	Viral Gene Therapy	25 April 2024
Beqvez	Approval (U.S.)	Hemophilia B	Viral Gene Therapy	26 April 2024
IGNK001	Orphan Drug Designation (U.S.)	Acute Myelogenous Leukemia (AML)	Cellular	30 April 2024
TSHA-102	Regenerative Medicine Advanced Therapy (RMAT) Designation	Rett Syndrome	Viral Gene Therapy	02 May 2024
Olezarsen	NDA/BLA Filing	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Antisense	07 May 2024
FLT201	PRIME Designation (Europe); Regenerative Medicine Advanced Therapy (RMAT) Designation	Gaucher Disease	Viral Gene Therapy	09 May 2024
Upstaza	Priority Review	Aromatic L-amino acid decarboxylase (AADC) deficiency	Viral Gene Therapy	14 May 2024
WU-CART-007	Regenerative Medicine Advanced Therapy (RMAT) Designation; PRIME Designation (Europe)	Adult T-cell Leukemia/Lymphoma (ATL)	Cellular	20 May 2024
IGV-001	Fast Track Status	Brain Cancer (Malignant Glioma; AA and glioblastoma (GBM))	Antisense	21 May 2024
UCART22	Orphan Drug Designation (Europe)	Acute Lymphoblastic Leukemia (ALL)	Cellular	24 May 2024
RP-A601	Orphan Drug Designation (Europe)	Cardiovascular Disease	Viral Gene Therapy	24 May 2024
TSC-100	Regenerative Medicine Advanced Therapy (RMAT) Designation	Hematologic Cancer	Cellular	29 May 2024
SPL84	Fast Track Status	Cystic Fibrosis (CF)	Antisense	29 May 2024
QALSODY	Approval (Europe)	Amyotrophic Lateral Sclerosis (ALS)	Antisense	29 May 2024
BRT-DA01	Regenerative Medicine Advanced Therapy (RMAT) Designation	Parkinson's Disease (PD)	Cellular	30 May 2024
Beqvez	CHMP (European Panel) Results (Positive)	Hemophilia B	Viral Gene Therapy	30 May 2024
mRESVIA	Approval (U.S.)	Respiratory Syncytial Virus Prophylaxis	mRNA vaccine	31 May 2024
NGN-401	Innovative Licensing and Access Pathway (ILAP) (U.K.)	Rett Syndrome	Viral Gene Therapy	03 June 2024
AMT-130	Regenerative Medicine Advanced Therapy (RMAT) Designation	Huntington's Disease	Viral Gene Therapy	03 June 2024

Source: Biomedtracker | Citeline, July 2024

Key highlights in Q2 2024 (2/2)

Noteworthy events that happened in Q2 2024

Drug	Event Type	Indication	Molecule	Event Date
Rytelo	Approval (U.S.)	Myelodysplastic Syndrome (MDS)	New Molecular Entity (NME)	06 June 2024
AGTC-501	Innovative Licensing and Access Pathway (ILAP) (U.K.); PRIME Designation (Europe); Fast Track Status	Retinitis Pigmentosa (RP) (Ophthalmology)	Viral Gene Therapy	12 June 2024
NRTX-1001	Regenerative Medicine Advanced Therapy (RMAT) Designation	Partial/Focal Seizures (Epilepsy)	Cellular	18 June 2024
Fitusiran	Filing for Approval (China); NDA/BLA Filing	Hemophilia A and B - General Clotting Products	siRNA/RNAi	21 June 2024
VX-880	Regenerative Medicine Advanced Therapy (RMAT) Designation	Diabetes Mellitus, Type I	Cellular	21 June 2024
Olezarsen	Priority Review	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Antisense	25 June 2024
CT-0525	Fast Track Status	Solid Tumors	Cellular	25 June 2024
Kresladi	Complete Response Letter (CRL)	Leukocyte Adhesion Deficiency-I (LAD-I)	Viral Gene Therapy	28 June 2024
Amtagvi	MAA Submission (Europe)	Melanoma	Cellular	28 June 2024

Source: Biomedtracker | Citeline, July 2024

Pipeline overview

Q2 2024

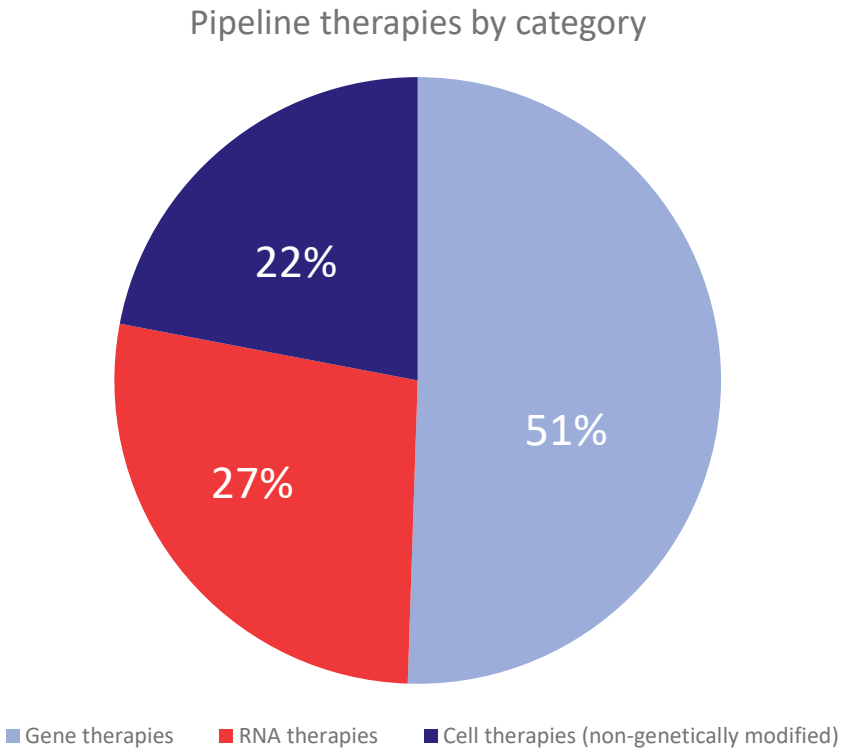
CITELINE
a norstella company

American Society
of Gene + Cell Therapy

Pipeline of gene, cell, and RNA therapies

4,047 therapies are in development, ranging from preclinical through pre-registration

- 2,068 gene therapies (including genetically modified cell therapies such as CAR-T cell therapies) are in development, accounting for 51% of gene, cell, and RNA therapies
- 901 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies



Source: Pharmaprojects | Citeline, July 2024

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q2 2024

CITELINE
a norstella company

American Society
of Gene + Cell Therapy

Gene therapy pipeline: quarterly comparison

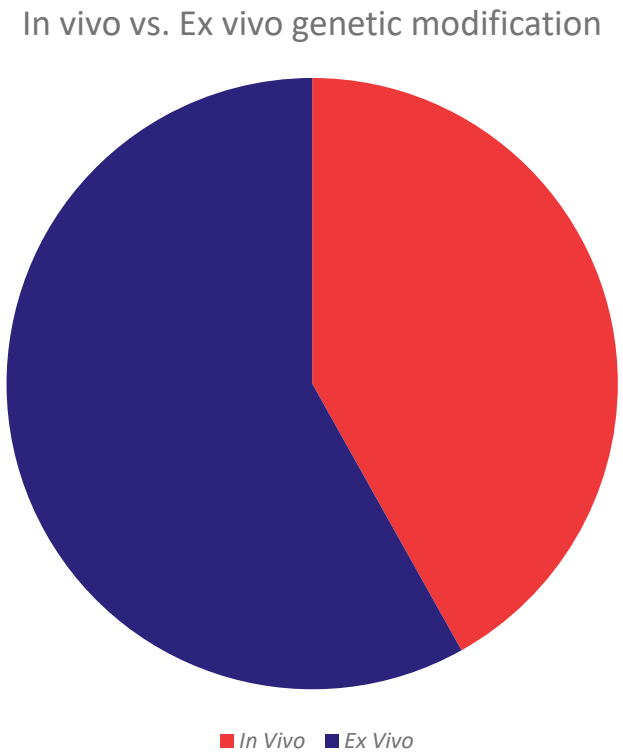
- For the first time in over a year, the number of Phase II and Phase III candidates have seen a decrease since the previous quarter, while the number of gene therapies at Phase I continues to increase
- Rocket Pharmaceuticals has filed for approval for a second gene therapy, RP-L102. The filing was made to the EMA for the treatment of Fanconi anemia
- Therapies currently in pre-registration:
  - In the US
    - RP-L201 (Rocket Pharmaceuticals)
    - EB-101 (Abeona Therapeutics)
    - afami-cel (Adaptimmune Therapeutics)
  - In the US and EU
    - obe-cel (Autolus Therapeutics)
  - In the EU
    - RP-L102 (Rocket Pharmaceuticals)

Global Status	Q2 2023	Q3 2023	Q4 2023	Q1 2024	Q2 2024
Preclinical	1,539	1,522	1,528	1,471	1,436
Phase I	240	256	270	301	314
Phase II	260	267	274	282	279
Phase III	30	30	33	35	34
Pre-registration	6	7	6	4	5
Total	**2,075**	**2,082**	**2,111**	**2,093**	**2,068**

