Gene, Cell, + RNA Therapy Landscape Report

Q3 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.

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.

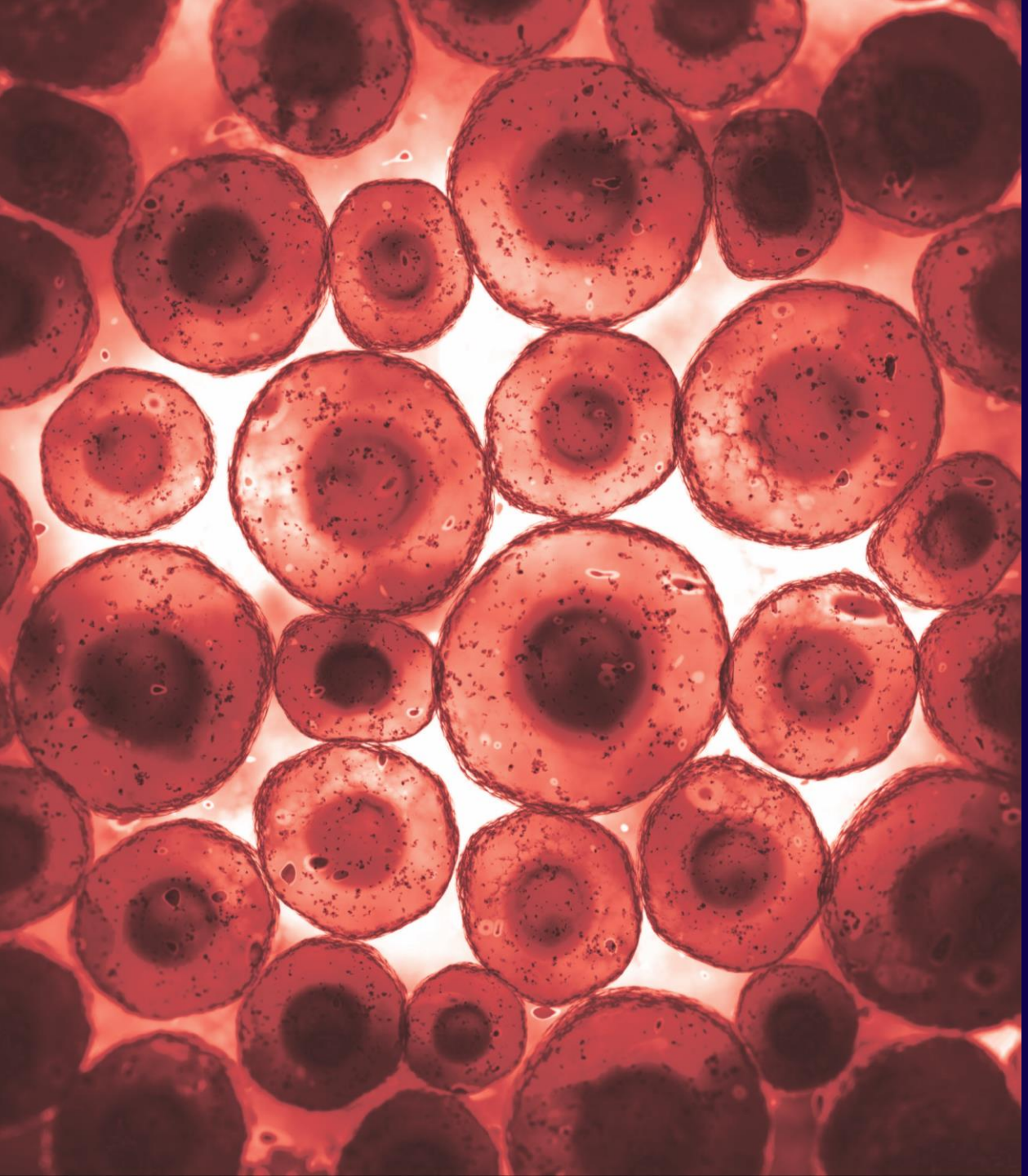


Table of contents

American Society of Gene + Cell Therapy

Introduction

Welcome to the third quarterly report of 2023 from ASGCT and Citeline! This past quarter, an anti-BCMA-targeting CAR-T cell therapy, Fucaso, was approved in China for multiple myeloma and an mRNA vaccine, Daichirona, was approved in Japan for COVID-19. There are currently 3,866 therapies in development from pre-clinical through pre-registration; 53% of those are gene therapies, 25% are RNA therapies, and 22% are non-genetically modified cell therapies.

In the gene therapy pipeline, the number of therapies in Phase 1 development has increased—by 7% since the previous quarter—for the first time in the past year. The number of Phase III gene therapies has remained unchanged for the fourth consecutive quarter. In Q3, 58 trials were initiated for gene therapies, with trials for non-oncology indications increasing by 6 points, to 38%. The proportion of non-oncology trials has increased since Q4 last year. For the first time in more than a year in the cell therapy pipeline, COVID-19 complications is no longer listed in the top three specified indications for non-genetically modified cell therapy development. Twenty-one cell therapy trials were initiated in Q3, 10 fewer than the previous quarter. Among RNA therapies, the top-specified rare oncology indications are pancreatic, liver, and ovarian cancer. The most common non-oncology rare indications are Duchenne muscular dystrophy, amyotrophic lateral sclerosis, and Huntington's disease.

