Gene, Cell, + RNA Therapy Landscape Report

Q2 2023 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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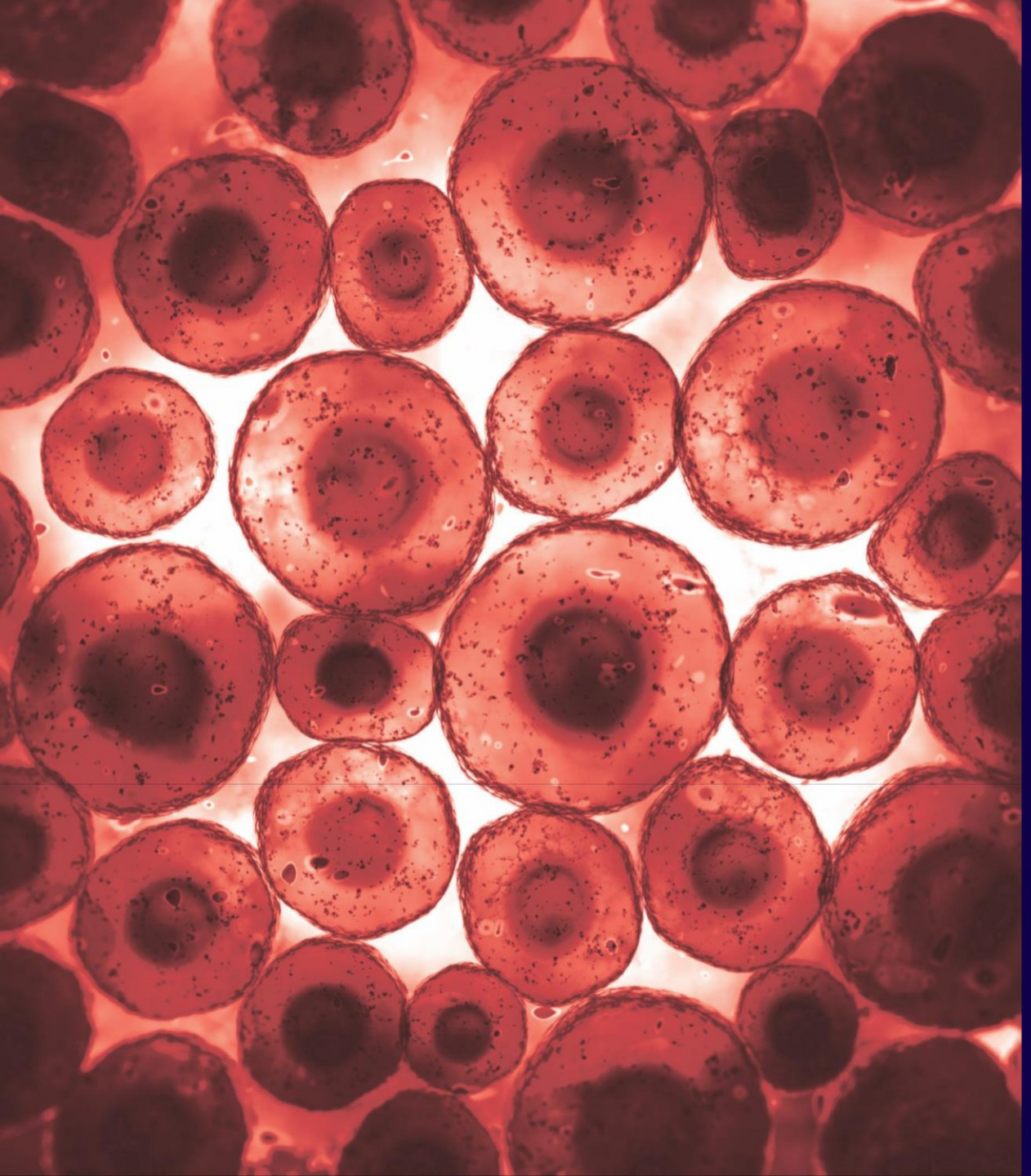
Our global teams of analysts, journalists and consultants keep their fingers on the pulse of the pharmaceutical, biomedical and medtech industries, covering it all with expert insights: key diseases, clinical trials, drug R&D and approvals, market forecasts and more. For more information on one of the world's most trusted life science partners, visit Citeline.



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American Society of Gene + Cell Therapy

Introduction

Welcome to the latest quarterly report from ASGCT and Citeline! Six new therapies were approved in the 2nd quarter of 2023, including two each in the gene, cell, and RNA therapy categories. The gene therapies—Elevidys for Duchenne muscular dystrophy and Vyjuvek for dystrophic epidermyolysis bullosa—are both the first to be approved for their respective indications. Additionally, Roctavian for hemophilia A was approved in the US and a COVID-19 mRNA vaccine was approved in Japan.

More gene therapies moved into Phase II trials in the past quarter than have in more than a year. Companies behind gene therapies for hemophilia B and sickle cell disease also filed for approval in Q2. In the gene therapy pipeline, oncology and rare diseases remain the top areas of development both overall and in the clinic. In Q2, 60 clinical trials for gene therapies were initiated. The proportion of those trials for non-oncology indications has increased five percent since last quarter, to 32 percent, which continues the trend of non-oncology gene therapy trials increasing in proportion since Q4 of 2022. In the non-genetically modified cell therapy pipeline, oncology and rare diseases are also the top areas of development. Of 31 trials initiated for non-genetically modified cell therapies in Q2, 58 percent were for non-oncology indications, an increase of five percent from Q1.

In Q2, companies made 117 deals—a six percent increase over the previous quarter and a quarterly high in the last year. The increase was driven by a rebound in financing—a 39 percent increase over Q1—and a slight jump in acquisitions. Alliances, however, decreased 26 percent from 54 to 40 partnerships. Start- up financing has continued to rise. In Q2, 21 companies announced seed or Series A rounds, the highest quarterly amount in the last year. The $1.3 billion raised was more than double the amount the previous quarter.

Key takeaways from Q2 2023

Q2 2023 was a notable quarter for approvals, with 6 new therapies being approved, 2 for each of the gene, cell, and RNA therapy categories

- All of the 6 new approvals were granted by the US FDA, with the exception of Arcturus Therapeutics' ARCT-154 COVID-19 mRNA vaccine, which was approved in Japan
- Both new gene therapy approvals (Elevidys in Duchenne muscular dystrophy and Vyjuvek for dystrophic epidermolysis bullosa) are the first gene therapies to be approved in their respective indications

Gene therapies have seen the greatest increase in the number of therapies in Phase II development in over a year

- By the end of Q1 2023 there were 247 gene therapies in Phase II, and this has since grown by 5% to 260 at the end of Q2
- More broadly, rare disease and oncology indications continue to be the most targeted diseases by gene therapies in clinical development, while sensory indications have overtaken alimentary/metabolic diseases in third place

Dealmaking in Q2 2023 reached a quarterly high, with a big rebound in financings

- Advanced molecular companies signed a total of 117 deals, the highest quarterly amount within the last year, and a 6% increase over Q1 2023's 110 aggregate
- Start-up financing was a big driver of the increase and continues to rise quarter over quarter, with $1.3 billion in aggregate raised from 21 companies in Q2 2023, double the amount brought in during the previous quarter
- In the largest Series A round of the quarter, MPM BioImpact and F2 Ventures led a $300 million financing for ReNAgade Therapeutics, which is launching with an RNA platform capable of RNA delivery, reprogramming cells, editing genes, and gene insertion

Key highlights in Q2 2023

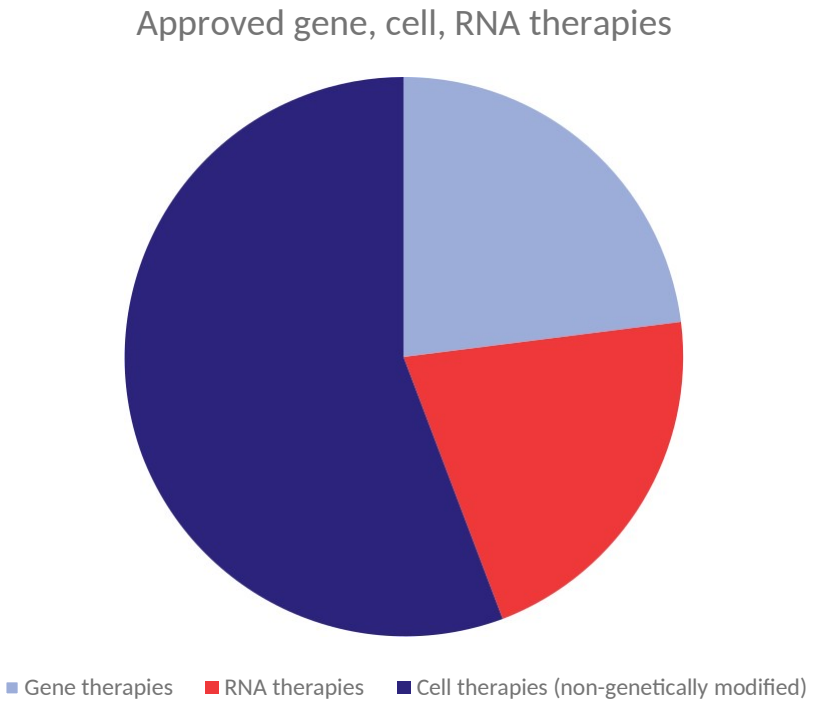
Q2 2023

American Society of Gene + Cell Therapy

Approved gene, cell, and RNA therapies

Globally, for clinical use:

- 26 gene therapies are approved (including genetically modified cell therapies)
  - In Q2 2023, both Elevidys and Vyjuvek were approved in the US for Duchenne muscular dystrophy and dystrophic epidermolysis bullosa, respectively
- 24 RNA therapies are approved
  - In Q2 2023, Qalsody was approved in the US for amyotrophic lateral sclerosis, and Arcturus Therapeutics' ARCT-154 COVID-19 mRNA vaccine was approved in Japan
- 63 non-genetically modified cell therapies are approved
  - In Q2 2023, Omisirge and Lantidra were approved in the US for allogeneic stem cell transplantation and type 1 diabetes, respectively



Source: Pharmaprojects | Citeline, July 2023

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Approved gene therapies as of Q2 2023 (1/2)

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	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, July 2023

Text highlighted in yellow represents new approvals during Q2 2023

Approved gene therapies as of Q2 2023 (2/2)

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	Orchard Therapeutics
Breyanzi	lisocabtagene maraleucel	2021	Diffuse large B-cell lymphoma; follicular lymphoma	US, Japan, EU, Switzerland, UK, Canada	Celgene (Bristol Myers Squibb)
Abecma	idecabtagene vicleucel	2021	Multiple myeloma	US, Canada, EU, UK, Japan	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	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	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

Source: Pharmaprojects | Citeline, July 2023

Text highlighted in yellow represents new approvals during Q2 2023

Approved RNA therapies as of Q2 2023 (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 Argentina	Ionis Pharmaceuticals
Ampligen	rintatolimod	2016	Chronic fatigue syndrome		AIM ImmunoTech
Tegsedi	inotersen	2018	Amyloidosis, transthyretin-related hereditary	EU, UK, Canada, US, Brazil	Ionis Pharmaceuticals
Onpattro	patisiran	2018	Amyloidosis, transthyretin-related	US, EU, UK, Japan, Canada, Switzerland, Brazil, Taiwan, Israel, Turkey	Alnylam
Vyondys 53	golodirsen	2019	hereditary 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 2023

Text highlighted in yellow represents new approvals during Q2 2023

Approved RNA therapies as of Q2 2023 (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	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