Source: Pharmaprojects | Citeline, July 2024

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

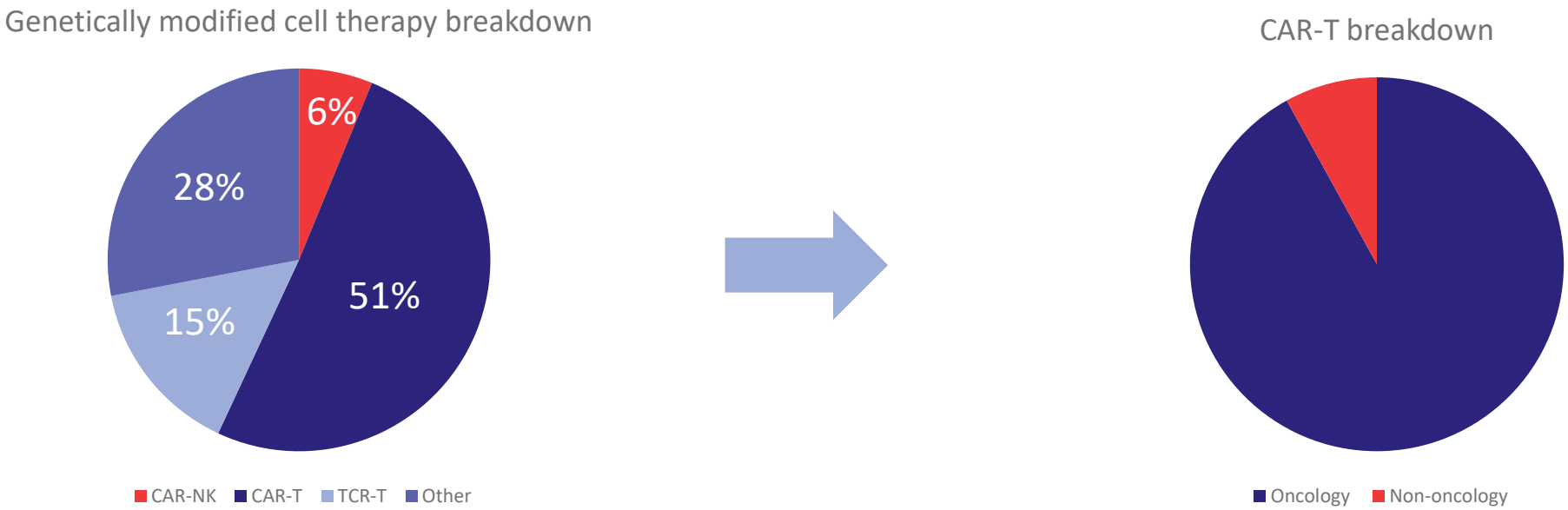
- *Ex vivo* genetic modification is more widely used for gene therapies in pipeline development
- In Q2 2024, *in vivo* delivery techniques were used in 42% of gene therapies



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

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 51%, followed by the “other” category at 28%, 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)

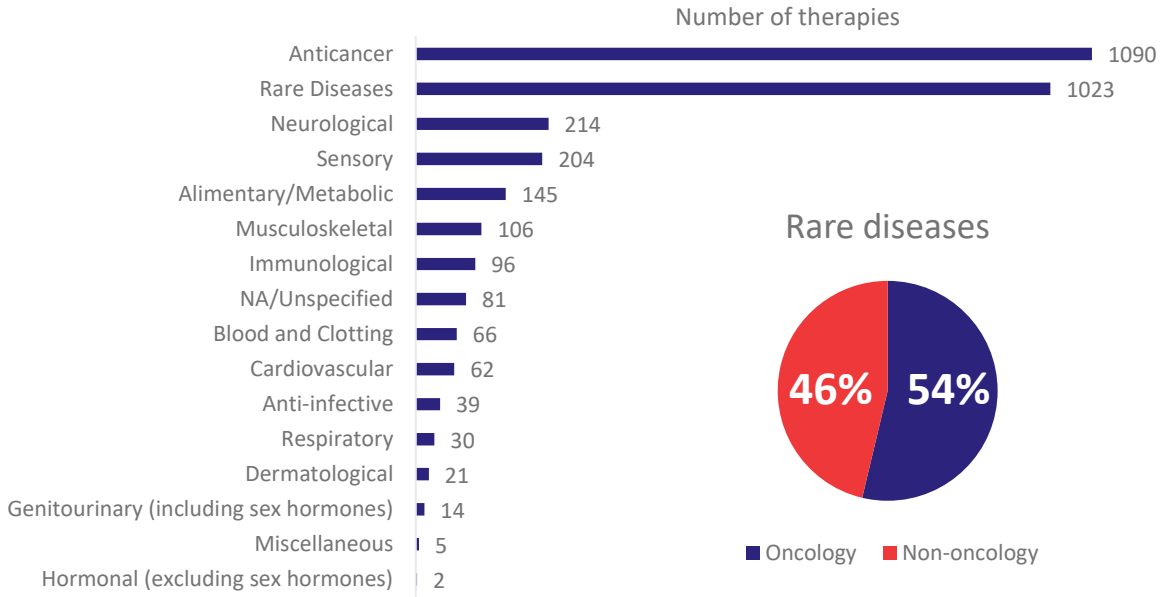


Source: Cell and Gene Therapy dashboard | Citeline, July 2024

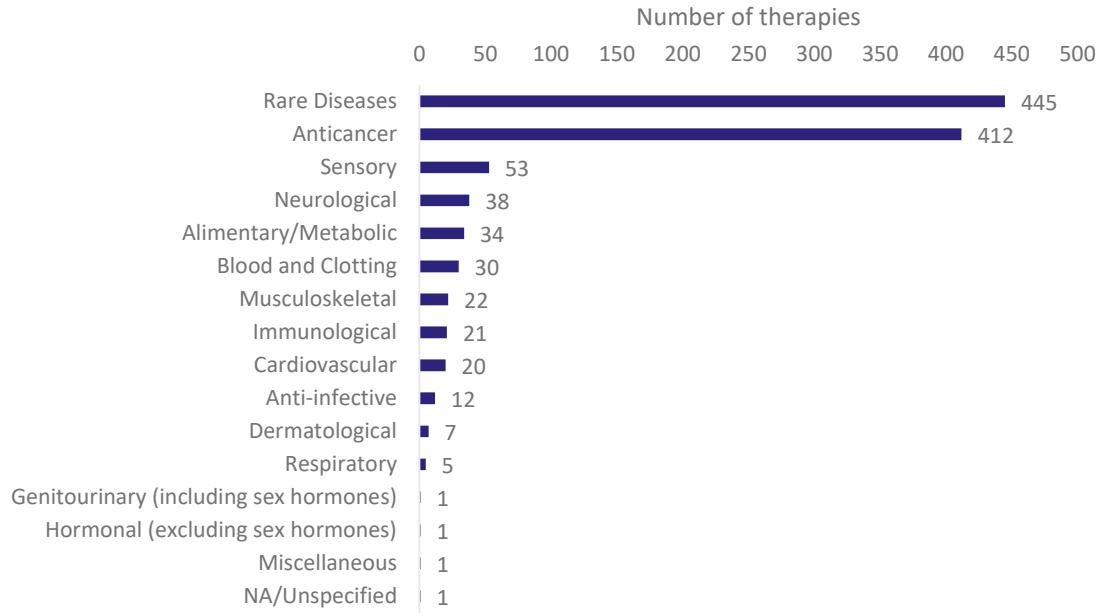
Gene therapy pipeline: most commonly targeted therapeutic areas

- 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, as seen in the previous quarter

Number of therapies from preclinical through pre-registration



Therapies in the clinic (excludes preclinical development)



Source: Pharmaprojects | Citeline, July 2024

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

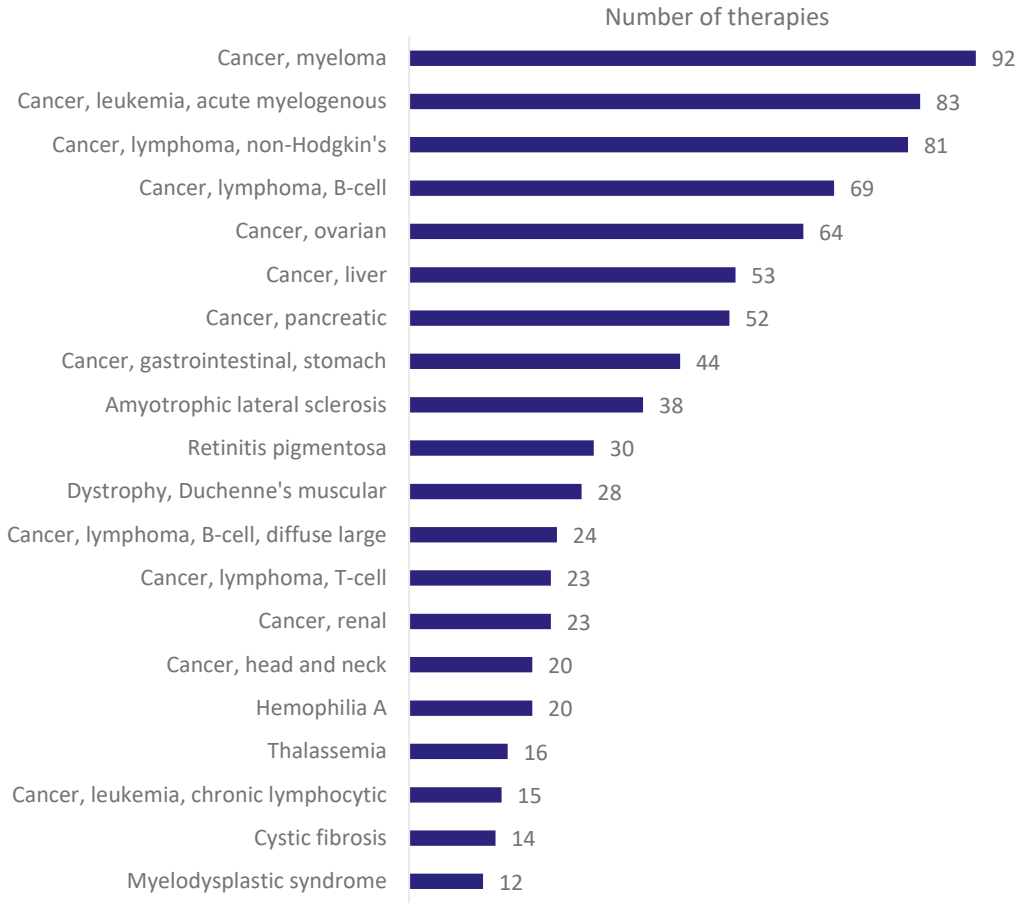
CITELINE a norstella company

American Society of Gene + Cell Therapy

Gene therapy pipeline: most common rare diseases targeted

- For the 1,023 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, 2023, and Q1 2024
- 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