Q3's deal activity represented a 5% increase over the 110 deals signed the same quarter one year ago. Overall, total financings, alliances, and acquisitions amounted to 116 transactions compared with last quarter's 117 transactions. The volume of seed and Series A financing decreased 15% compared with the last quarter. Aggregate dollar value saw a steeper decrease of 73% to $348.2 million.

Key takeaways from Q3 2023

Q3 2023 was a quiet time for approvals in comparison to the previous quarter

- Both of the new approvals seen across the gene, cell, and RNA landscape in Q3 were in Asia, with a new anti-BCMA-targeting CAR-T therapy, Fucaso, being approved in China for multiple myeloma, and the new mRNA COVID-19 vaccine Daichirona from Daiichi Sankyo approved in Japan

For the first time in over a year, COVID-19 complications is no longer in the top 3 specified indications for non-genetically modified cell therapy development

- Taking third place instead of COVID-19 complications is now Parkinson's disease research, closely followed by type 1 diabetes
- Outside of this change, the main focus of non-genetically modified cell therapy development has remained consistent with findings from previous quarters; the top disease areas continue to be research in anti-cancer indications such as solid tumors (unspecified), and rare diseases such as acute respiratory distress syndrome

Advanced molecular companies maintained steady deal activity in Q3 2023, but start-ups faced a tougher financing environment

- Q3 2023's total deal activity reached 116 transactions, which was virtually flat to Q2 2023's 117 aggregate, but a 5% increase over the volume one year ago
- The number of seed and Series A rounds decreased by 15% to 17 financings in Q3, with aggregate dollar value experiencing a much steeper decrease of 73% to $348.2 million
- The quarter featured Novartis's acquisition of RNA delivery firm DTx Pharma for up to $1 billion, as well as the $70 million Series A financing of Tenpoint Therapeutics, which is focused on vision-restoring engineered cell-based therapeutics and *in vivo* reprogramming

Key highlights in Q3 2023

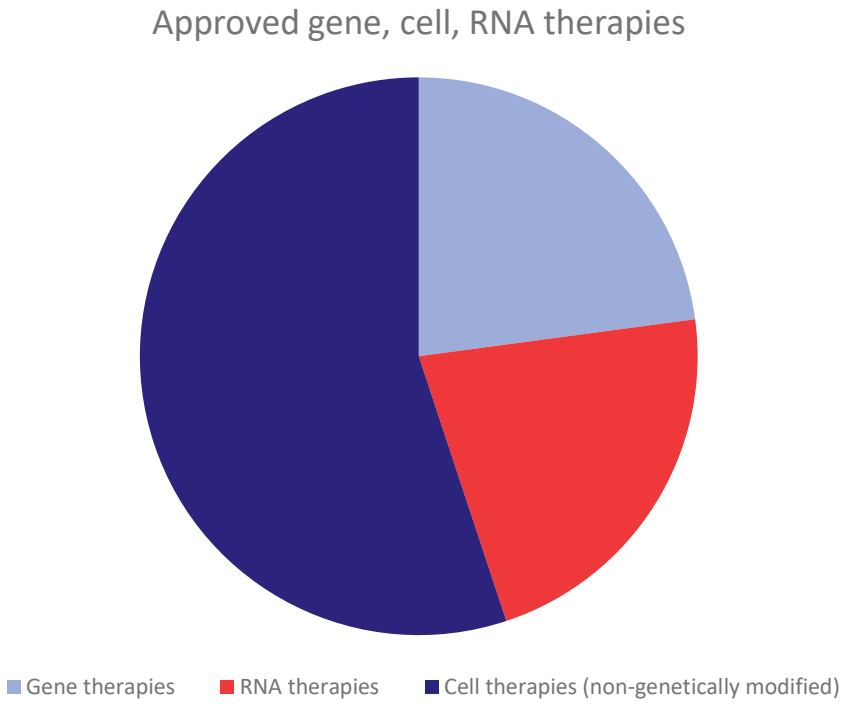
Q3 2023

American Society of Gene + Cell Therapy

Approved gene, cell, and RNA therapies

Globally, for clinical use:

- 27 gene therapies are approved (including genetically modified cell therapies)
  - In Q3 2023, Fucaso, an anti-BCMA-targeting CAR-T therapy, was approved in China for multiple myeloma
- 26 RNA therapies are approved
  - In Q3 2023, Daiichi Sankyo's Daichirona COVID-19 mRNA vaccine was approved in Japan
- 65 non-genetically modified cell therapies are approved



Source: Pharmaprojects | Citeline, October 2023

Approved gene therapies as of Q3 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, Japan	Spark Therapeutics (Roche)
Yescarta	axicabtagene ciloleucel	2017	Diffuse large B-cell lymphoma; non-Hodgkin's lymphoma; follicular lymphoma	US, EU, UK, Japan, Canada, China, Australia	Kite Pharma (Gilead)
Collategene	beperminogene perplasmid	2019	Critical limb ischemia	Japan	AnGes
Zolgensma	onasemnogene abeparvovec	2019	Spinal muscular atrophy	US, EU, UK, Japan, Australia, Canada, Brazil, Israel, Taiwan, South Korea	Novartis
Zynteglo	betibeglogene autotemcel	2019	Transfusion-dependent beta thalassemia	US	bluebird bio