Source: Pharmaprojects | Citeline, July 2023

Text highlighted in yellow represents new approvals during Q2 2023

Approved RNA therapies as of Q2 2023 (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

*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 2023

Text highlighted in yellow represents new approvals during Q2 2023

Key highlights in Q2 2023

Noteworthy events that happened in Q2 2023

Drug	Event Type	Indication	Molecule	Event Date
CB-011	Fast Track Status	Multiple Myeloma (MM)	Cellular	04 April 2023
SynKIR-110	Fast Track Status	Mesothelioma	Cellular	05 April 2023
Omisirge	Approval (U.S.)	Bone Marrow Transplant and Stem Cell Transplant	Cellular	17 April 2023
Ixo-vec	Innovative Licensing and Access Pathway (ILAP) (U.K.)	Wet Age-Related Macular Degeneration (Wet AMD) (Ophthalmology)	Viral Gene Therapy	18 April 2023
Lumevoq	MAA Withdrawal	Leber's Hereditary Optic Neuropathy (LHON) (Ophthalmology)	Viral Gene Therapy	20 April 2023
Lovotibeglogene Autotemcel	NDA/BLA Filing	Sickle Cell Anemia	Viral Gene Therapy	24 April 2023
AOC 1044	Fast Track Status	Duchenne Muscular Dystrophy (DMD)	siRNA/RNAi	24 April 2023
QALSODY	Accelerated/Conditional Approval (U.S.)	Amyotrophic Lateral Sclerosis (ALS)	Antisense	25 April 2023
ARCT-154	Approval (Japan)	COVID-19 prophylaxis	mRNA vaccine	28 April 2023
SC291	Fast Track Status	Hematologic Cancer	Cellular	08 May 2023
OTL-200	Meeting with FDA; Rolling NDA/BLA Initiated	Metachromatic Leukodystrophy	Viral Gene Therapy	15 May 2023
Vyjuvek	Approval (U.S.)	Epidermolysis Bullosa	Viral Gene Therapy	19 May 2023
Isaralgagene Civaparvovec	Fast Track Status	Fabry's Disease	Viral Gene Therapy	22 May 2023
RGX-121	Regenerative Medicine Advanced Therapy (RMAT) Designation	Mucopolysaccharidosis II (MPS II; Hunter Syndrome)	Viral Gene Therapy	23 May 2023
INO-3107	Orphan Drug Designation (Europe)	Head and Neck Cancer	Other Nucleic Acid	23 May 2023
RP-L301	Regenerative Medicine Advanced Therapy (RMAT) Designation	Pyruvate Kinase Deficiency	Viral Gene Therapy	23 May 2023
DYNE-101	Orphan Drug Designation (Europe)	Muscular Dystrophy	Antisense	25 May 2023
LN-144	Priority Review	Melanoma	Cellular	26 May 2023
RP-A501	PRIME Designation (Europe)	Glycogen Storage Disease (GSD)	Viral Gene Therapy	31 May 2023
ADI-001	Meeting with FDA	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	Cellular	31 May 2023
ARCT-810	Fast Track Status	Urea Cycle Disorders and Derangements (UCD)	siRNA/RNAi	01 June 2023
Vididencel	Advanced Therapy Medicinal Product (ATMP) Classification	Acute Myelogenous Leukemia (AML)	Cellular	19 June 2023
Lovotibeglogene Autotemcel	Priority Review	Sickle Cell Anemia	Viral Gene Therapy	21 June 2023
Elevidys	Accelerated/Conditional Approval (U.S.)	Duchenne Muscular Dystrophy (DMD)	Viral Gene Therapy	22 June 2023
CD388	Fast Track Status	Influenza (including vaccines)	Antisense	22 June 2023
Fidanacogene Elaparvovec	NDA/BLA Accepted; MAA Submission (Europe)	Hemophilia B	Viral Gene Therapy	27 June 2023
Lantidra	Approval (U.S.)	Diabetes Mellitus, Type I	Cellular	28 June 2023
Roctavian	Approval (U.S.)	Hemophilia A	Viral Gene Therapy	29 June 2023

Source: Biomedtracker | Citeline, July 2023

Pipeline overview

Q2 2023

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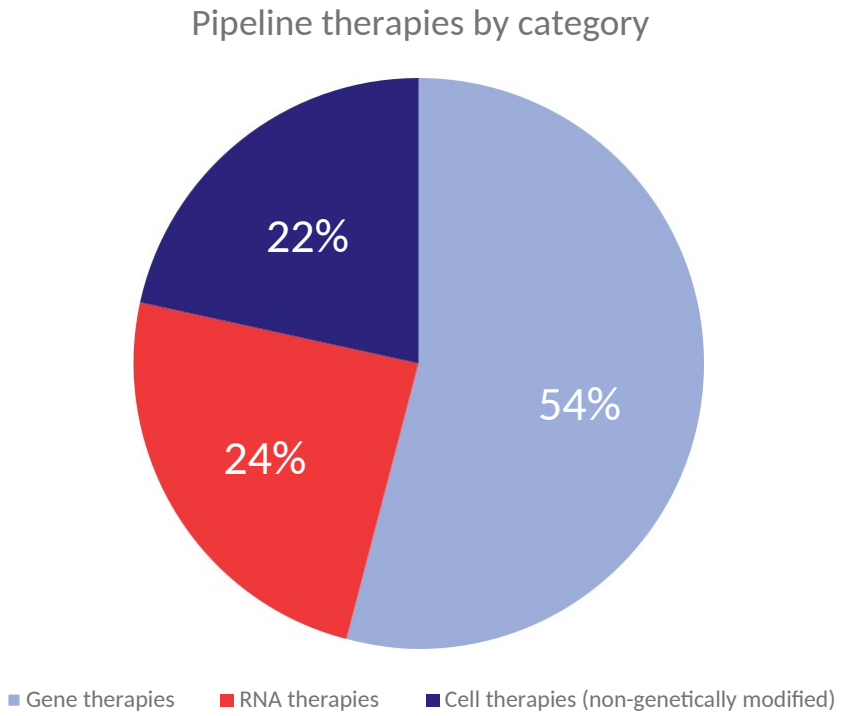
Pipeline of gene, cell, and RNA therapies

3,905 therapies are in development, ranging from preclinical through pre-registration

- 2,075 gene therapies (including genetically modified cell therapies such as CAR T-cell therapies) are in development, accounting for 54% of gene, cell, and RNA therapies
- 828 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies



Source: Pharmaprojects| Citeline, July 2023

American Society of Gene + Cell Therapy

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q2 2023

American Society of Gene + Cell Therapy

Gene therapy pipeline: Quarterly comparison

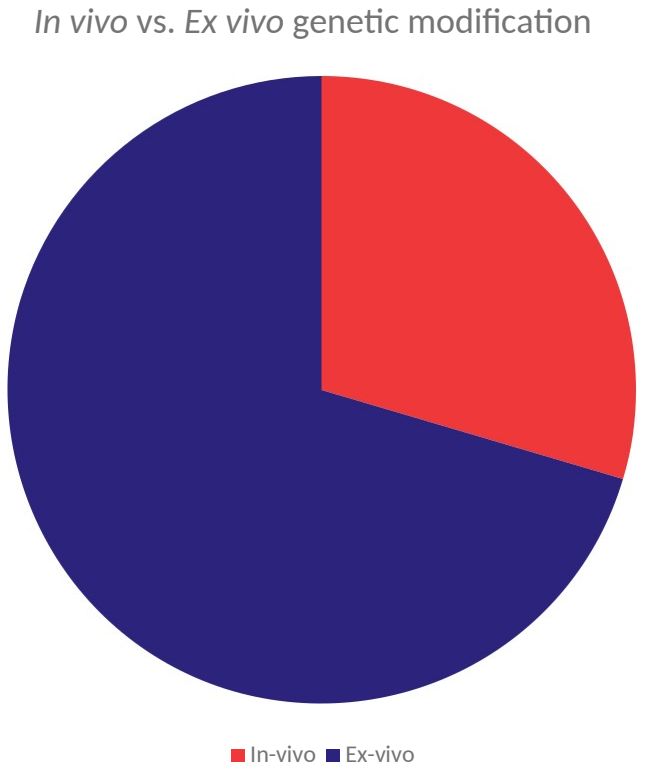
- While Phase I therapies declined in Q2 2023, and Phase III therapies remained the same as the previous 2 quarters, Q2 saw the greatest increase in Phase II therapies in over a year
- Fidanacogene elaparvovec in hemophilia B, and lovotibeglogene autotemcel in sickle cell anemia, filed for approval in Q2 2023
- The EMA filing for lenadogene nolparvovec (Lumevoq) was withdrawn due to the Committee for Advanced Therapies indicating the data so far would be insufficient for a positive opinion
- Therapies currently in pre-registration:
  - In China
    - equecabtagene autoleucel (Nanjing IASO Biotherapeutics, Innovent)
    - zevor-cel (CARsgen Therapeutics)
    - inaticabtagene autoleucel (CASI Pharmaceuticals, Juventas Cell Therapy)
  - In the EU, UK, and US
    - exagamglogene autotemcel (CRISPR Therapeutics, Vertex Pharmaceuticals)
  - In the EU and US
    - fidanacogene elaparvovec (Pfizer)
  - In the US
    - lovotibeglogene autotemcel (Bluebird Bio)

Global Status	Q2 2022	Q3 2022	Q4 2022	Q1 2023	Q2 2023
Preclinical	1,482	1,480	1,515	1,493	1,539
Phase I	258	264	254	245	240
Phase II	248	249	248	247	260
Phase III	28	32	30	30	30
Pre-registration	8	6	6	7	6
Total	**2,024**	**2,031**	**2,053**	**2,022**	**2,075**

Source: Pharmaprojects| Citeline, July 2023

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

- *Ex vivo* genetic modification is more widely used for gene therapies in pipeline development
- In Q2 2023, *in vivo* delivery techniques were used in 30% of gene therapies, 2% higher than the previous quarter



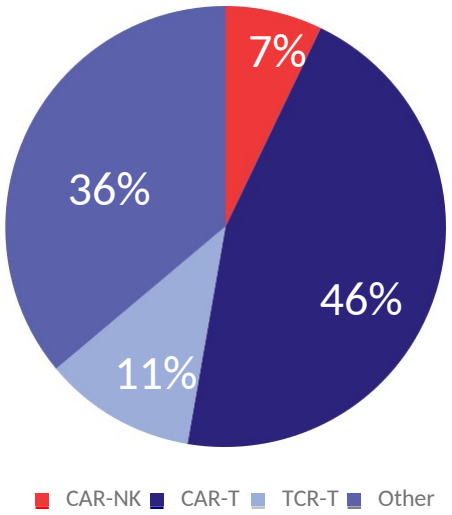
Source: Cell and Gene Therapy dashboard | Citeline, July 2023

American Society of Gene + Cell Therapy

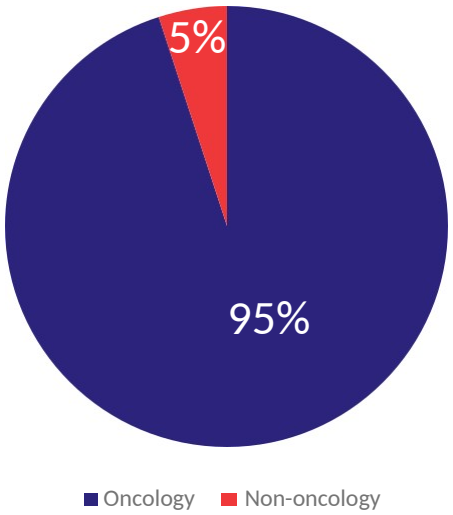
Gene therapy breakdown: CAR-Ts continue to dominate pipeline