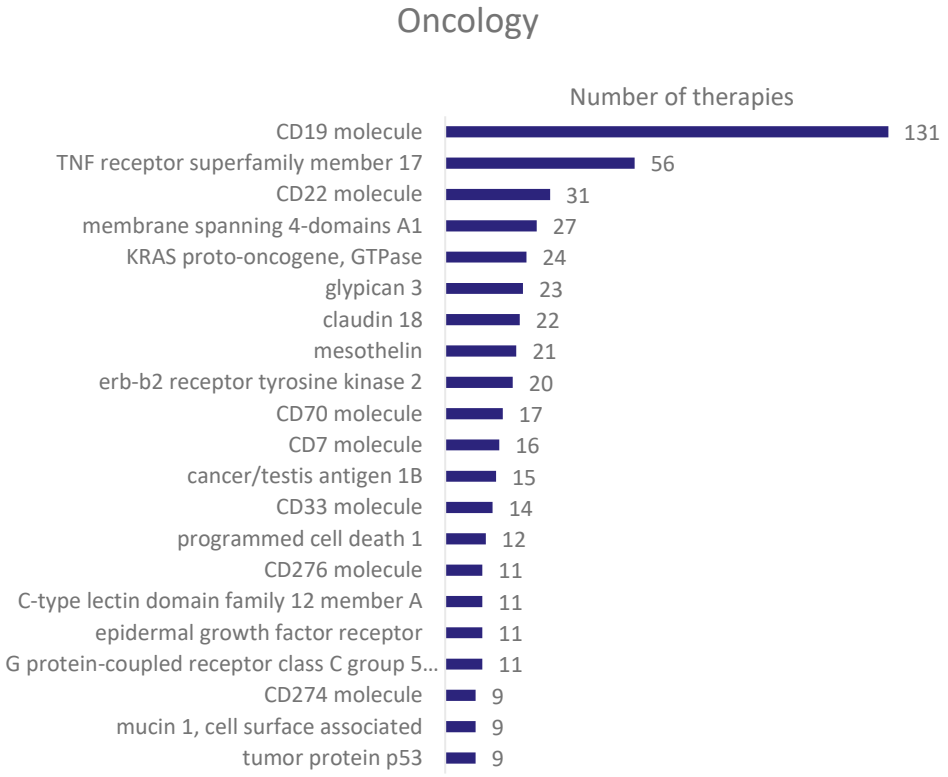
Source: Pharmaprojects | Citeline, July 2024

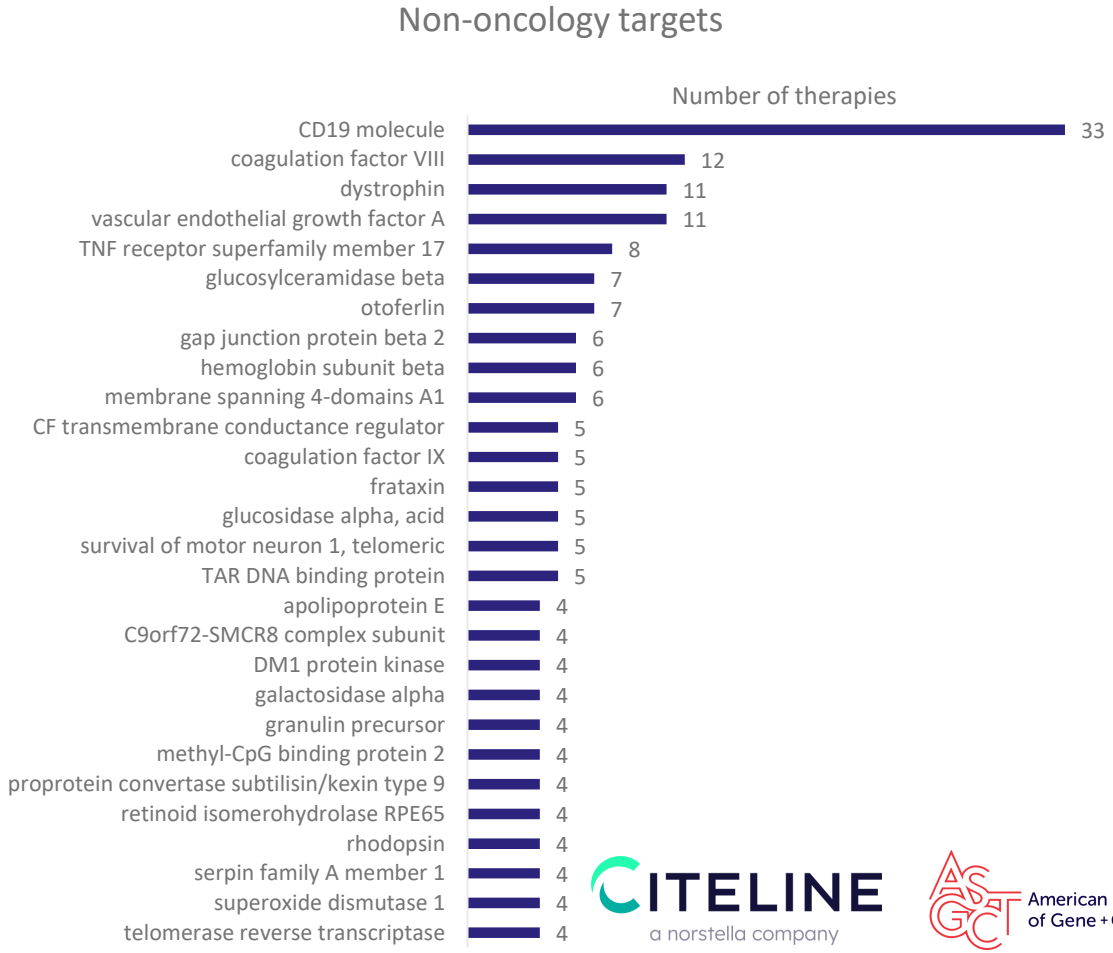
Note: Figures based on indications in pipeline development only for each therapy

Gene therapy pipeline: most common targets

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

- CD19, 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 Q2 2024, as seen in the previous three quarters





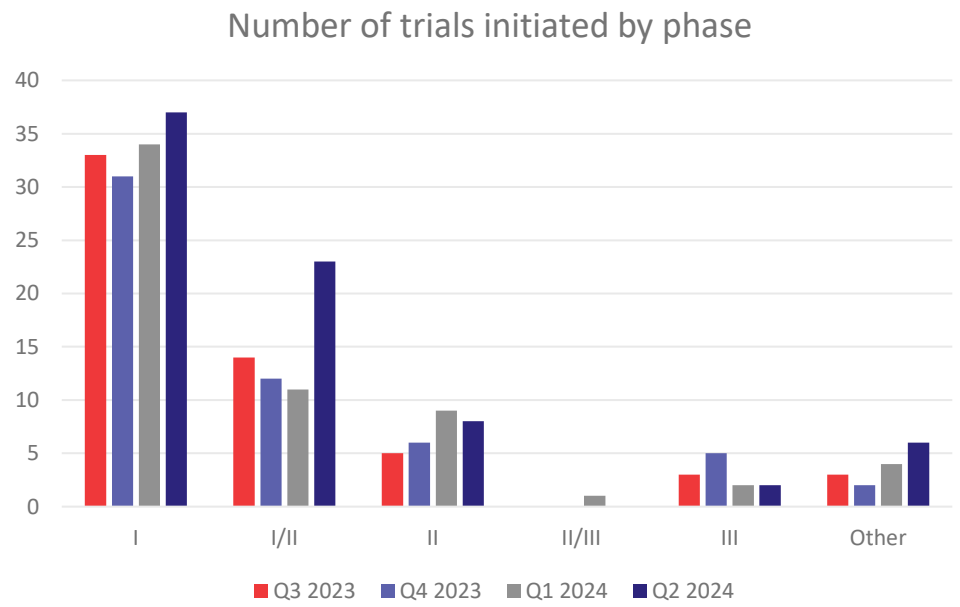
Source: Pharmaprojects | Citeline, July 2024