Source: Pharmaprojects | Citeline, October 2023

Text highlighted in yellow represents new approvals during Q3 2023

Approved gene therapies as of Q3 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
Fucaso	equecabtagene autoleucel	2023	Multiple myeloma	China	Nanjing IASO Biotechnology

Source: Pharmaprojects | Citeline, October 2023

Text highlighted in yellow represents new approvals during Q3 2023

Approved RNA therapies as of Q3 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	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, October 2023

Text highlighted in yellow represents new approvals during Q3 2023

Approved RNA therapies as of Q3 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, Saudi Arabia	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	Sinocelltech

Source: Pharmaprojects | Citeline, October 2023

Text highlighted in yellow represents new approvals during Q3 2023

Approved RNA therapies as of Q3 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
Daichirona	COVID-19 vaccine, Daiichi Sankyo	2023	Infection, coronavirus, novel coronavirus prophylaxis	Japan	Daiichi Sankyo

*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, October 2023

Text highlighted in yellow represents new approvals during Q3 2023

Key highlights in Q3 2023

Noteworthy events that happened in Q3 2023

Drug	Event Type	Indication	Molecule	Event Date
Fucaso	Approval (China)	Multiple Myeloma (MM)	Cellular	02 July 2023
NS-089/NCNP-02	Rare Pediatric Disease (RPD) Designation	Duchenne Muscular Dystrophy (DMD)	Antisense	04 July 2023
HEMO-CAR-T	FDA Response	Acute Myelogenous Leukemia (AML)	Cellular	10 July 2023
EBT101	Fast Track Status	HIV / AIDS	Viral Gene Therapy	20 July 2023
NS-089/NCNP-02	Breakthrough Therapy Designation (U.S.)	Duchenne Muscular Dystrophy (DMD)	Antisense	27 July 2023
RP-L301	PRIME Designation (Europe)	Pyruvate Kinase Deficiency	Viral Gene Therapy	31 July 2023
NS-089/NCNP-02	Orphan Drug Designation (U.S.)	Duchenne Muscular Dystrophy (DMD)	Antisense	31 July 2023
IVS-3001	Fast Track Status	Renal Cell Cancer (RCC)	Cellular	31 July 2023
VP-001	Fast Track Status	Retinitis Pigmentosa (RP) (Ophthalmology)	Antisense	02 August 2023
Ryoncil	Complete Response Letter (CRL)	Graft vs. Host Disease (GVHD) - Treatment	Cellular	03 August 2023
OTL-200	Rolling NDA/BLA Completed	Metachromatic Leukodystrophy	Viral Gene Therapy	03 August 2023
RP-L201	NDA/BLA Filing	Autoimmune Disorders	Viral Gene Therapy	10 August 2023
AOC 1044	Orphan Drug Designation (U.S.)	Duchenne Muscular Dystrophy (DMD)	siRNA/RNAi	10 August 2023
Biostage Esophageal Implant	Orphan Drug Designation (Europe)	Esophageal Cancer	Cellular	21 August 2023
TSHA-102	Fast Track Status	Rett Syndrome	Viral Gene Therapy	24 August 2023
EB-101	Meeting with FDA	Epidermolysis Bullosa	Viral Gene Therapy	30 August 2023
KB408	Orphan Drug Designation (U.S.)	Alpha-1 Antitrypsin Deficiency (A1AD or AATD)	Viral Gene Therapy	01 September 2023
INO-3107	Breakthrough Therapy Designation (U.S.)	Head and Neck Cancer	Other Nucleic Acid	07 September 2023
Vididencel	Fast Track Status	Acute Myelogenous Leukemia (AML)	Cellular	08 September 2023
OTL-200	Priority Review	Metachromatic Leukodystrophy	Viral Gene Therapy	18 September 2023
DYNE-101	Orphan Drug Designation (U.S.)	Myotonic Muscular Dystrophy	Antisense	19 September 2023
Ryoncil	Meeting with FDA	Graft vs. Host Disease (GVHD) - Treatment	Cellular	20 September 2023
EB-101	NDA/BLA Filing	Epidermolysis Bullosa	Viral Gene Therapy	26 September 2023