- CAR T-cell therapies remain the most common technology used in the pipeline of genetically modified cell therapies (preclinical through to pre-registration), representing 46%, followed by the “other” category at 36%, which includes a list of less commonly used technologies including TCR-NK, CAR-M, and TAC-T
- 95% of CAR T-cell therapies are in development for cancer indications. The remaining non-oncology indications include scleroderma, HIV/AIDS, and autoimmune disease (unspecified)

Genetically modified cell therapy breakdown



CAR-T breakdown

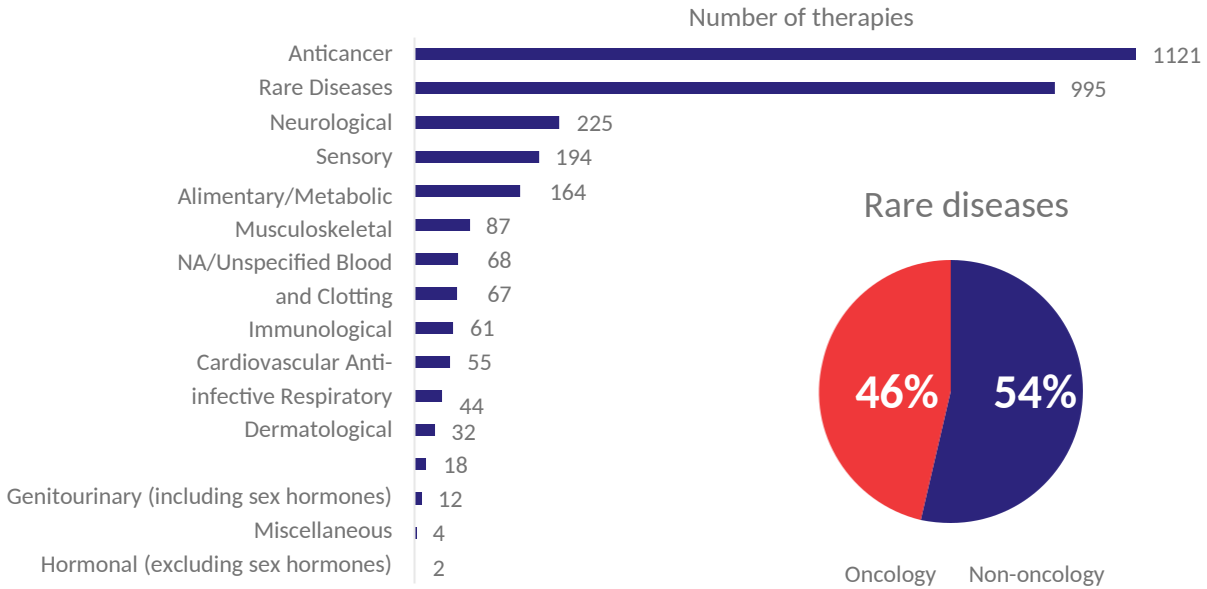


Source: Cell and Gene Therapy dashboard | Citeline, July 2023

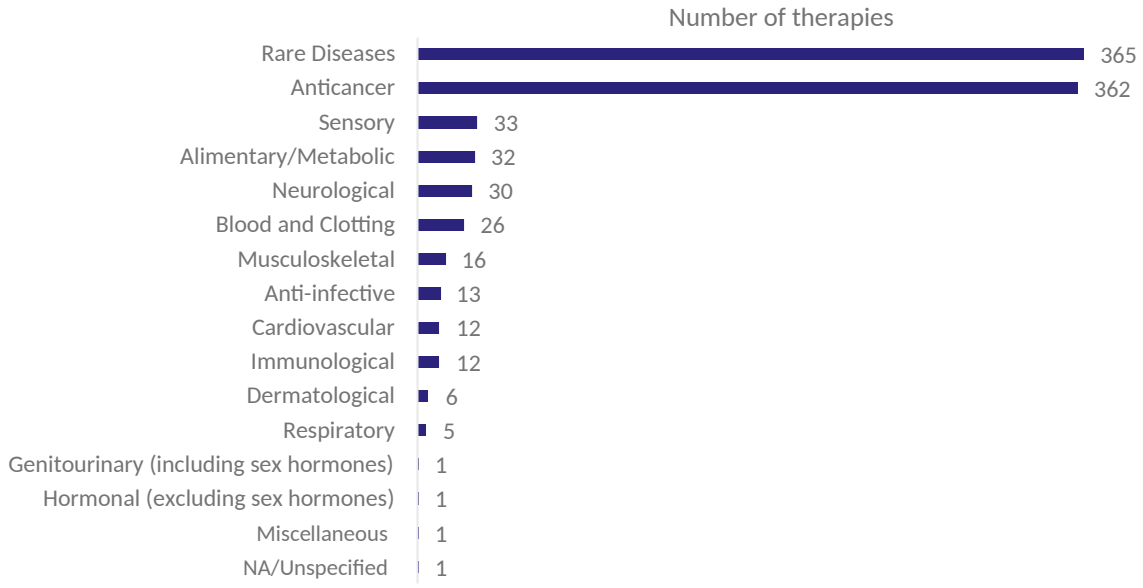
Gene therapy pipeline: Most commonly targeted therapeutic areas

- Oncology and rare diseases remain 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 occurs in oncology, representing a majority of 54% compared to non-oncology rare disease gene therapy pipeline development

Number of therapies from preclinical through pre-registration



Therapies in the clinic (excludes preclinical development)



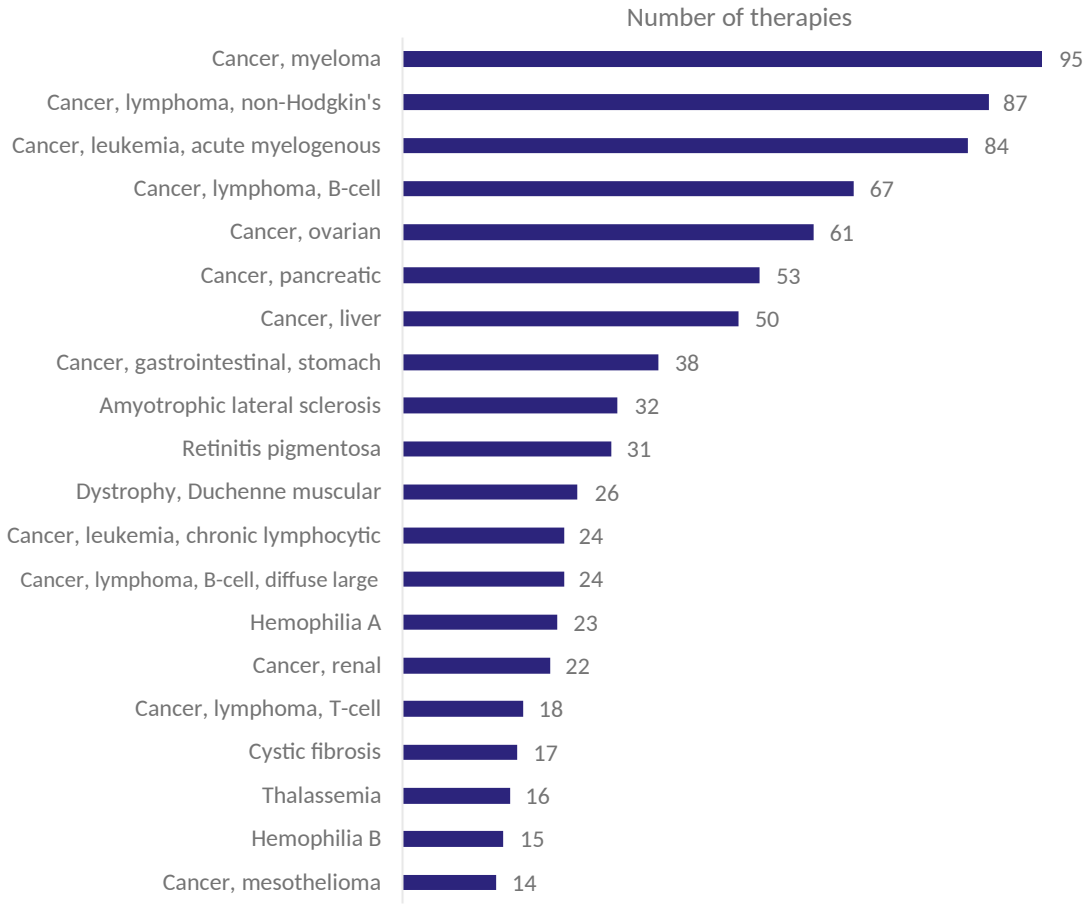
Source: Pharmaprojects| Citeline, July 2023

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 995 pipeline (preclinical to pre-registration) gene therapies which are being developed for rare diseases, eight out of the top 10 rare diseases are oncological, as seen all throughout 2022 and Q1 2023
- In the same order as the previous seven quarters, the top five rare diseases for which gene therapies are being developed are:
  1. Myeloma
  2. Non-Hodgkin's lymphoma
  3. Acute myelogenous leukemia
  4. B-cell lymphoma
  5. Ovarian cancer



Source: Pharmaprojects| Citeline, July 2023

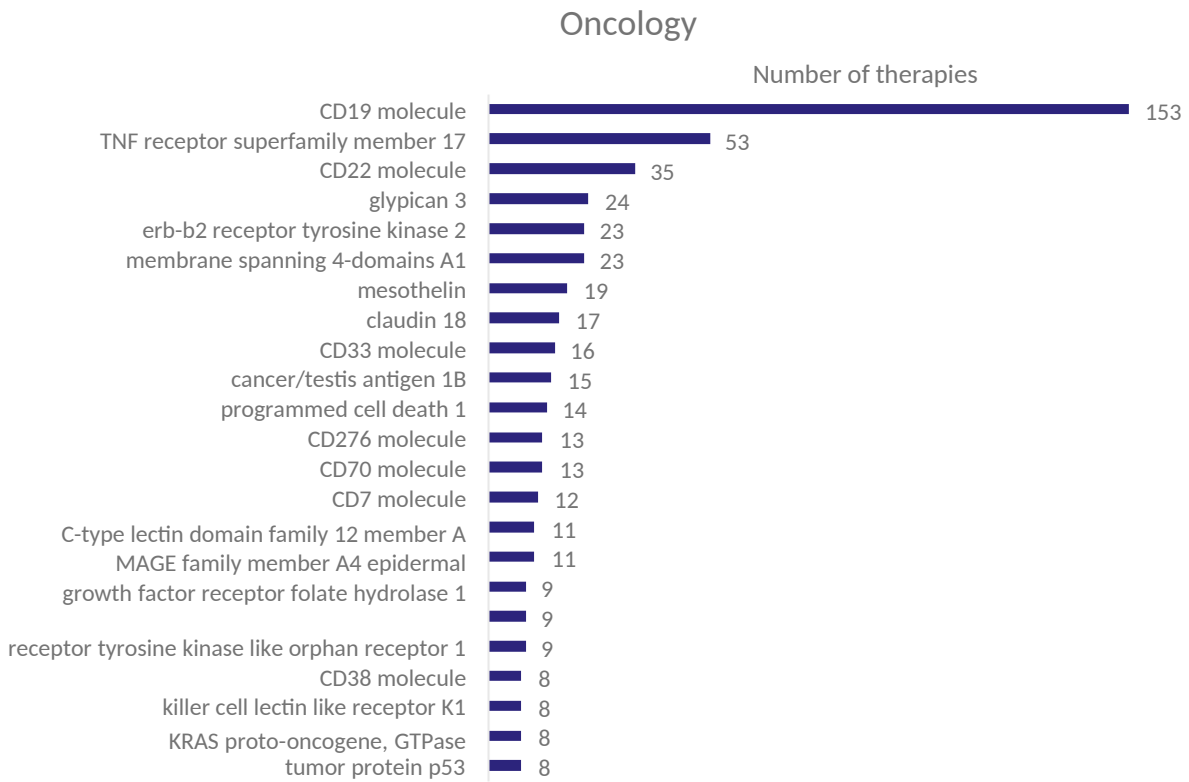
Note: Figures based on indications in pipeline development only for each therapy