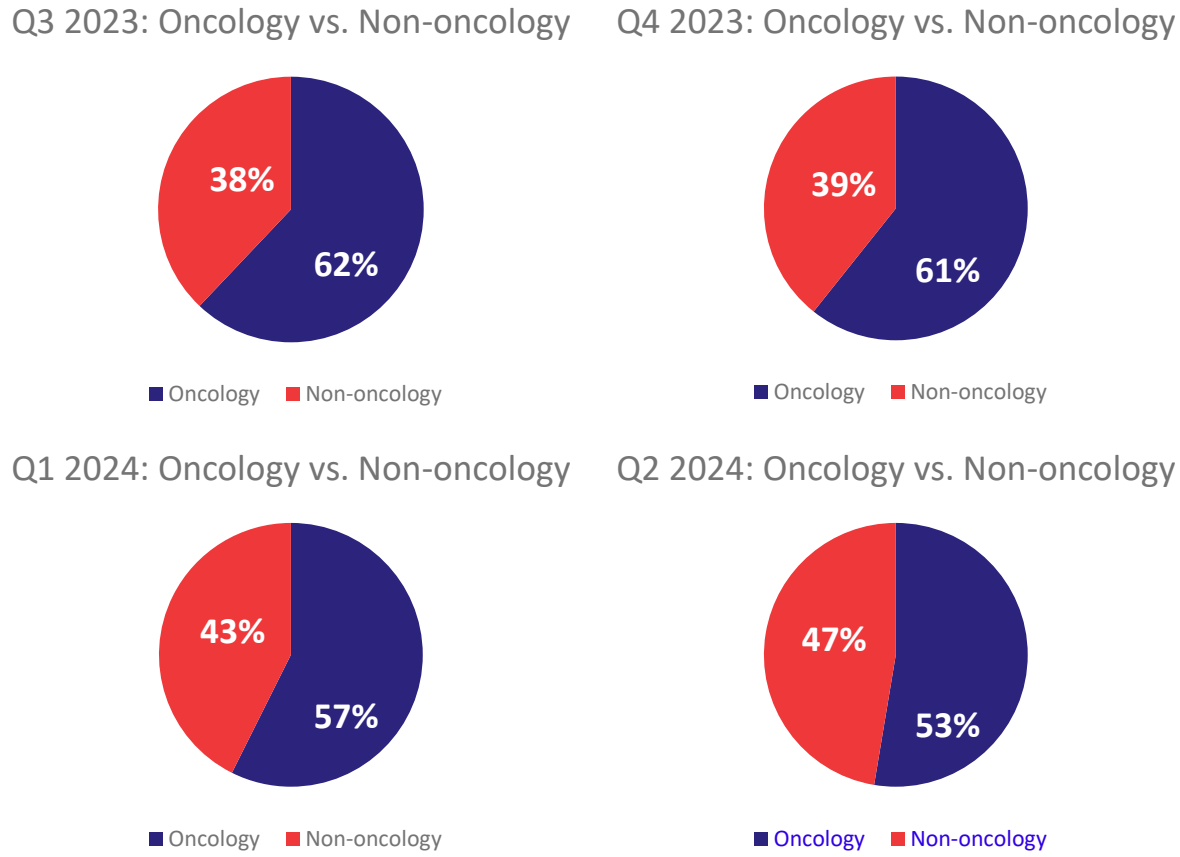
CITELINE a norstella company

American Society of Gene + Cell Therapy

Gene therapy clinical trial activity

- The proportion of gene therapy trials for non-oncology indications has increased by another four percentage points since the previous quarter, to 47%, continuing the trend of an increasing proportion of non-oncology gene therapy trials
- 76 gene therapy trials were initiated in Q2 2024, a 25% increase since the previous quarter





Source: Trialtrove | Citeline, July 2024

CITELINE a norstella company

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline

Q2 2024

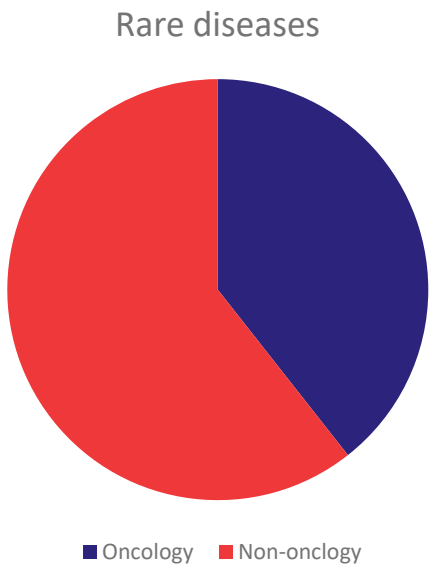
CITELINE
a norstella company

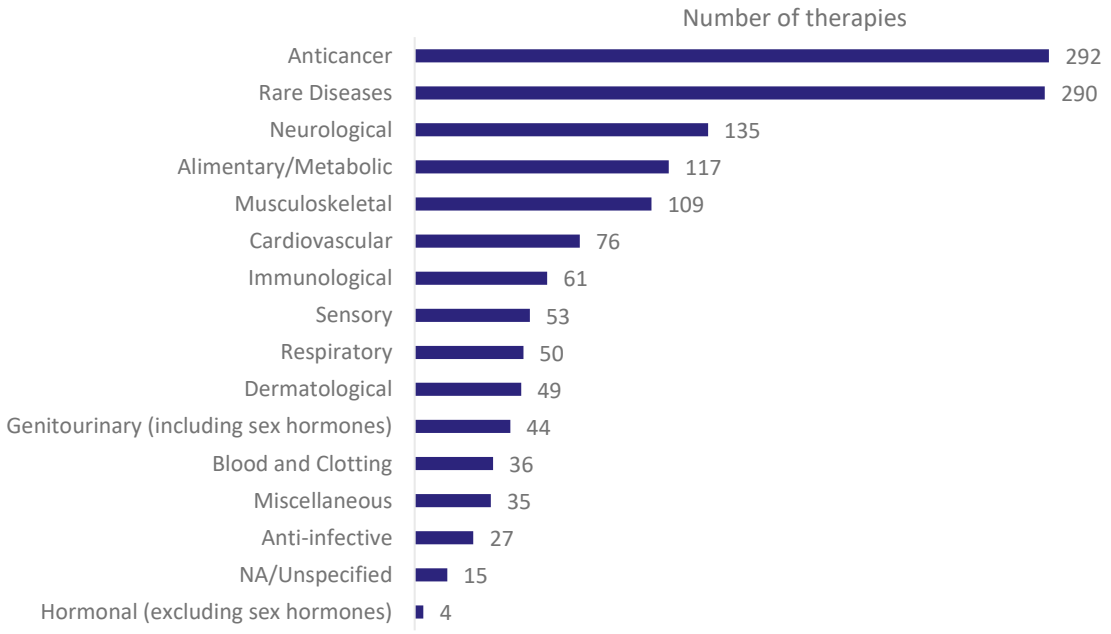
American Society of Gene + Cell Therapy

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, 62% were in development for non-oncology rare diseases, 2 percentage points lower than in the previous three quarters





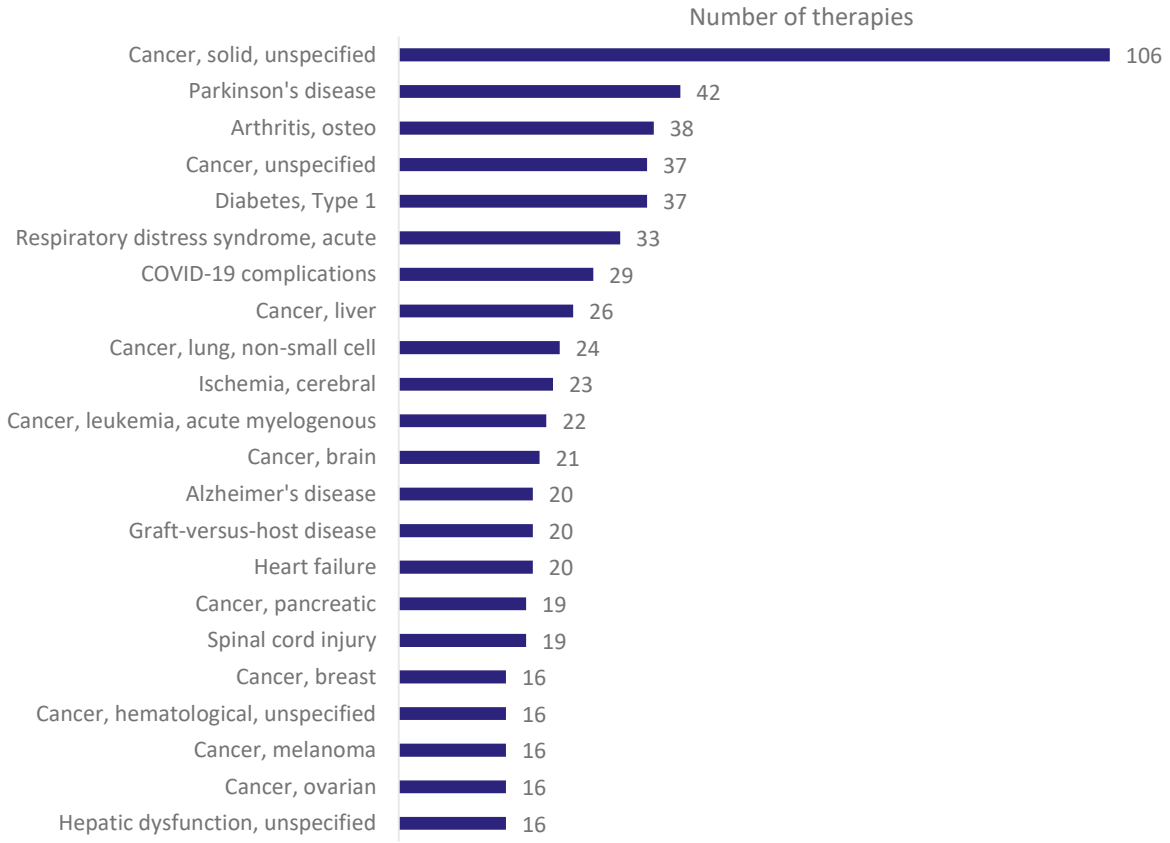
Source: Pharmaprojects | Citeline, July 2024