Source: Biomedtracker | Citeline, October 2023

Pipeline overview

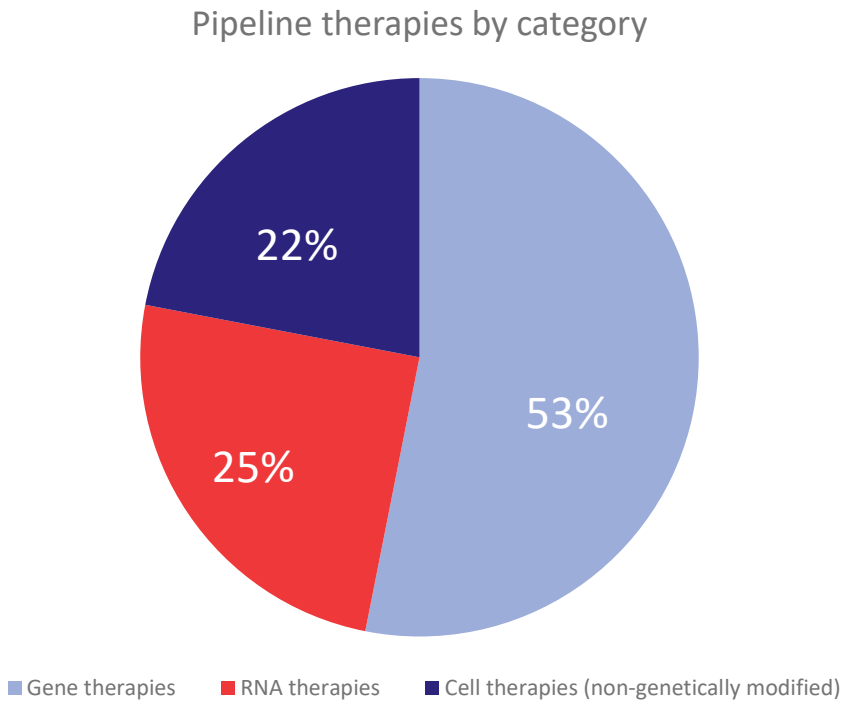
Q3 2023

American Society of Gene + Cell Therapy

Pipeline of gene, cell, and RNA therapies

3,866 therapies are in development, ranging from preclinical through pre-registration

- 2,082 gene therapies (including genetically modified cell therapies such as CAR T-cell therapies) are in development, accounting for 53% of gene, cell, and RNA therapies
- 862 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies



Source: Pharmaprojects| Citeline, October 2023

American Society of Gene + Cell Therapy

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q3 2023

American Society of Gene + Cell Therapy

Gene therapy pipeline: Quarterly comparison

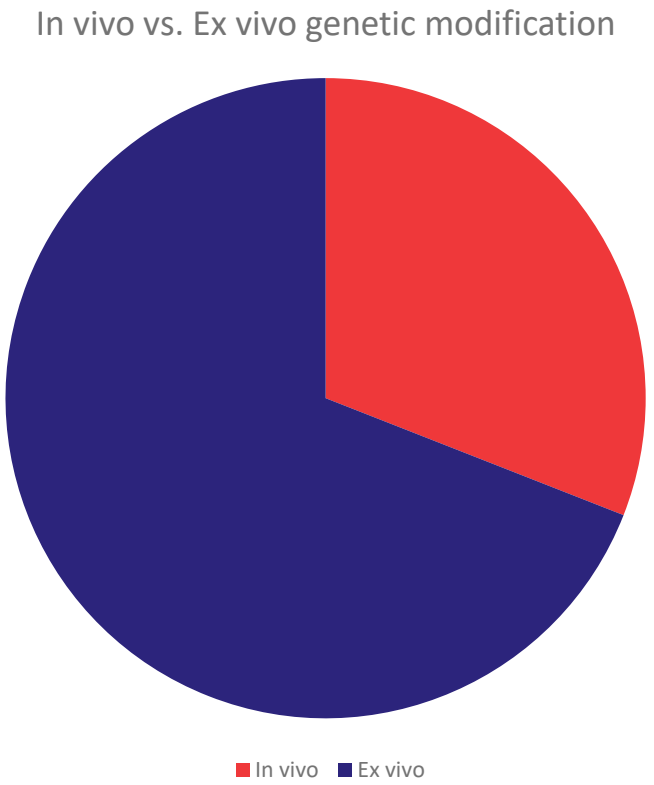
- For the first time in the past year, the number of gene therapies in Phase I development has increased since the previous quarter, increasing by 7%
- For the fourth quarter in a row, the number of Phase III gene therapies has remained unchanged at 30 therapies
- Rocket Pharmaceutical filed for approval in the US for its lentiviral gene therapy, RP-L201, in leukocyte adhesion deficiency
- Abeona Therapeutics filed for approval in the US for its engineered cell therapy, EB-101, in epidermolysis bullosa
- Therapies currently in pre-registration:
  - In China
    - 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)
    - RP-L201 (Rocket Pharmaceuticals)
    - EB-101 (Abeona Therapeutics)

Global Status	Q3 2022	Q4 2022	Q1 2023	Q2 2023	Q3 2023
Preclinical	1,480	1,515	1,493	1,539	1,522
Phase I	264	254	245	240	256
Phase II	249	248	247	260	267
Phase III	32	30	30	30	30
Pre-registration	6	6	7	6	7
Total	**2,031**	**2,053**	**2,022**	**2,075**	**2,082**

Source: Pharmaprojects | Citeline, October 2023

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

- *Ex vivo* genetic modification is more widely used for gene therapies in pipeline development
- In Q3 2023, *in vivo* delivery techniques were used in 31% of gene therapies, one percentage point higher than the previous quarter



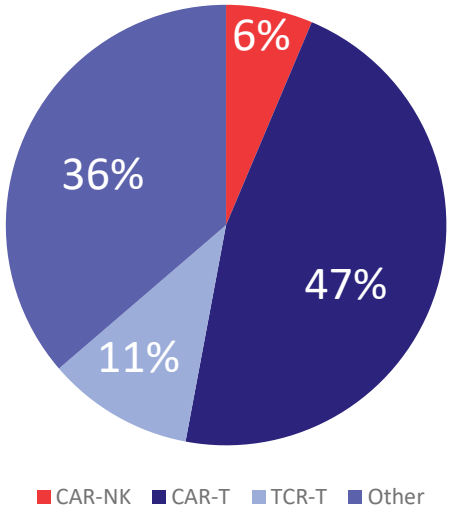
Source: Cell and Gene Therapy dashboard | Citeline, October 2023