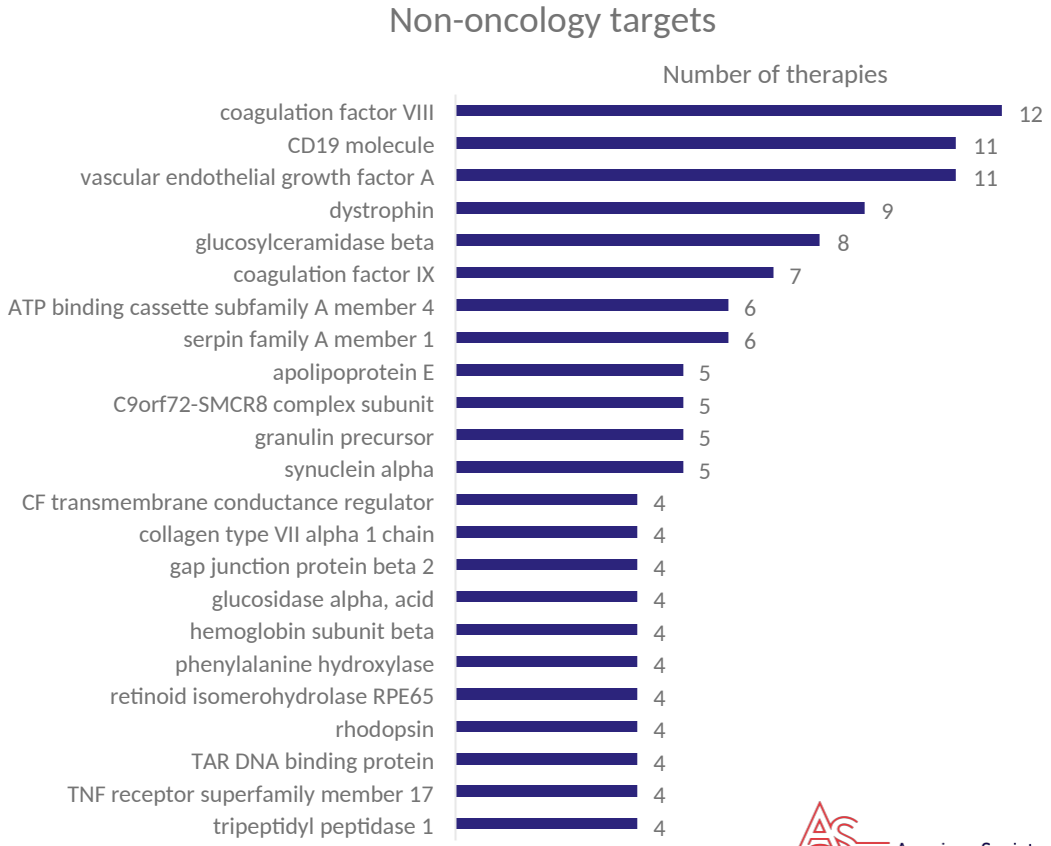
American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common targets

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

- CD19, B-cell maturation antigen (BCMA), also known as TNF receptor superfamily member 17, and CD22 molecule continue to be the top three most common targets for oncology indications
- Coagulation factor VIII remains the most common target for non-oncology indications, while CD19 molecule joins vascular endothelial growth factor A as the second most common in Q2 2023



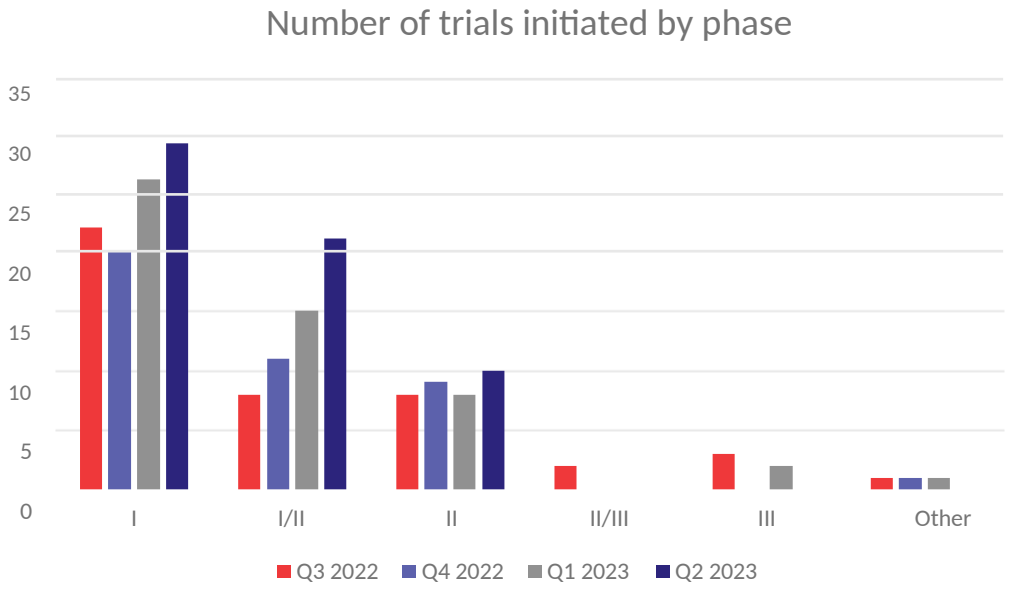


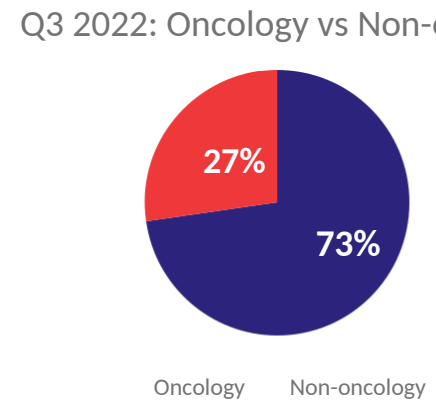
Source: Pharmaprojects| Citeline, July 2023

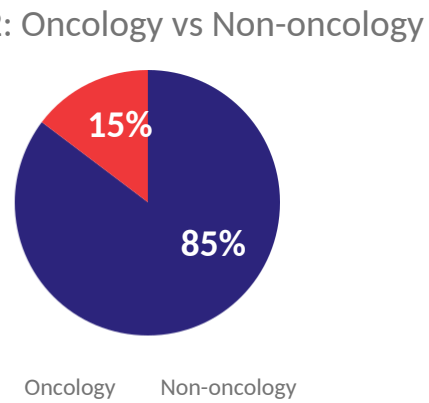
American Society of Gene + Cell Therapy

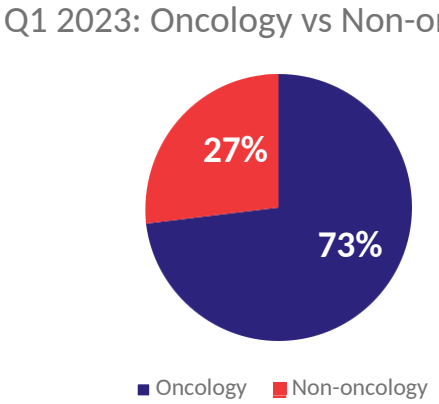
Gene therapy clinical trial activity

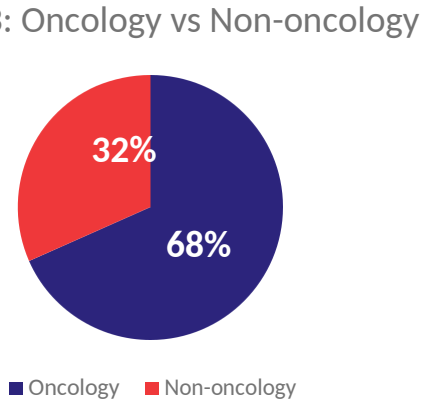
- 60 trials were initiated in Q2 2023 for gene therapies
- The proportion of gene therapy trials for non-oncology indications has increased by 5 percentage points since the previous quarter, to 32%, continuing the trend of increasing proportion of non-oncology gene therapy trials initiating each quarter since Q4 2022











Source: Trialtrove| Citeline, July 2023

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline

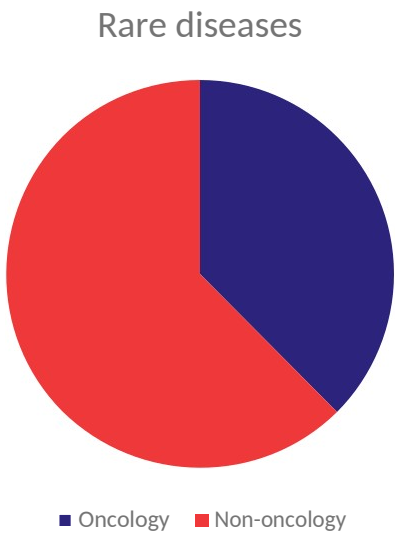
Q2 2023

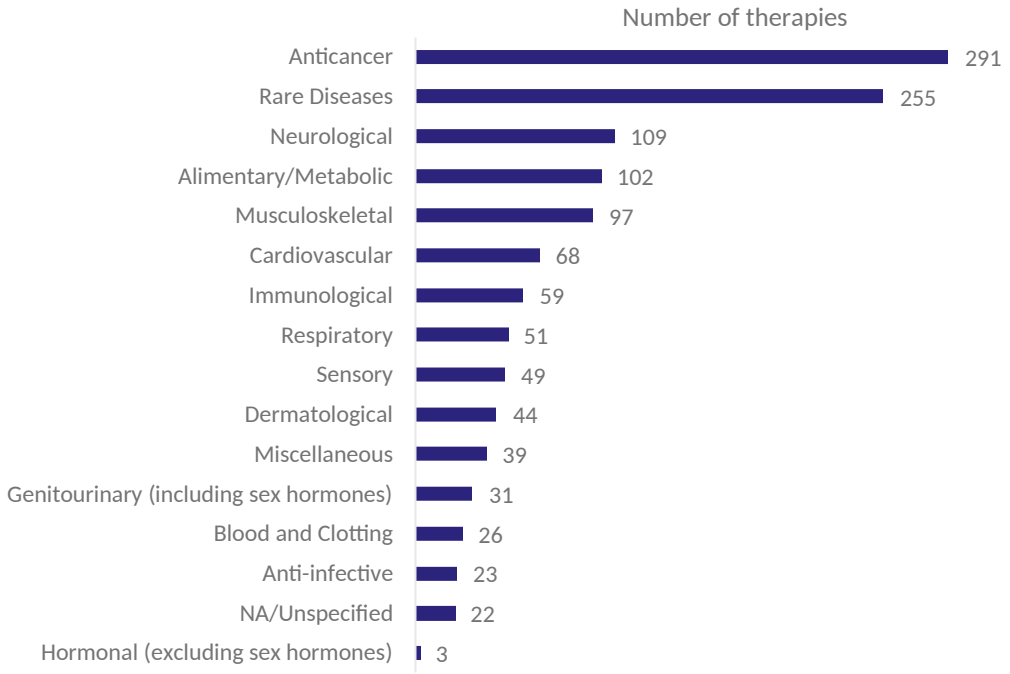
American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline: Most common therapeutic areas targeted