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, Parkinson's disease continues to be the most targeted disease:

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



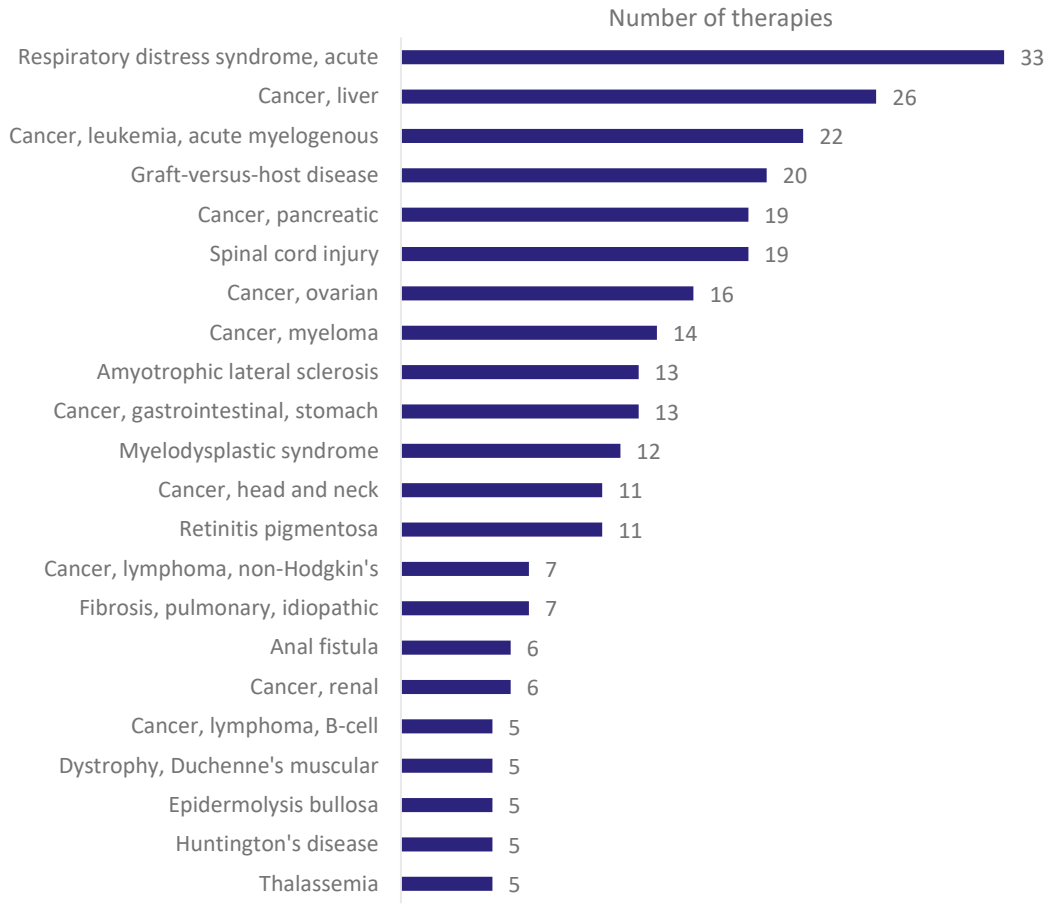
Source: Pharmaprojects | Citeline, July 2024

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 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

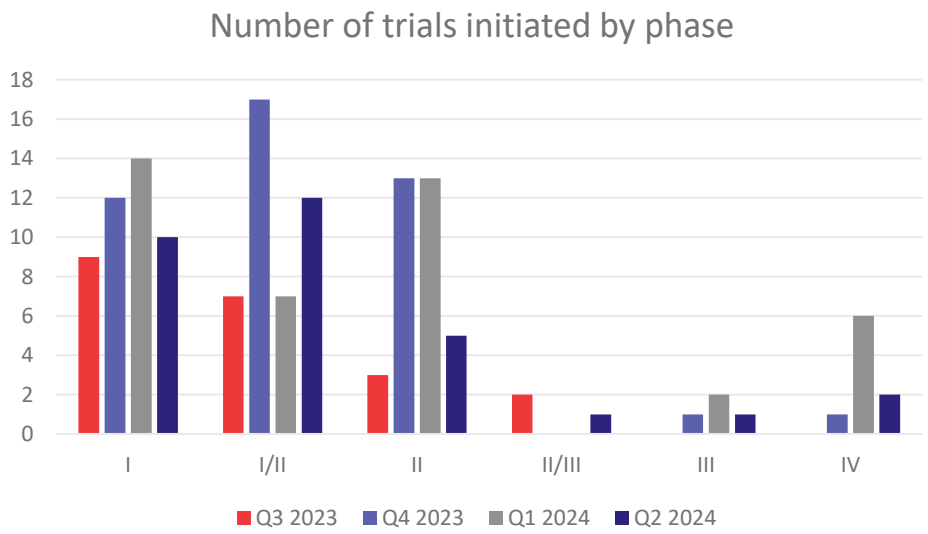


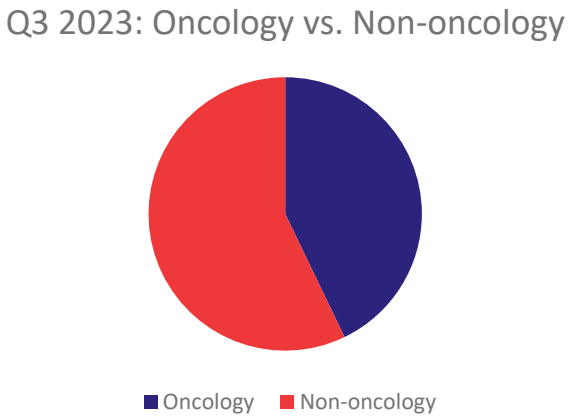
Source: Pharmaprojects | Citeline, July 2024

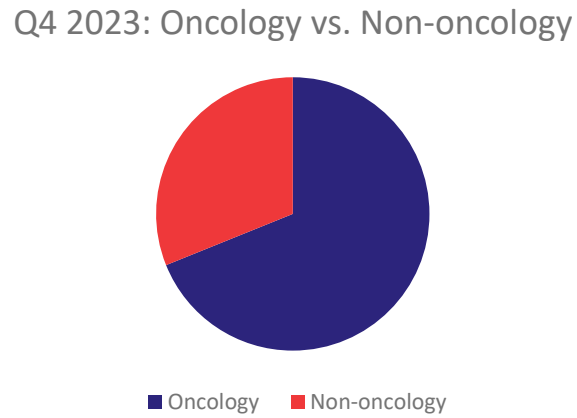
Note: Figures based on indications in pipeline development only for each therapy

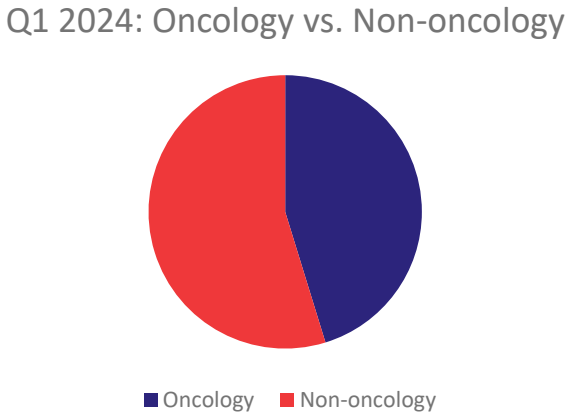
Non-genetically modified cell therapy trial activity

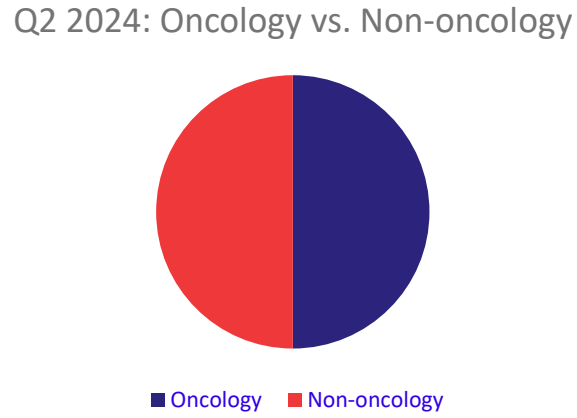
- 31 trials were initiated for non-genetically modified cell therapies in Q2 2024, 11 fewer than in the previous quarter
- Of these 31, 52% were for non-oncology indications