American Society of Gene + Cell Therapy

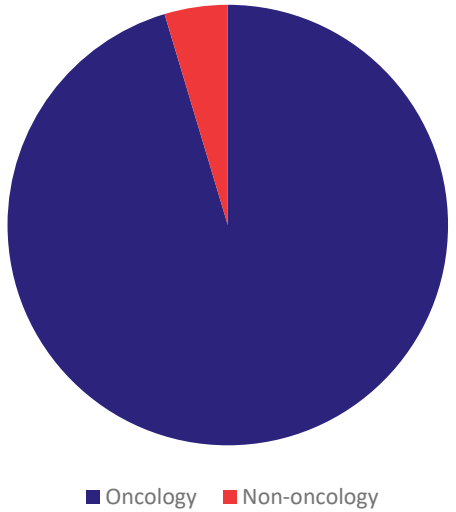
Gene therapy breakdown: CAR-Ts continue to dominate pipeline

- CAR-T cell therapies remain the most common technology used in the pipeline of genetically modified cell therapies (preclinical through to pre-registration), representing 47%, followed by the “other” category at 36%, which includes a list of less commonly used technologies including TCR-NK, CAR-M, and TAC-T
- 97% 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



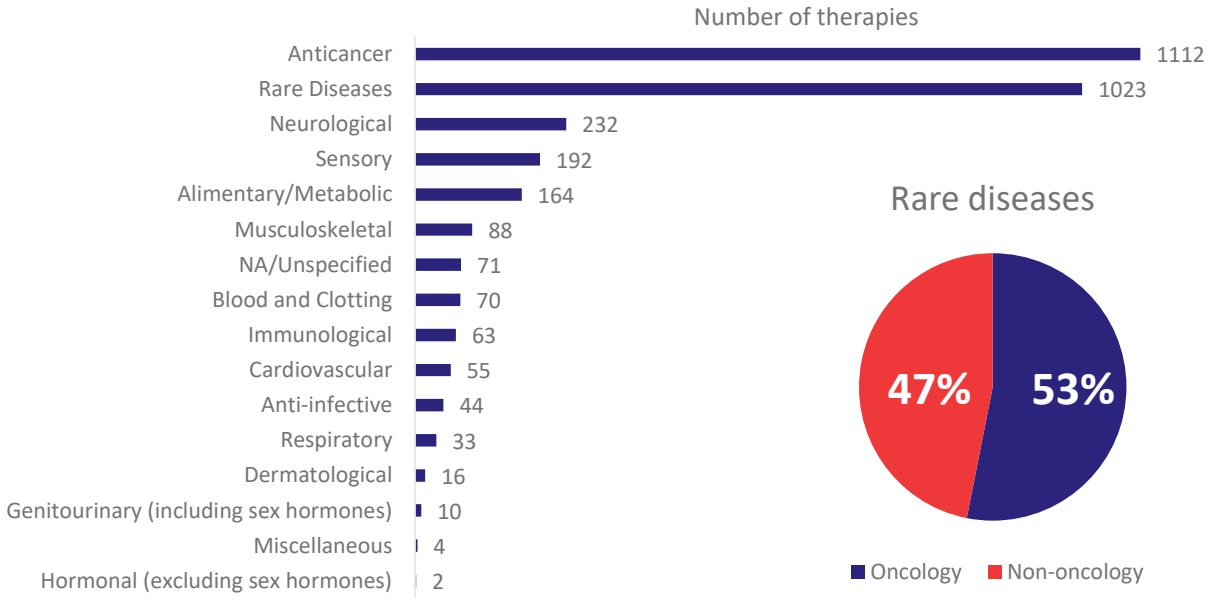
Source: Cell and Gene Therapy dashboard | Citeline, October 2023

American Society of Gene + Cell Therapy

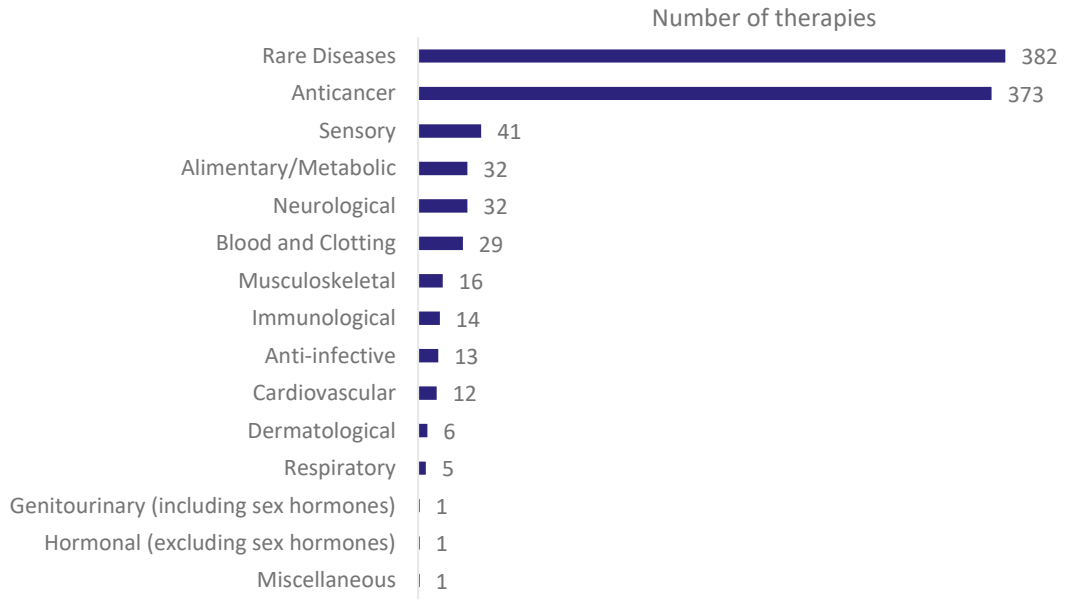
Gene therapy pipeline: Most commonly targeted therapeutic areas