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

- Oncology and rare diseases remain 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% are in development for non-oncology rare diseases, a decrease of one percentage point from the previous quarter





Source: Pharmaprojects| Citeline, July 2023

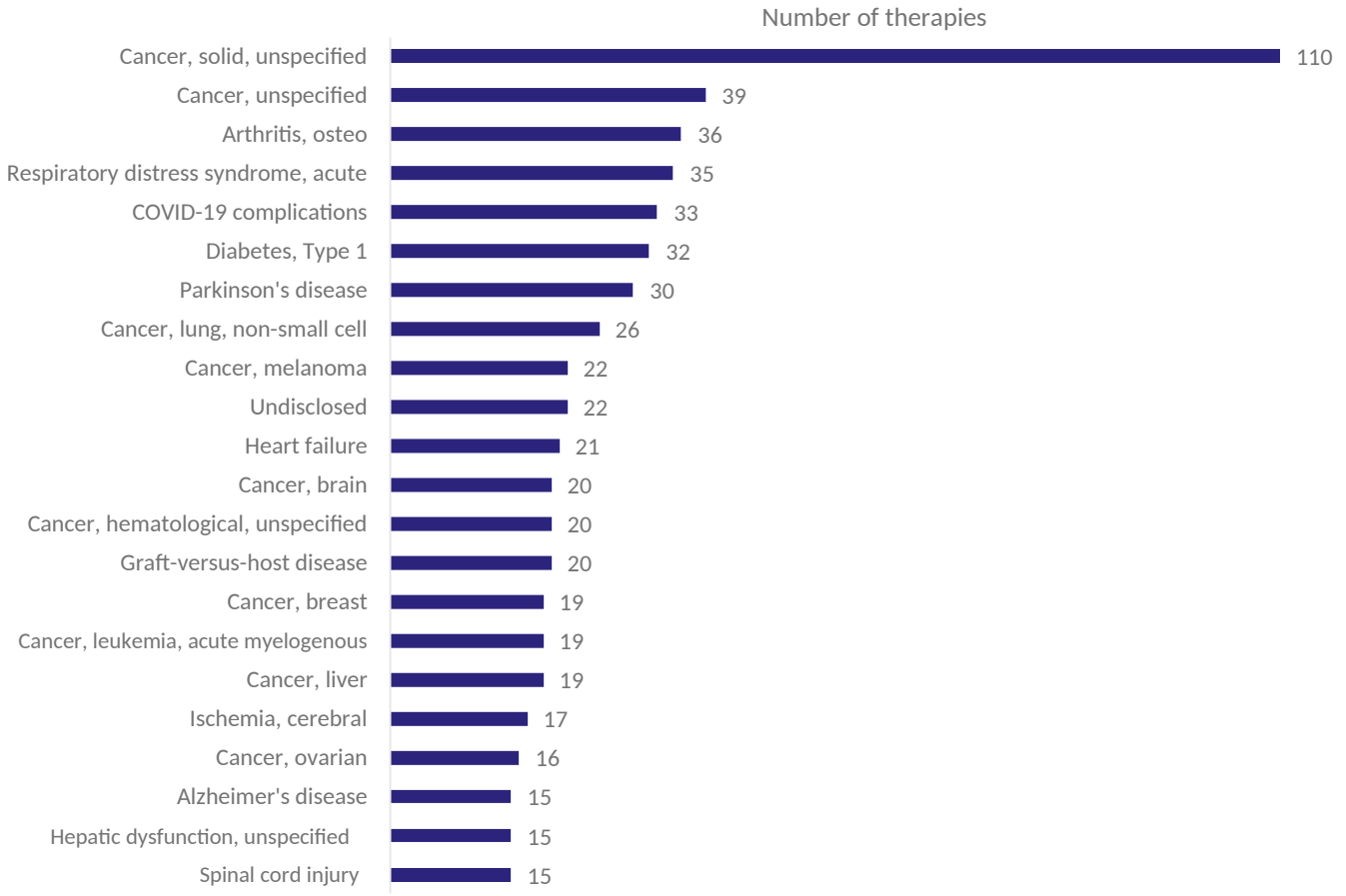
Note: Figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

Of the therapies for which indications are specified, the top three indications remain the same as in Q4 2021, throughout 2022, and Q1 2023:

1. Osteoarthritis
2. Acute respiratory distress syndrome
3. COVID-19 complications



Source: Pharmaprojects| Citeline, July 2023

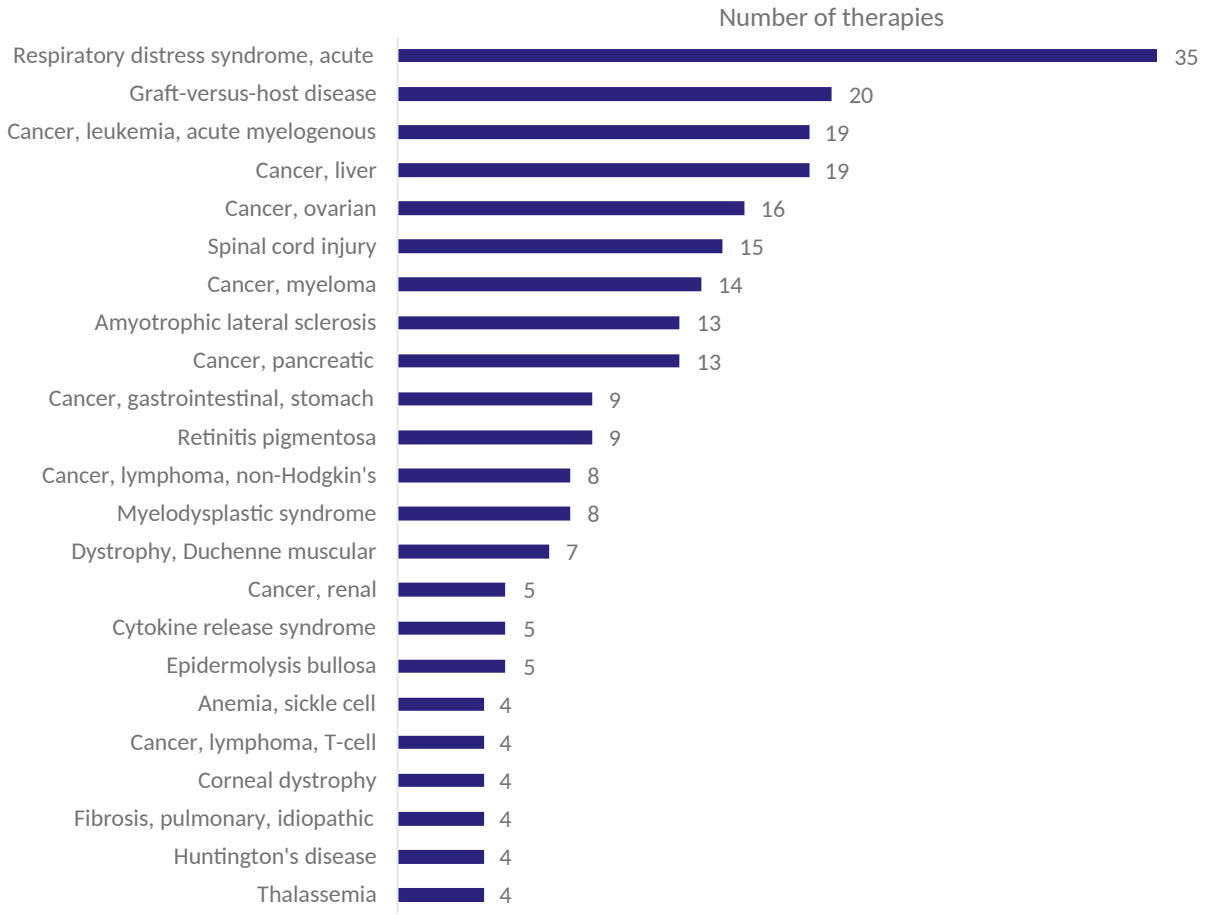
Note: Figures based on indications in pipeline development only for each therapy

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



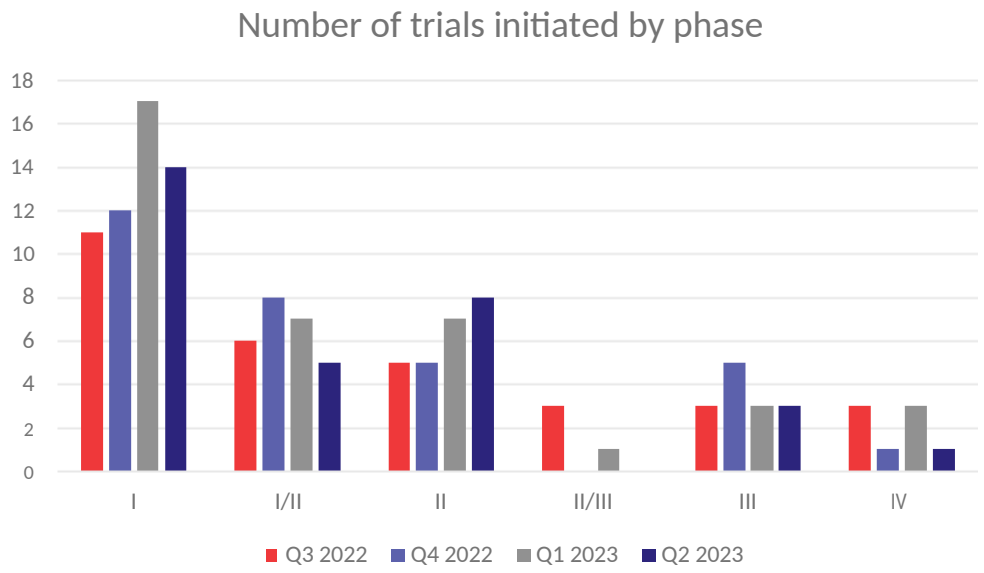
Source: Pharmaprojects| Citeline, July 2023

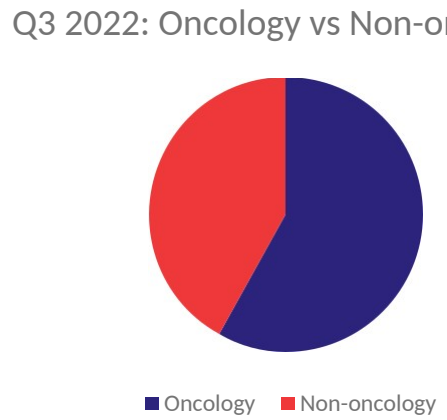
Note: Figures based on indications in pipeline development only for each therapy

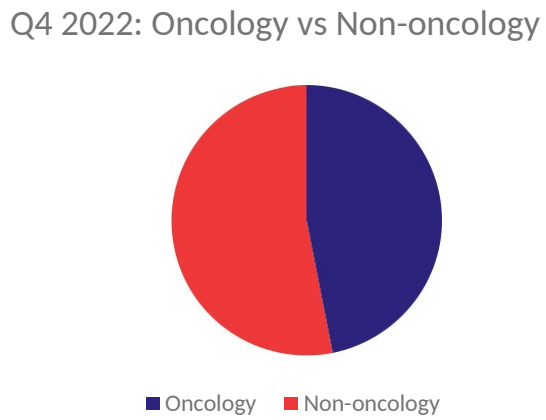
American Society of Gene + Cell Therapy

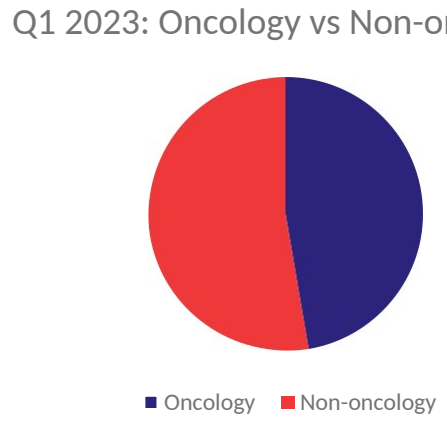
Non-genetically modified cell therapy trial activity