Source: Trialtrove | Citeline, July 2024

RNA therapy pipeline

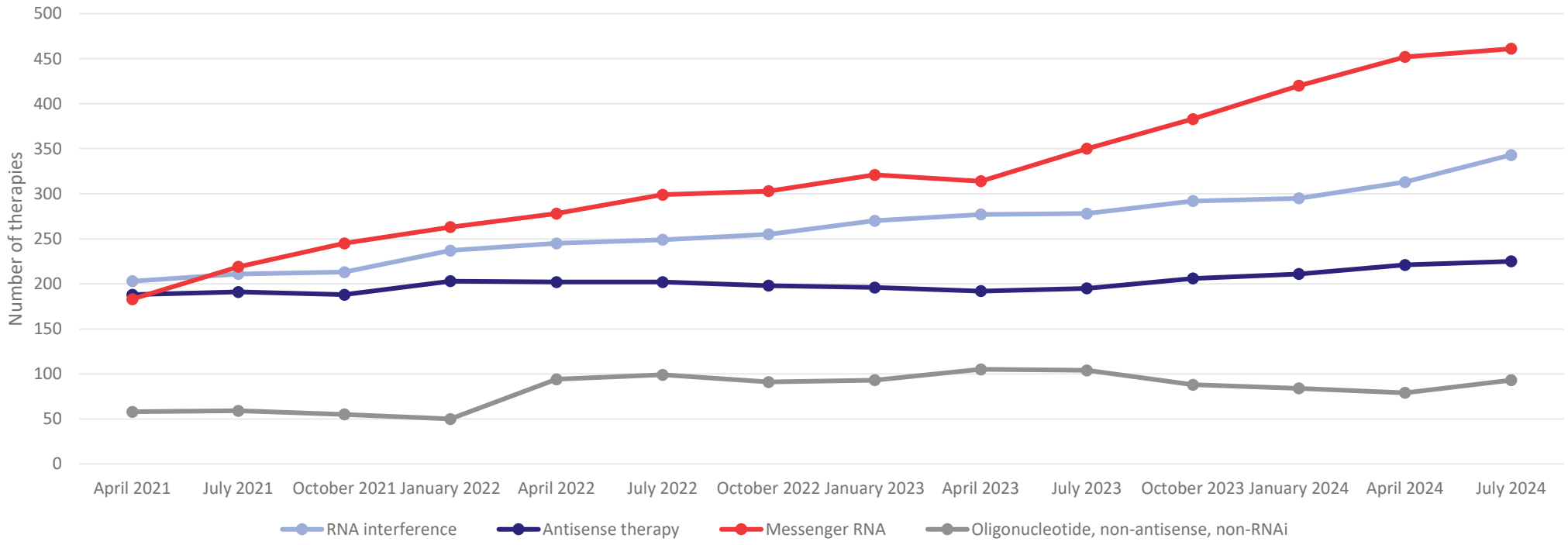
Q2 2024

CITELINE
a norstella company

American Society
of Gene + Cell Therapy

RNA therapy pipeline: most common modalities

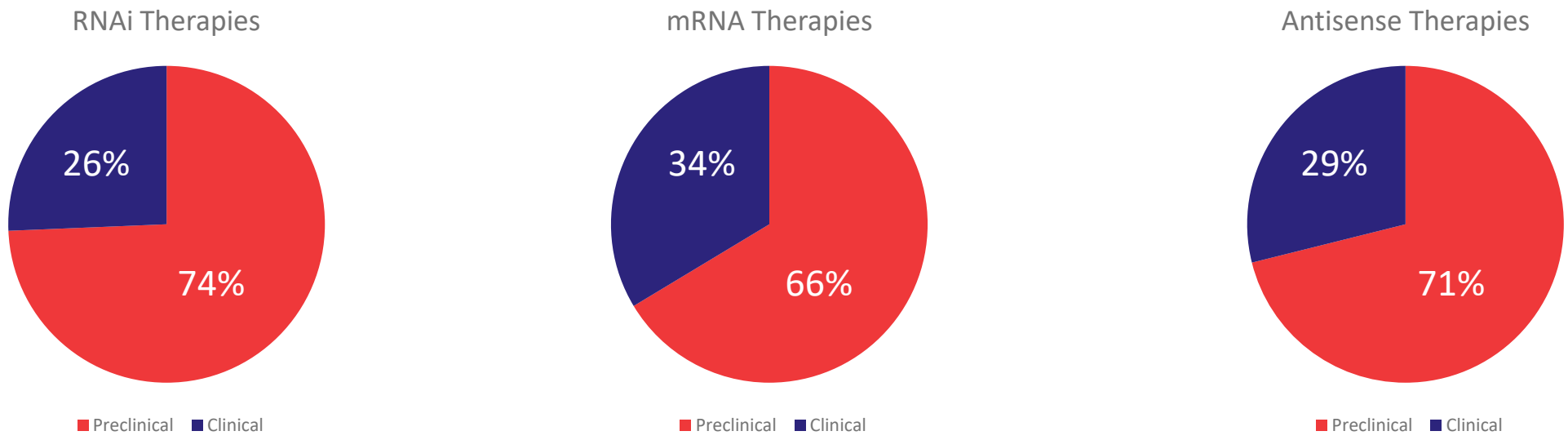
- Of RNA therapies in the pipeline, messenger RNA (mRNA) and RNA interference (RNAi) continued to be the preferred RNA modalities for research



Source: Pharmaprojects | Citeline, July 2024

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

- The majority of RNAi, mRNA, and antisense therapies in development were in the preclinical stage, representing 74%, 66%, and 71% of their respective pipelines

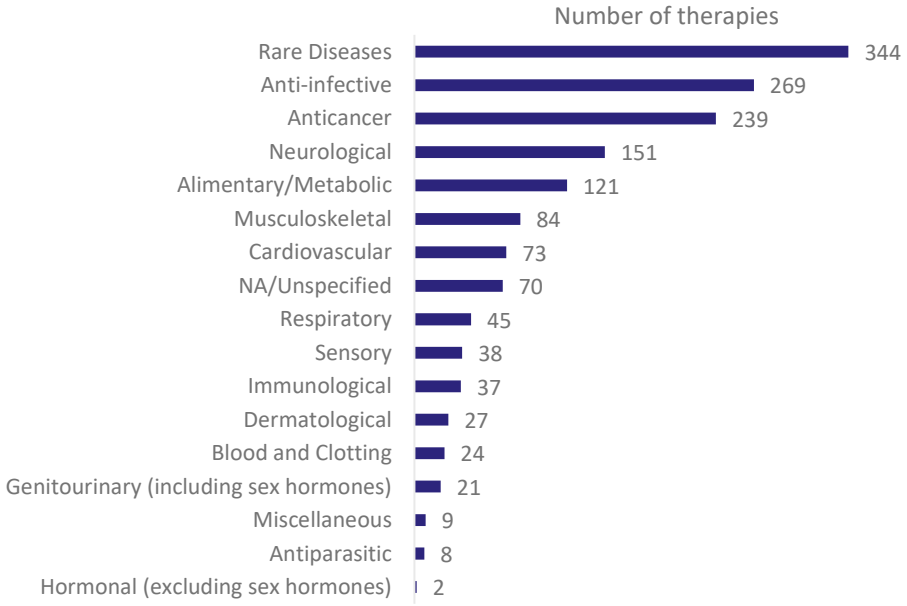


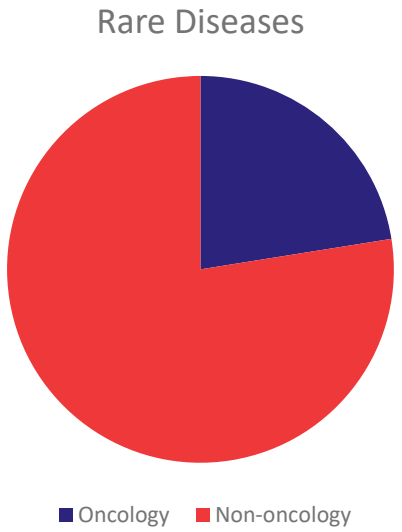
Source: Pharmaprojects | Citeline, July 2024