- 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 53% 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)



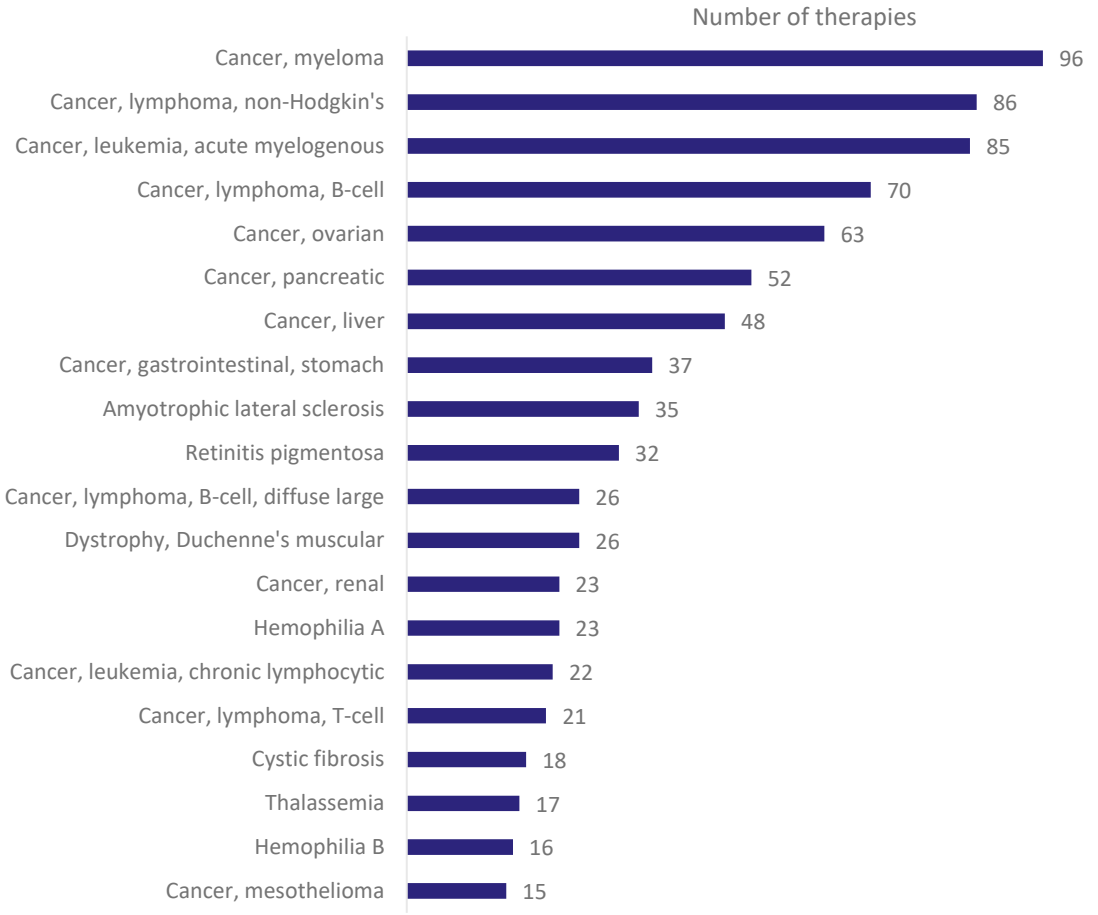
Source: Pharmaprojects | Citeline, October 2023

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 1,023 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 H1 2023
- In the same order as the previous eight 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, October 2023

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

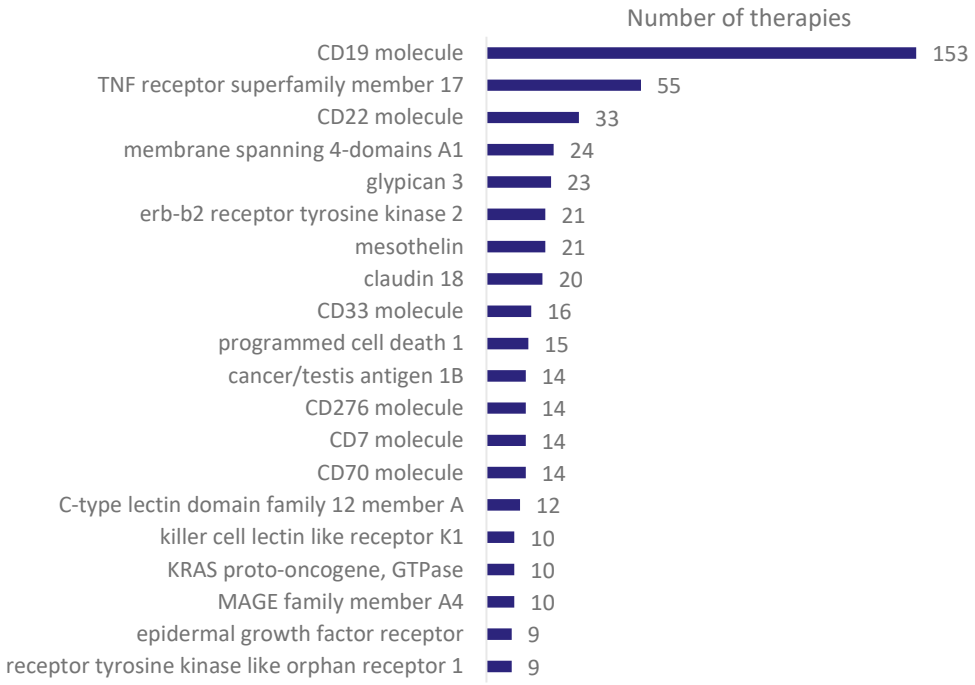
American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common targets