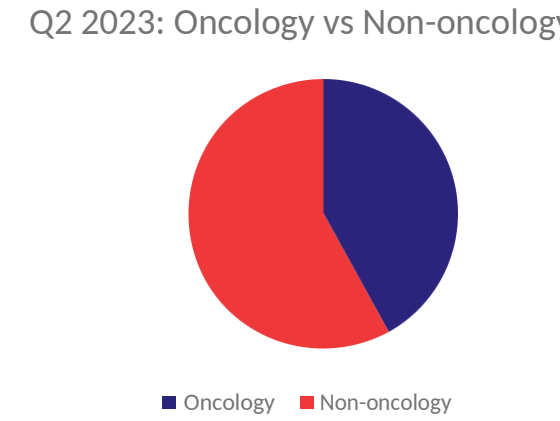
- 31 trials were initiated for non-genetically modified cell therapies in Q2 2023, 7 less than the previous quarter
- Of these 31, 58% are for non-oncology indications, an increase of 5 percentage points from Q1 2023











Source: Trialtrove| Citeline, July 2023

American Society of Gene + Cell Therapy

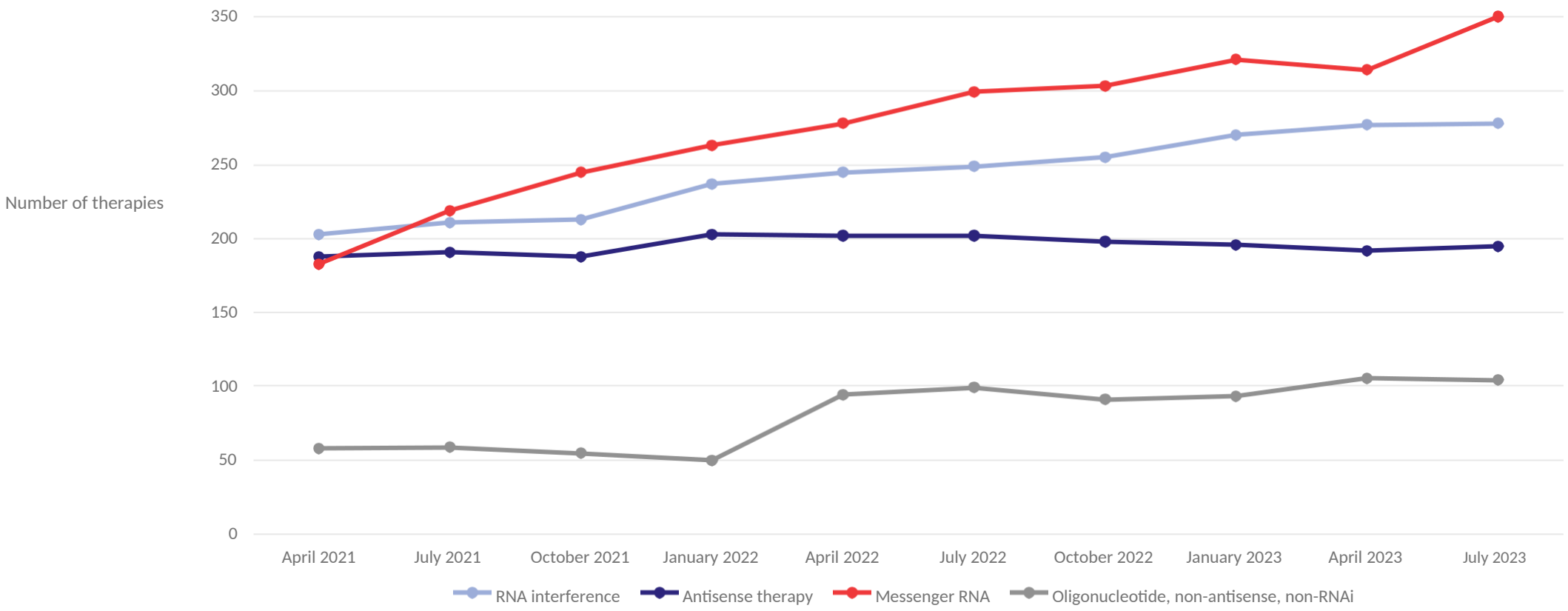
RNA therapy pipeline

Q2 2023

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) continue to be the preferred RNA modalities for research

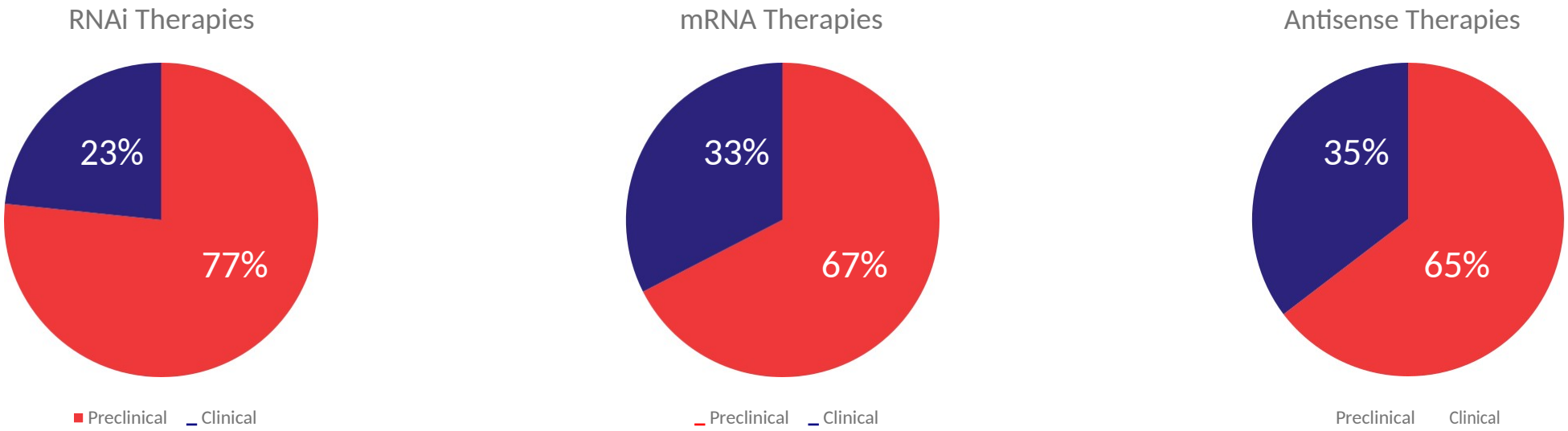


Source: Pharmaprojects| Citeline, July 2023

American Society of Gene + Cell Therapy

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

- The majority of RNAi, mRNA, and antisense therapeutics in development are in preclinical development, representing 77%, 67%, and 65% of their respective pipelines



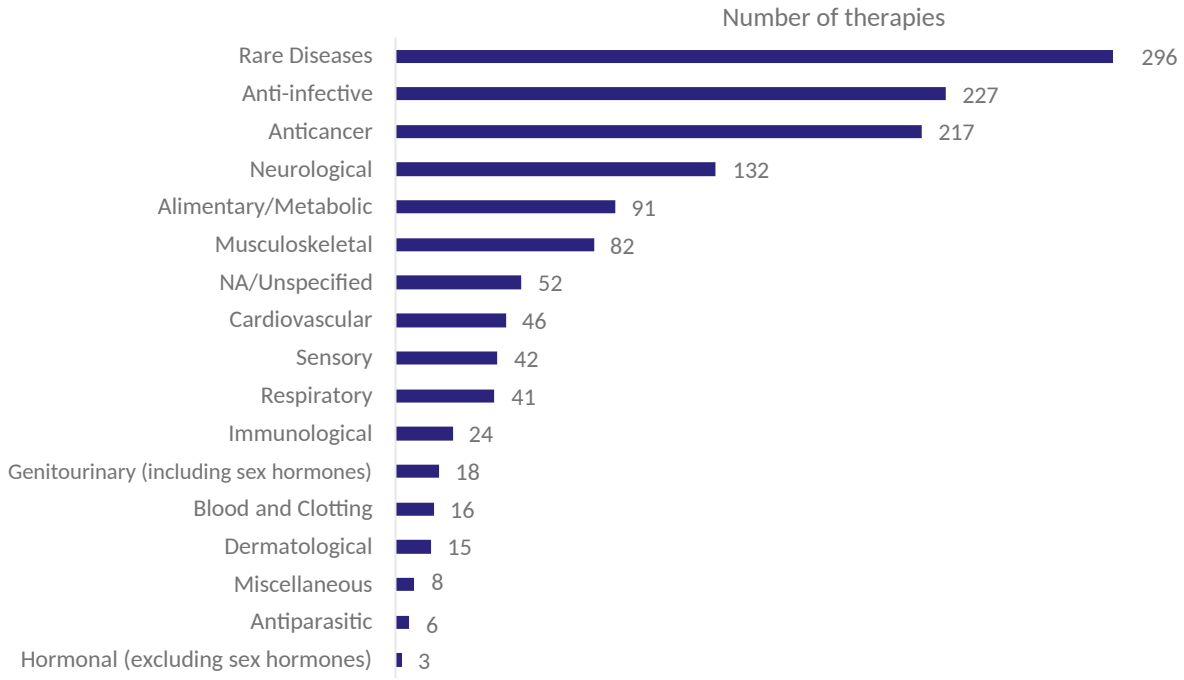
Source: Pharmaprojects| Citeline, July 2023

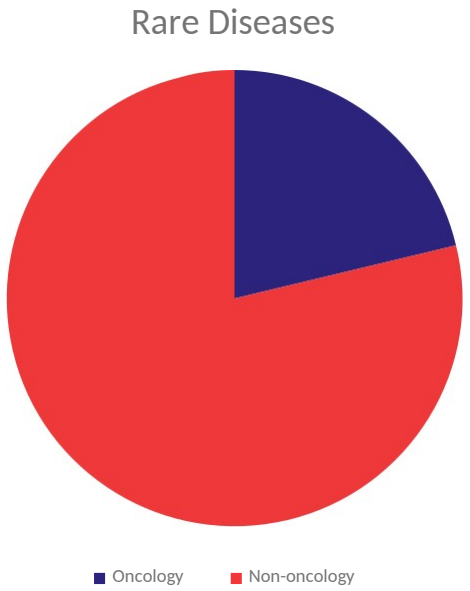
American Society of Gene + Cell Therapy

RNA therapies: Most commonly targeted therapeutic areas

Of the 934 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Rare diseases remains the top targeted therapeutic area by RNA therapies, while anti-infective indications regain their position as the second most commonly targeted, above oncology indications
- Non-oncology indications continue to be the most targeted rare diseases by RNA therapies, representing a majority of 80%