RNA therapies: most commonly targeted therapeutic areas

Of the 1,125 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 78%





Source: Pharmaprojects | Citeline, July 2024

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

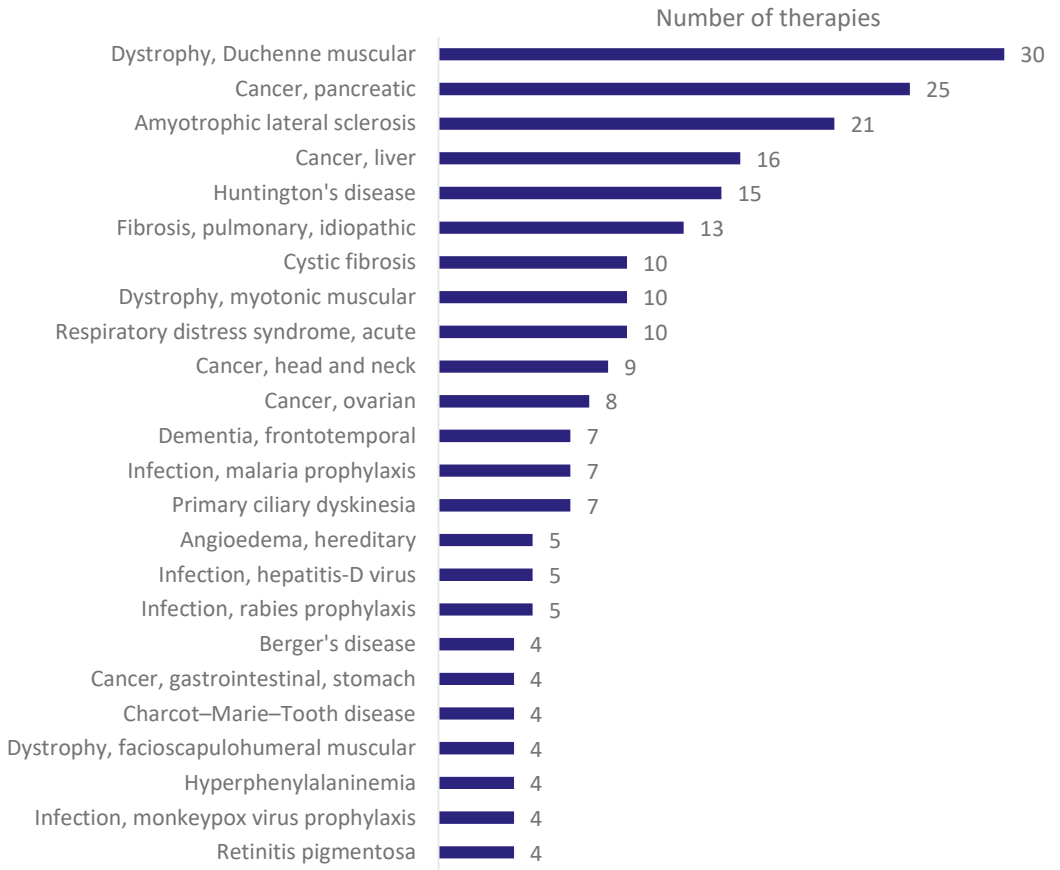
CITELINE a norstella company

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 head and neck cancer
- For non-oncology rare diseases, Duchenne muscular dystrophy, amyotrophic lateral sclerosis, and Huntington's disease were the most targeted indications

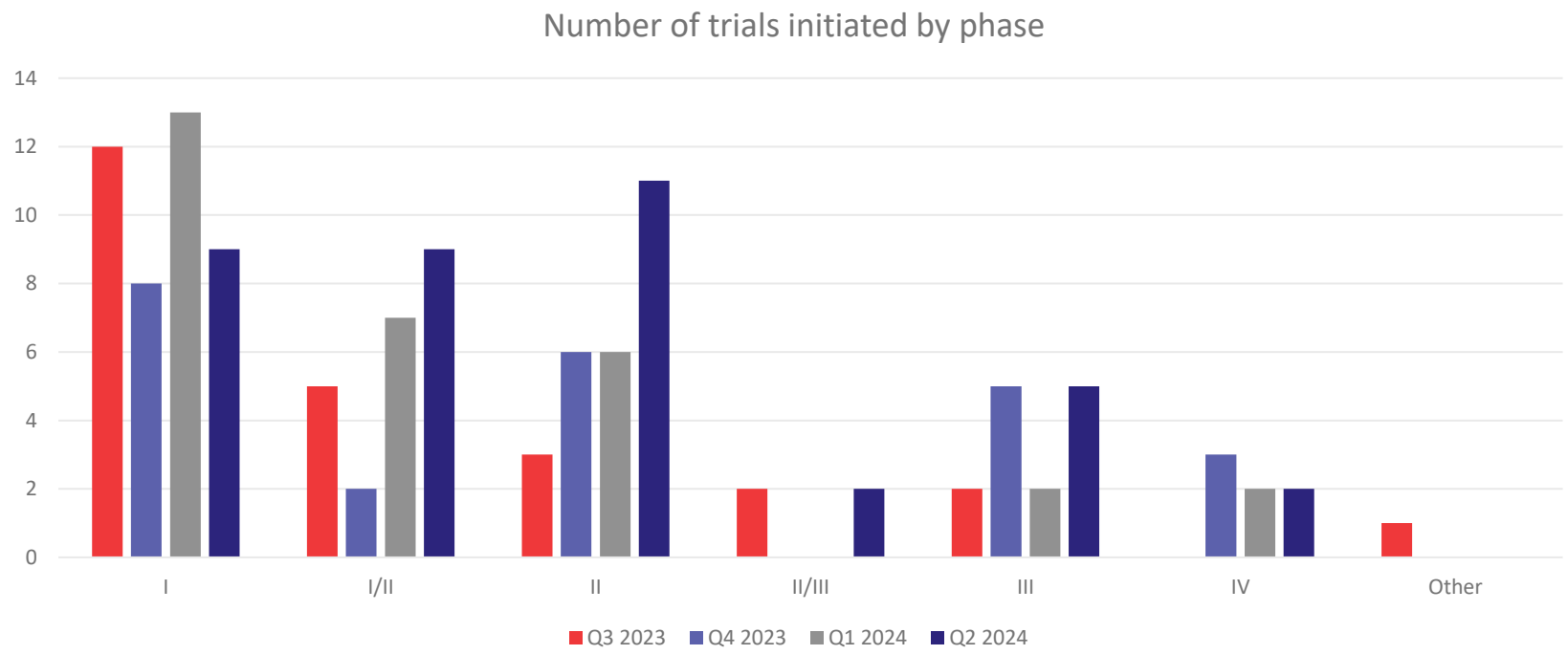


Source: Pharmaprojects | Citeline, July 2024

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

RNA therapy pipeline: clinical trial activity

- 38 RNA trials were initiated in Q2 2024, compared to 30 in Q1 2024, 82% of which were for non-oncology indications



Source: Trialtrove | Citeline, July 2024

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

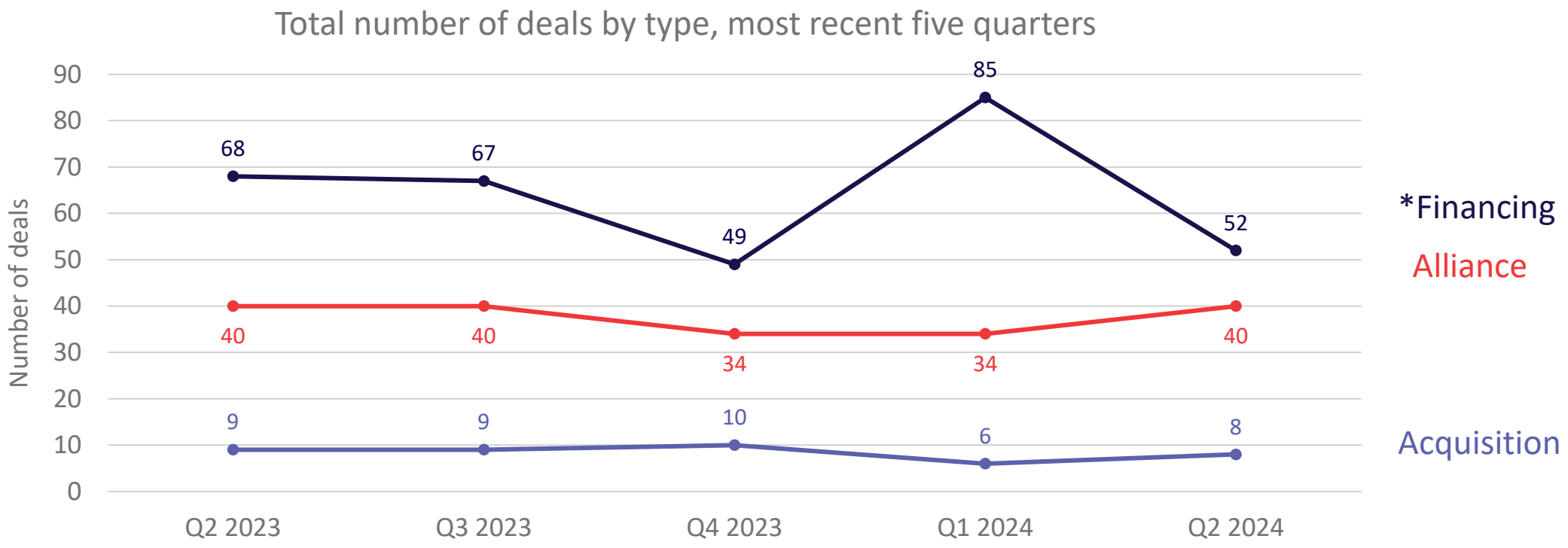
Q2 2024

CITELINE
a norstella company

American Society of Gene + Cell Therapy

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

- In Q2 2024, advanced molecular therapy companies reached a total of 100 deals, representing a 20% decrease from the previous quarter's 125 agreements, and also down 15% from 117 in the same quarter last year
- Alliances and acquisitions each trended slightly upward in Q2 2024
- The decrease in the current quarter was due to a big drop (-39%) in financings, which totaled just above the low seen in Q4 2023



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

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

CITELINE a norstella company

American Society of Gene + Cell Therapy

Q2 2024 acquisitions in gene, cell, and RNA therapy

- Acquisitions of advanced molecular therapy companies was up slightly in Q2 2024, totaling 8 transactions
- The quarter's largest deal saw MilliporeSigma buy Mirus Bio for $600 million, gaining a portfolio of transfection agents to be used in viral vector manufacturing
- In a $50 million agreement, big pharma company GlaxoSmithKline purchased Elsie Biotechnologies and its encoding technology for increasing activity, reducing toxicity, and improving delivery of oligonucleotide therapies