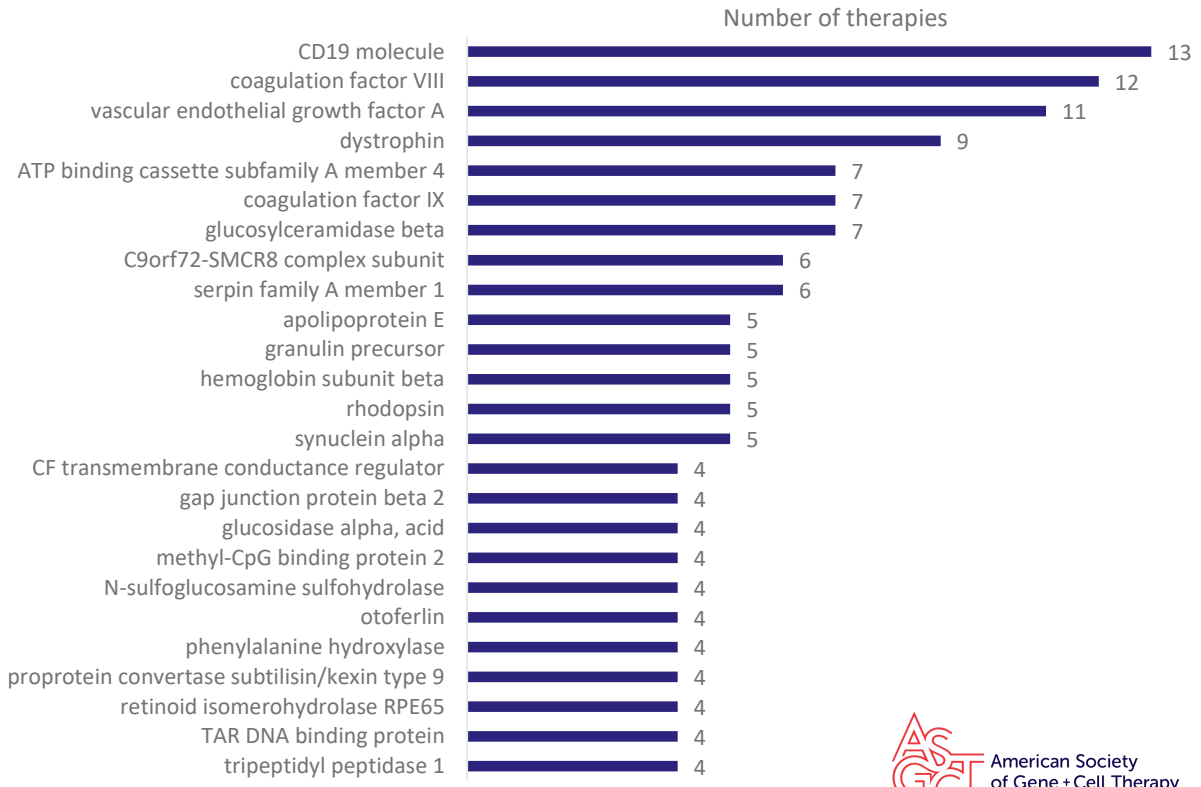
Of the gene therapies in preclinical trials through pre-registration for which targets are disclosed:

- 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
- CD19 molecule is the most common target for non-oncology indications, while coagulation factor VIII moves down to second most common in Q3 2023