Source: Pharmaprojects| Citeline, July 2023

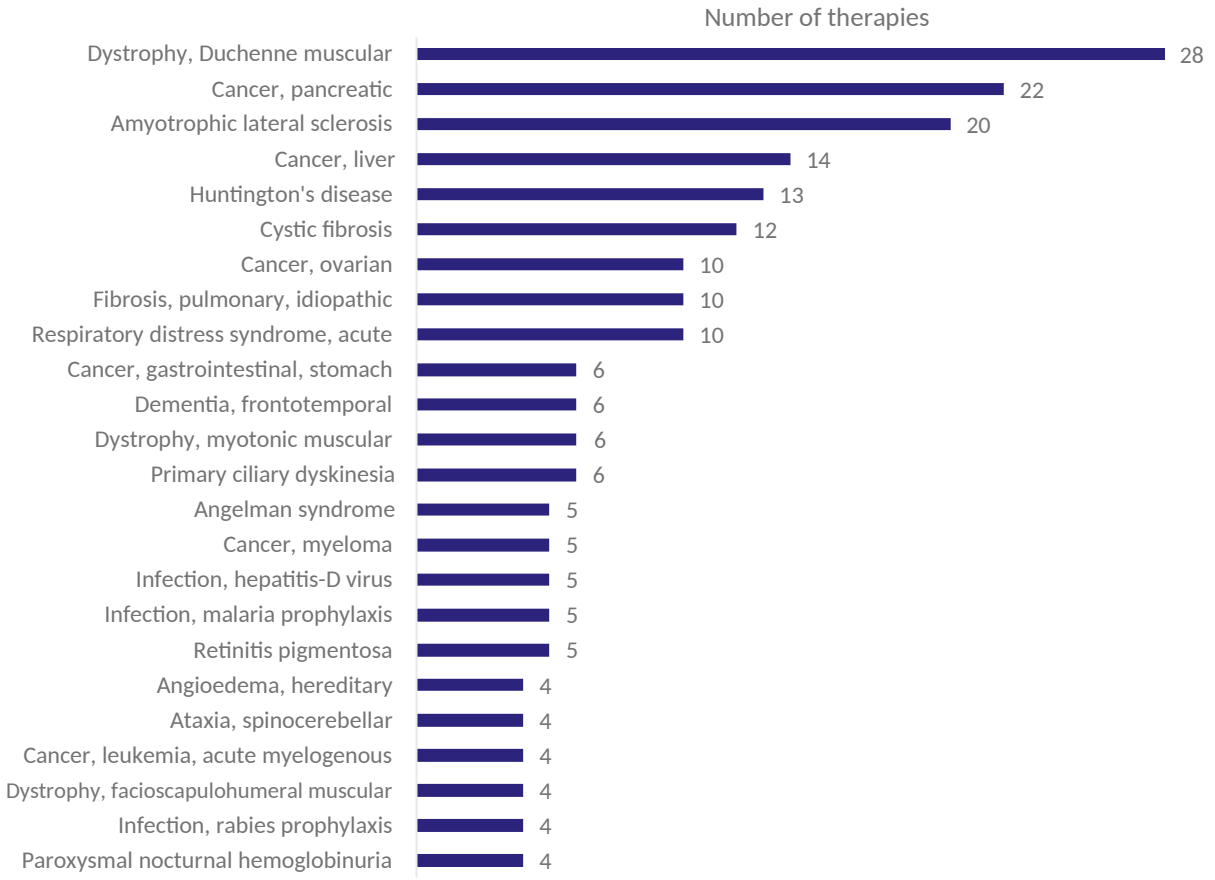
Note: Figures based on indications in pipeline development only for each therapy

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



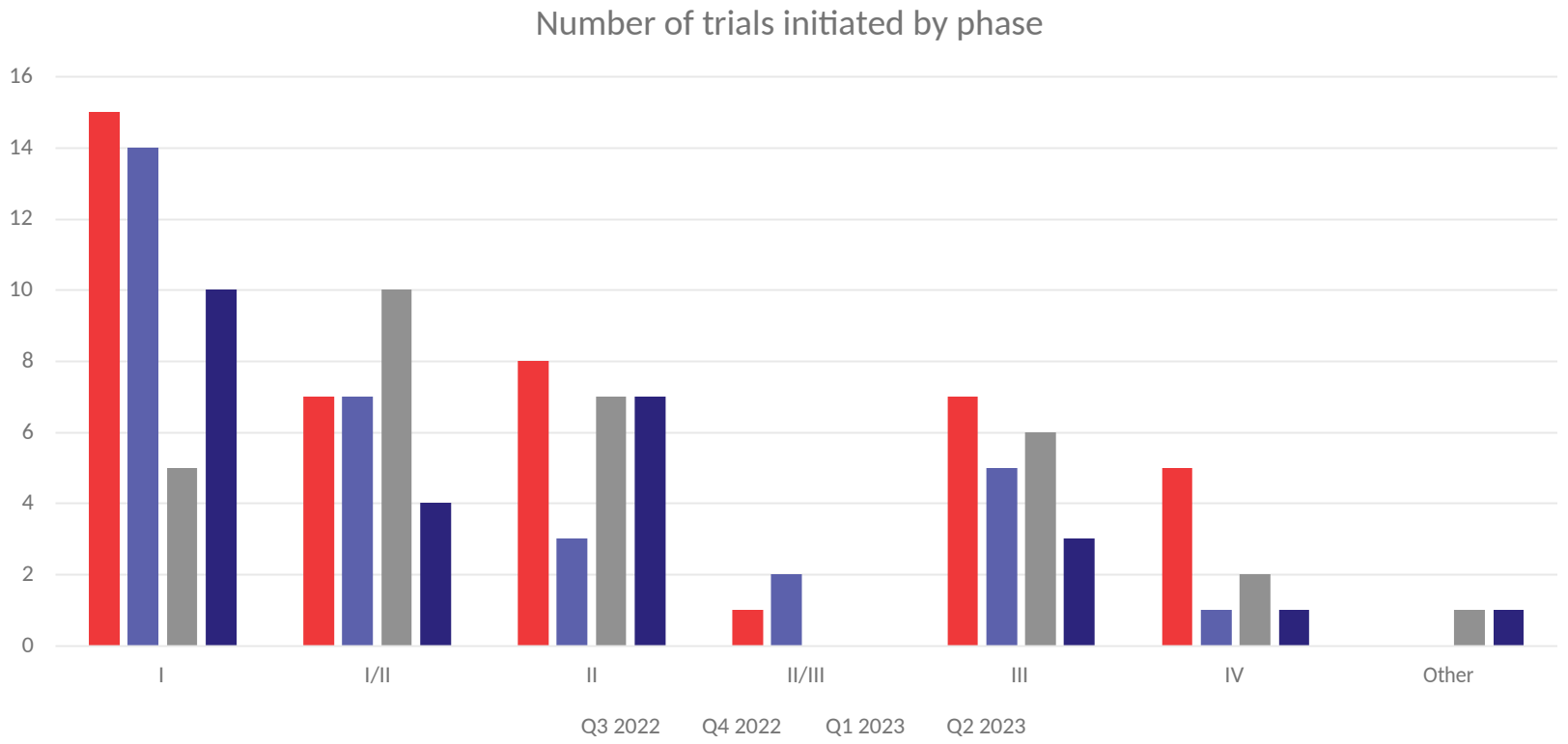
Source: Pharmaprojects| Citeline, July 2023

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

American Society of Gene + Cell Therapy

RNA therapy pipeline: Clinical trial activity

- 26 RNA trials were initiated in Q2 2023, compared to 31 in Q1 2023, 88% of which were for non-oncology indications



Source: Trialtrove| Citeline, July 2023

American Society of Gene + Cell Therapy

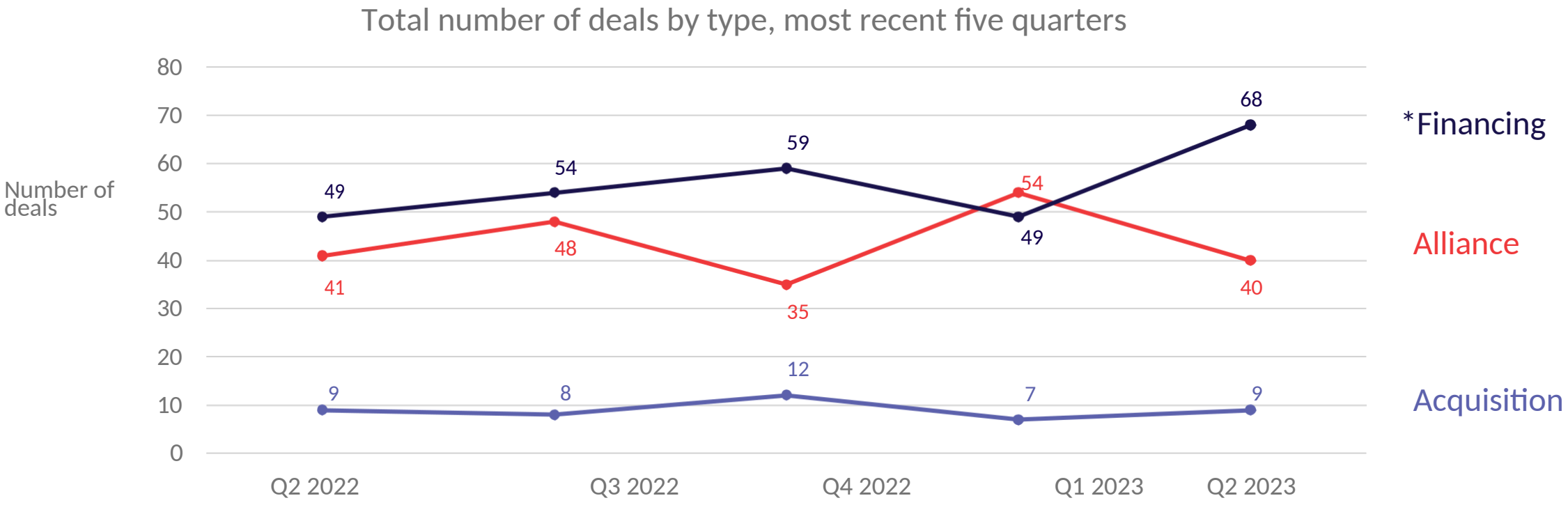
Overview of dealmaking for gene, cell, and RNA therapy companies

Q2 2023

American Society of Gene + Cell Therapy

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

- In Q2 2023, advanced molecular therapy companies penned 117 total deals – not only a 6% increase over the previous quarter's total, but also a quarterly high in the last year
- Q2 increase driven by a rebound in financing volume (+39% over Q1) and a slight jump in the number of acquisitions
- Alliances, however, experienced a slowdown, decreasing by 26% from 54 to 40 partnerships from Q1 to Q2



Source: Biomedtracker| Citeline, BioSciDB| Evaluate, July 2023

*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

Q2 2023 acquisitions in gene, cell, and RNA therapy

- Nine advanced molecular therapy acquisitions announced in Q2 2023, an increase over 7 acquisitions in Q1 2023
- Eli Lilly will pay approximately $35 million upfront, plus up to $309 million in contingent value rights, for partner Sigilon and its non-viral engineered cell-based therapy platform, Shielded Living Therapeutics, used in diabetes development
- Astellas' $5.9 billion purchase of Iveric Bio includes pipeline of AAV gene therapies for rare ophthalmic diseases