Deal date	Deal title	Potential deal value (USD $)
3 April 2024	Kintara Therapeutics and TuHURA Biosciences Enter into Merger Agreement	Undisclosed
11 April 2024	Century Therapeutics to Acquire Clade Therapeutics for up to $45M; Acquisition Closed	45,000,000
8 May 2024	Arbor Biotechnologies Announces Acquisition of Serendipity	Undisclosed
20 May 2024	InDex Pharmaceuticals Enters into Reverse Merger Agreement with Flerie	Undisclosed
23 May 2024	Orna Therapeutics Acquires ReNAgade Therapeutics	Undisclosed
23 May 2024	MilliporeSigma Acquires Mirus Bio for $600M	600,000,000
6 June 2024	GSK Acquires Elsie Biotechnologies	50,000,000
17 June 2024	Spur Therapeutics Acquires SwanBio Therapeutics	Undisclosed

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

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

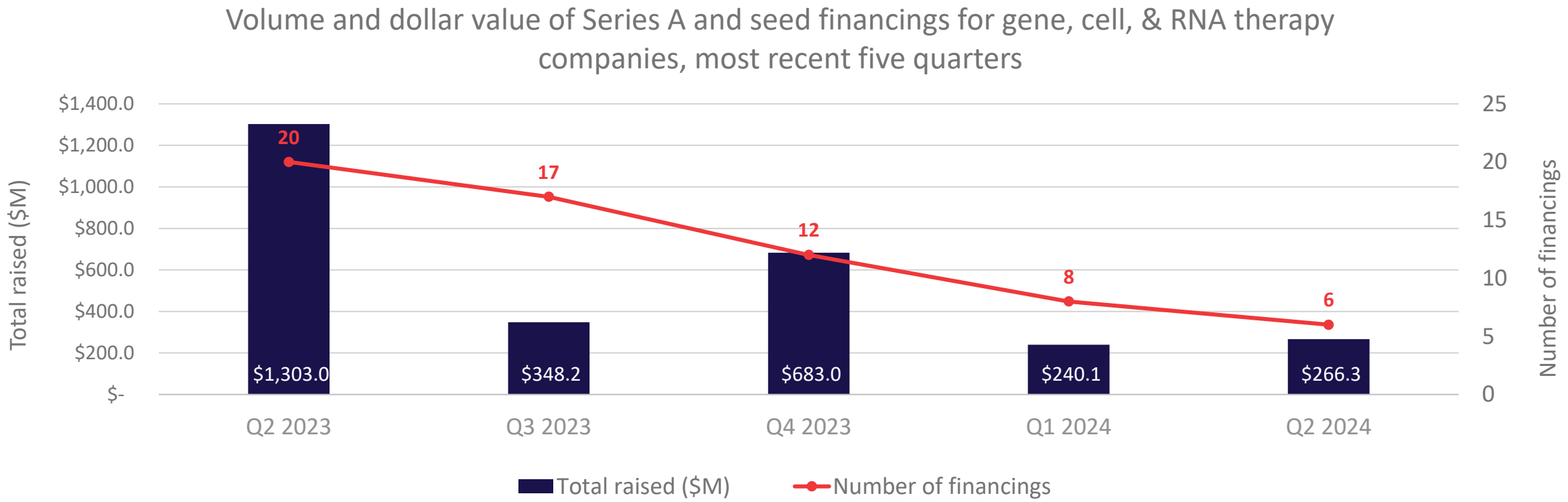
Q2 2024

CITELINE
a norstella company

American Society of Gene + Cell Therapy

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

- Seed and Series A financings again saw a quarterly decrease in volume, with 6 transactions done in Q2 2024
- The number of financings was down from the 8 completed in Q1 2024, and also ~3x less than the total 20 from the same quarter in 2023
- The aggregate raised in Q2 2024, $266.3 million, represents an 11% increase over the previous quarter's $240.1 million



Source: Biomedtracker | Citeline, Evaluate, July 2024

CITELINE a norstella company

American Society of Gene + Cell Therapy

Q2 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)
09 April 2024	Nvelop Therapeutics Launches with $100M Seed Round*	Gene editing delivery	United States / Massachusetts / Cambridge	Broad Institute; Massachusetts General Hospital	100
02 May 2024	Latus Launches with $54M Series A Financing	Gene therapy	United States / Pennsylvania / Philadelphia	Center for Cellular and Molecular Therapeutics at Children's Hospital of Philadelphia	54
21 May 2024	Limula Raises CHF6.2M in Seed Financing	Cell therapy manufacturing	Switzerland / Epalinges	Unknown	6.9
23 May 2024	Radar Therapeutics Raises $13.4M in Seed Funding	RNA sensors for genetic delivery	United States / California / Berkeley	Stanford University; Massachusetts Institute of Technology	13.4
24 June 2024	EpilepsyGTx Raises $10M in Seed Round	Gene therapy	United Kingdom / Cambridgeshire	UCL Queen Square Institute of Neurology	10
25 June 2024	Exsilio Therapeutics Launches with $82M Series A Financing	Gene editing	United States / New York / New York	n/a - led by former Moderna exec	82

*Nvelop raised seed funding in 2022, but just announced it in Q2 2024

Source: Biomedtracker | Citeline, Evaluate, July 2024

Notable Q2 2024 start-up gene, cell, and RNA therapy companies

Company details	Academic source	Financing type/ amount raised	Lead investor(s)	Therapy areas of interest
DLVR-X and DLVR-M modular non-viral vehicles that enable in vivo delivery for gene editing	Broad Institute; Massachusetts General Hospital	Seed/$100M*	Undisclosed lead investors; investors include Newpath Partners; Atlas Venture; F-Prime Capital; 5AM Ventures; GV; ARCH Venture Partners	Undisclosed
Uses mRNA intermediates for gene insertion	n/a - led by former Moderna exec	Series A/$82M	Novartis Venture Fund; Delos Capital	Undisclosed
Gene therapies delivered via novel adeno-associated virus capsid variants	Center for Cellular and Molecular Therapeutics at Children's Hospital of Philadelphia	Series A/$54M	8VC; DCVC Bio	CNS diseases including CLN2 disease and Huntington's disease

Source: Biomedtracker | Citeline, Evaluate, July 2024

*Nvelop raised seed funding in 2022, but just announced it in Q2 2024

Upcoming catalysts

Q2 2024

CITELINE
a norstella company

American Society
of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward-looking events) expected in Q3 2024

Therapy	Generic name	Disease	Catalyst	Catalyst date
Afami-cel	afamitresgene autoleucel	Synovial Sarcoma	PDUFA/Approval Decision (U.S.)	04 August 2024 - 04 August 2024
Beqvez	fidanacogene elaparvovec	Hemophilia B	Approval Decision (Europe)	31 May 2024 - 05 August 2024
HPC-Cord Blood Therapy	n/a	Ischemic Stroke	PDUFA/Approval Decision (U.S.)	20 May 2024 - 31 August 2024
mRESVIA	mRNA-1345	Respiratory Syncytial Virus (RSV) Prevention	Approval Decision (Europe)	28 June 2024 - 03 September 2024
DCVax-L	n/a	Brain Cancer (Malignant Glioma; AA and glioblastoma (GBM))	Approval Decision (U.K.)	01 July 2024 - 30 September 2024
Wainua	eplontersen	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)	CHMP (European Panel) Results	07 May 2024 - 31 October 2024
Izervay	avacincaptad pegol	Dry Age-Related Macular Degeneration (Dry AMD)/Geographic Atrophy (Ophthalmology)	CHMP (European Panel) Results	01 May 2024 - 30 November 2024
Breyanzi	lisocabtagene maraleucel	Indolent Non-Hodgkin's Lymphoma - iNHL	PDUFA for sNDA/sBLA	01 January 2024 - 31 December 2024
Rytelo	imetelstat	Myelodysplastic Syndrome (MDS)	CHMP (European Panel) Results	01 June 2024 - 31 December 2024
Wainua	eplontersen	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)	Approval Decision (Europe)	08 January 2024 - 31 December 2024
Vyjuvek	beremagene geperpavec	Epidermolysis Bullosa	CHMP (European Panel) Results and Approval Decision (Europe)	01 July 2024 - 31 December 2024
Oxlumo	lumasiran	Hyperoxaluria	Supplemental Approval (Europe)	29 January 2024 - 31 January 2025
Rytelo	imetelstat	Myelodysplastic Syndrome (MDS)	Approval Decision (Europe)	01 August 2024 - 28 February 2025

Source: Biomedtracker | Citeline, July 2024

Appendix

Methodology, sources, and glossary of key terms

Q2 2024

CITELINE
a norstella company

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

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

Usage Guidelines

The Gene, Cell, + RNA Therapy Landscape Report, created by the American Society of Gene & Cell Therapy and Citeline, provides helpful overview graphics and data on cell and gene therapy trends. Readers are welcome to cite and share images and data from the report as-is with appropriate citations. When using any graphics or data, please include a citation stating "Data source: Gene, Cell, + RNA Therapy Landscape Report, American Society of Gene & Cell Therapy and Citeline, [year]" and link back to the original report source at https://asgct.org/publications/landscape-report to allow others to access the full context.

Data should not be modified or recreated in any way or suggest endorsement by ASGCT or Citeline. Contact ASGCT at media@asgct.org for any usage questions.

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

Contact:
clientservices@citeline.com