	Deal Title	Potential Deal Value (USD $)
05/01/2023	Astellas Enters Into Definitive Agreement to Acquire Iveric Bio for $5.9B	5,900,000,000
05/03/2023	Magenta Therapeutics and Dianthus Therapeutics Announce Merger Agreement	70,000,000
05/17/2023	enGene to Become Publicly Traded via Merger with Forbion European Acquisition Corp	Undisclosed
05/23/2023	CohBar, Inc. and Morphogenesis, Inc. Enter into Definitive Merger Agreement	Undisclosed
05/30/2023	GreenLight Biosciences Enters into Definitive Merger to Go Private Agreement	45,500,000
05/30/2023	Anew Medical Enters Into Merger Agreement with Redwoods Acquisition	Undisclosed
06/05/2023	CERo Therapeutics, Inc. and Phoenix Biotech Acquisition Corp. Announce Merger Agreement to Create Public Company	Undisclosed
06/29/2023	Lilly to Acquire Sigilon Therapeutics for up to $344.2M	344,200,000
06/30/2023	Baudax Bio Acquires TeraImmune, Inc.	Undisclosed

Source: Biomedtracker| Citeline, BioSciDB| Evaluate, July 2023

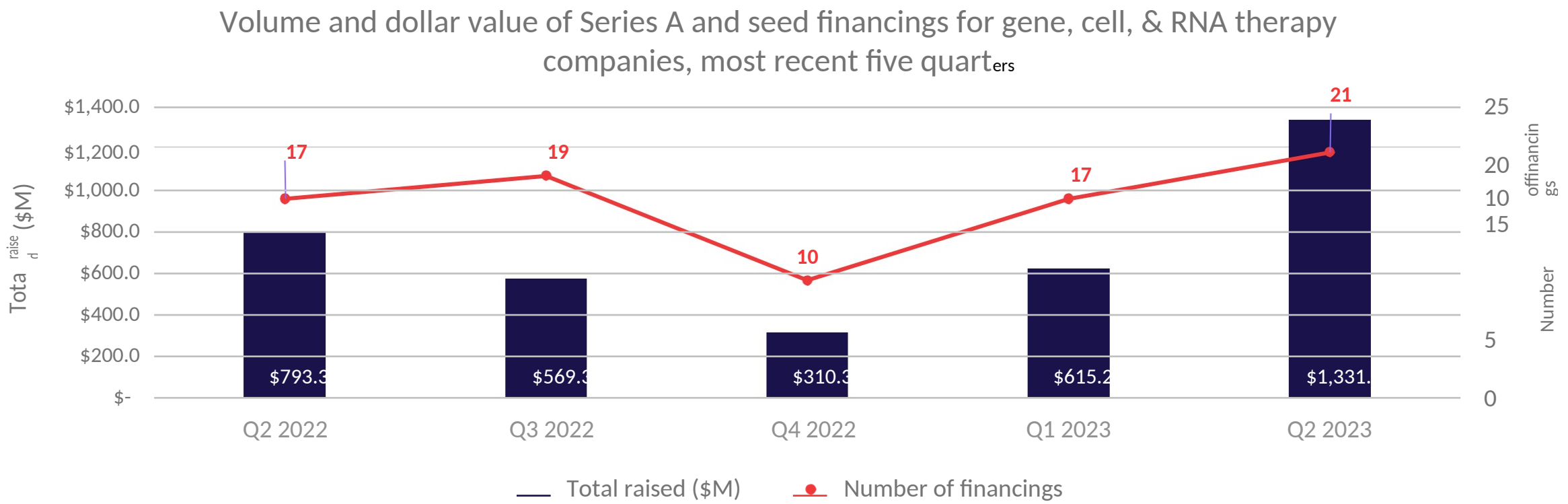
Start-up funding for gene, cell, and RNA therapy companies

Q2 2023

American Society of Gene + Cell Therapy

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

- Start-up financing activity continues to rise, with another quarterly increase seen in both volume and value
- 21 companies announced seed or Series A rounds in Q2 2023, the highest quarterly amount within the last year
- The aggregate $1.3 billion raised in these Q2 financing rounds was more than double the amount brought in during Q1



Source: Biomedtracker| Citeline, July 2023

American Society of Gene + Cell Therapy

Q2 2023 start-up financing for gene, cell, and RNA therapy companies (1/3)

04/10/2023	CTRL Therapeutics Launches with $10M Seed Financing	Cell therapy	Canada, Toronto	Northwestern University	10
04/11/2023	ImmuneBridge Raises $12M Seed Financing	NK cell therapy	United States, California, San Francisco	Undisclosed	12
04/17/2023	Complement Therapeutics Raises €72M Series A Financing	Gene therapy	United Kingdom, London	University of Manchester	79.1
04/18/2023	Brightstar Therapeutics Closes Series A Round to Fund Corneal Disease Treatment	Allografts	United States, Kentucky, Lexington	University of Minnesota	Undisclosed
04/26/2023	Orbital Therapeutics Raises $270M Series A Financing	Autologous cell therapy (CAR-T); RNA therapeutics	United States, Massachusetts, Cambridge	n/a - spun off from Beam Therapeutics	270
04/27/2023	Nkure Completes Pre-Series A Financing	NK cell therapy	India, Bangalore	Undisclosed	Undisclosed
05/02/2023	Odimma Therapeutics Raises €2M Seed Financing	Genetically modified viruses	France, Strasbourg	Undisclosed	2.2
05/04/2023	NeuExcell Raises $15m Pre-Series A+ Round	Gene therapy	United States, Pennsylvania, Philadelphia	Jinan University	15

Source: Biomedtracker| Citeline, July 2023

Q2 2023 start-up financing for gene, cell, and RNA therapy companies (2/3)

			Company Location	Academic Source	Potential Deal Value ($M)
05/09/2023	Ascend Gene & Cell Therapies Raises $130M in Seed and Series A Rounds	AAV manufacturing	United Kingdom, London	Undisclosed	132.5
05/11/2023	NewBiologix Launches With $50M Series A Financing	Engineered cell lines to manufacture gene and cell therapies	Switzerland, Lausanne	Undisclosed	50
05/16/2023	Ray Therapeutics Closes Oversubscribed $100M Series A Round	Engineered viruses	United States, California, San Diego	Undisclosed	100
05/17/2023	Siren Biotechnology Completes Initial Funding	Gene therapy	United States, California, San Francisco	UCSF's Paulk Lab	Undisclosed
05/18/2023	Myeloid Therapeutics Raises $73M in Series A2 Round	Cell therapy	United States, Massachusetts, Cambridge	Undisclosed	73
05/23/2023	ReNAgade Therapeutics Launches With $300M Series A Financing	RNA platform	United States, Massachusetts, Cambridge	Undisclosed	300
05/23/2023	Scarlet Therapeutics Raises Seed Financing	Cell therapy	United Kingdom, Bristol	University of Bristol	Undisclosed
05/30/2023	Lentitek Raises £250k Seed Funding	Lentiviral vector manufacturing	United Kingdom, Edinburgh	Undisclosed	0.3

Source: Biomedtracker| Citeline, July 2023

Q2 2023 start-up financing for gene, cell, and RNA therapy companies (3/3)

			Company Location	Academic Source	Potential Deal Value (USD, $M)
06/06/2023	AAVantgarde Bio Closes $65.3M Series A	Gene therapy	Italy, Milan	Telethon Institute of Genetics and Medicine; Telethon Foundation	65.3
06/07/2023	Hopewell Therapeutics Gets $25M in Seed Round	LNP technology for RNA and DNA delivery	United States, Massachusetts, Boston	Tufts University	25
06/08/2023	Kate Therapeutics Debuts with $51M Series A Financing	Gene therapy	United States, California, San Diego	Broad Institute	51
06/12/2023	Beacon Therapeutics Launches with £96M Financing	Gene therapy	United States, Florida, Alachua	University of Oxford	120
06/15/2023	Theradaptive Gets $26M in Series A Round	Bone and tissue regeneration	United States, Maryland, Frederick	Massachusetts Institute of Technology	26

Source: Biomedtracker| Citeline, July 2023

Notable Q2 2023 start-up gene, cell, and RNA therapy companies

ReNAgade Therapeutics	RNA technologies, including delivery, reprogramming cells, editing genes, and gene insertion	Undisclosed	Series A/$300M	MPM BioImpact, F2 Ventures	Undisclosed
Orbital Therapeutics	RNA technologies including delivery systems that extend therapeutic durability and delivery to a wider range of cells and tissues	Spun off from Beam Therapeutics	Series A/$270M	ARCH Venture Partners	Vaccines, immunomodulation, and protein replacement
ascend gene & cell therapies	AAV gene therapy manufacturing, including process development, clinical manufacturing, and analytical and regulatory support	Established by acquiring Freeline Therapeutics' manufacturing IP (CMC technologies and capabilities)	Combined seed and Series A/$132.5M	Abingworth, Petrichor	n/a

Source: Biomedtracker| Citeline, July 2023

Upcoming catalysts

Q2 2023

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward-looking events) expected in Q3 2023

AT-132	resamirigene bilparvovec	X-linked Myotubular Myopathy	Meeting with FDA	29 Mar 2023 - 31 Jul 2023
Ryoncil	remestemcel-L	Graft vs. Host Disease (GVHD) - Treatment	PDUFA for BLA - Second Review	2 Aug 2023 - 2 Aug 2023
OTL-200	atidarsagene autotemcel	Metachromatic Leukodystrophy	Approval Decision - Swissmedic	21 Jun 2023 - 31 Aug 2023
Honedra	autologous CD34+ cells	Peripheral Arterial Disease (PAD)	Japanese Approval Decision	21 Jun 2023 - 31 Aug 2023
Oxlumo	lumasiran	Hyperoxaluria	Supplemental Approval Europe (PH1)	28 Jun 2023 - 31 Aug 2023
Onpattro	patisiran	Transthyretin Amyloid Cardiomyopathy (ATTR-CM, Wild Type Or Hereditary)	Cardiovascular and Renal Drugs Advisory Committee Brief	11 Sep 2023 - 11 Sep 2023
Onpattro	patisiran	Transthyretin Amyloid Cardiomyopathy (ATTR-CM, Wild Type Or Hereditary)	Cardiovascular and Renal Drugs Advisory Committee Meeting	13 Sep 2023 - 13 Sep 2023
Exa-cel	exagamglogene autotemcel	Sickle Cell Anemia	Approval Decision (UK)	1 Jul 2023 - 30 Sep 2023
Exa-cel	exagamglogene autotemcel	Thalassemia	Approval Decision (UK)	1 Jul 2023 - 30 Sep 2023
Tab-cel	tabelecleucel	Hematologic Cancer	Approval Decision (U.K.)	13 Jun 2023 - 30 Sep 2023
DCR-PHXC	nedosiran	Hyperoxaluria	PDUFA for NDA - First Review	1 Sep 2023 - 30 Sep 2023
Leqvio	inclisiran	Dyslipidemia / Hypercholesterolemia	Approval Decision (Japan)	1 Jul 2023 - 31 Dec 2023
HPC-Cord Blood Therapy	umbilical cord blood mononuclear stem cell therapy	Ischemic Stroke	PDUFA for BLA - First Review	1 Jan 2023 - 31 Dec 2023
SB623	vandefitemcel	Traumatic Brain Injury (TBI)	Approval Decision (Japan)	20 Jun 2023 - 31 Jan 2024
Exa-cel	exagamglogene autotemcel	Sickle Cell Anemia	CHMP Opinion	1 Sep 2023 - 31 Mar 2024
Vyjuvek	beremagene geperpavec	Epidermolysis Bullosa	CHMP Opinion	1 Sep 2023 - 31 Mar 2024
Exa-cel	exagamglogene autotemcel	Thalassemia	CHMP Opinion	1 Sep 2023 - 31 Mar 2024

Source: Biomedtracker| Citeline, July 2023

Appendix

Methodology, sources, and glossary of key terms

Q2 2023

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 which 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 which 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 starts 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 which 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

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