Oncology



Non-oncology targets

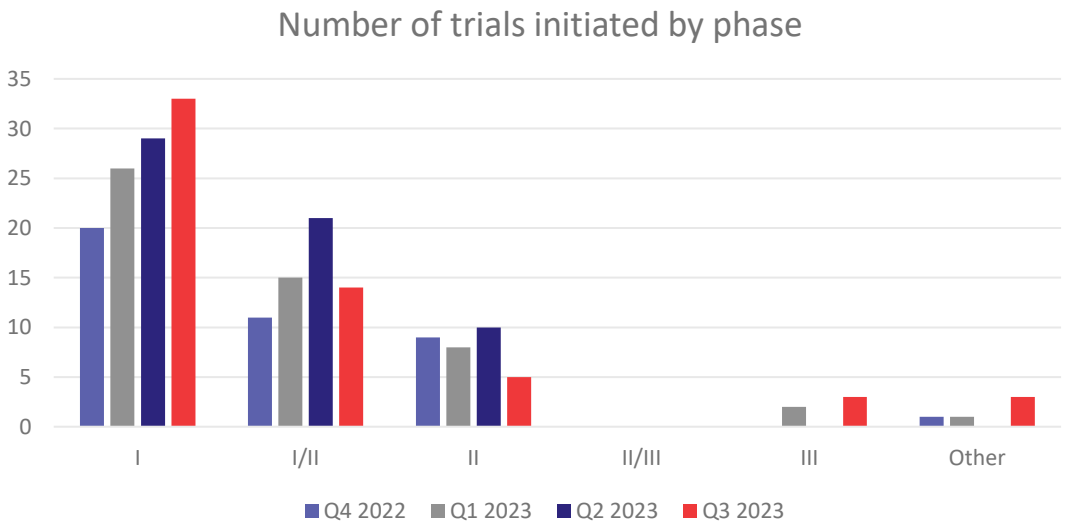


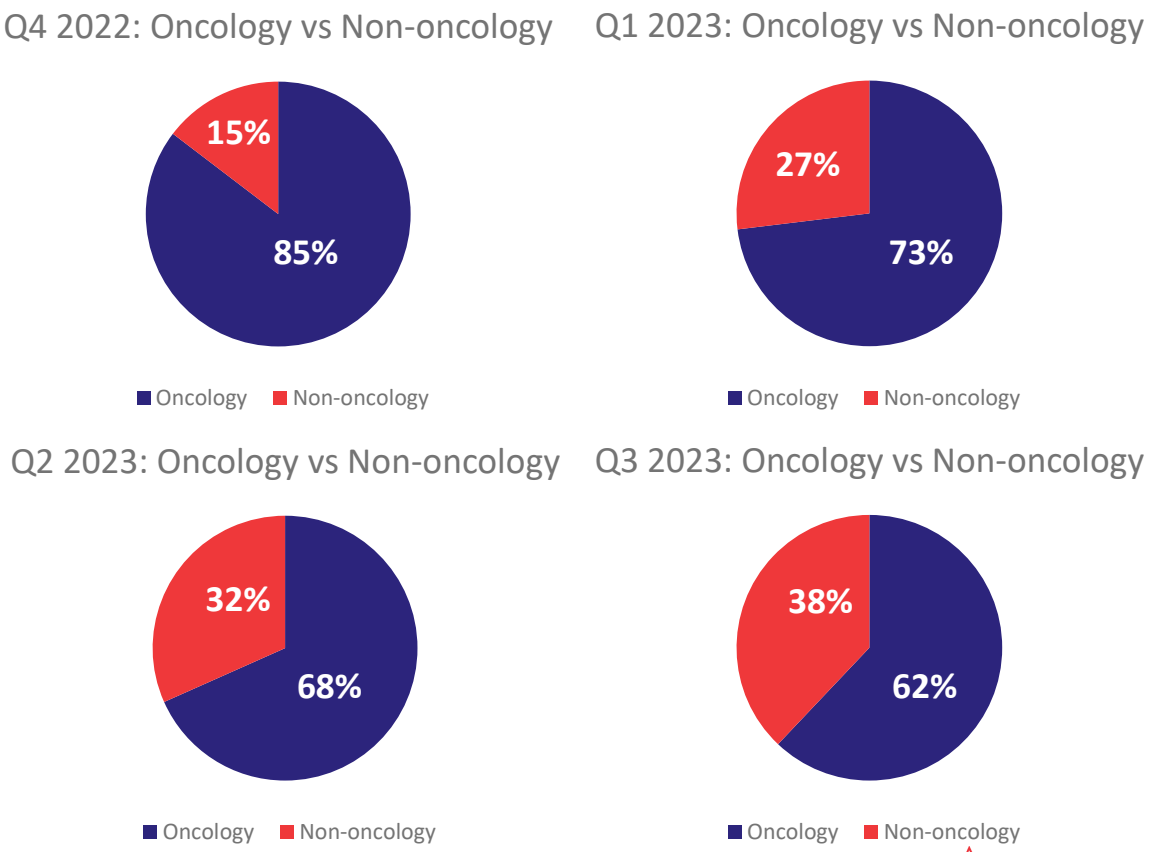
Source: Pharmaprojects| Citeline, October 2023

American Society of Gene + Cell Therapy

Gene therapy clinical trial activity

- 58 trials were initiated in Q3 2023 for gene therapies
- The proportion of gene therapy trials for non-oncology indications has increased by six percentage points since the previous quarter, to 38%, continuing the trend of an increasing proportion of non-oncology gene therapy trials initiating each quarter since Q4 2022





Source: Trialtrove| Citeline, October 2023

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline

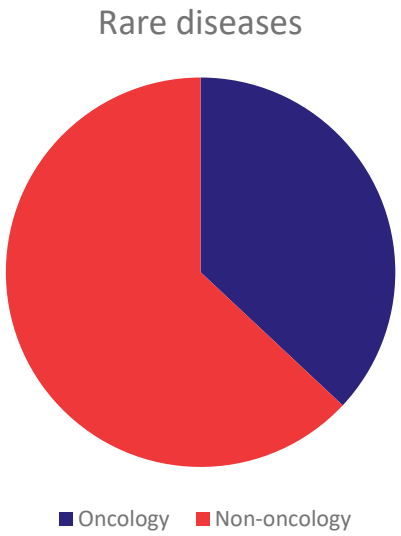
Q3 2023

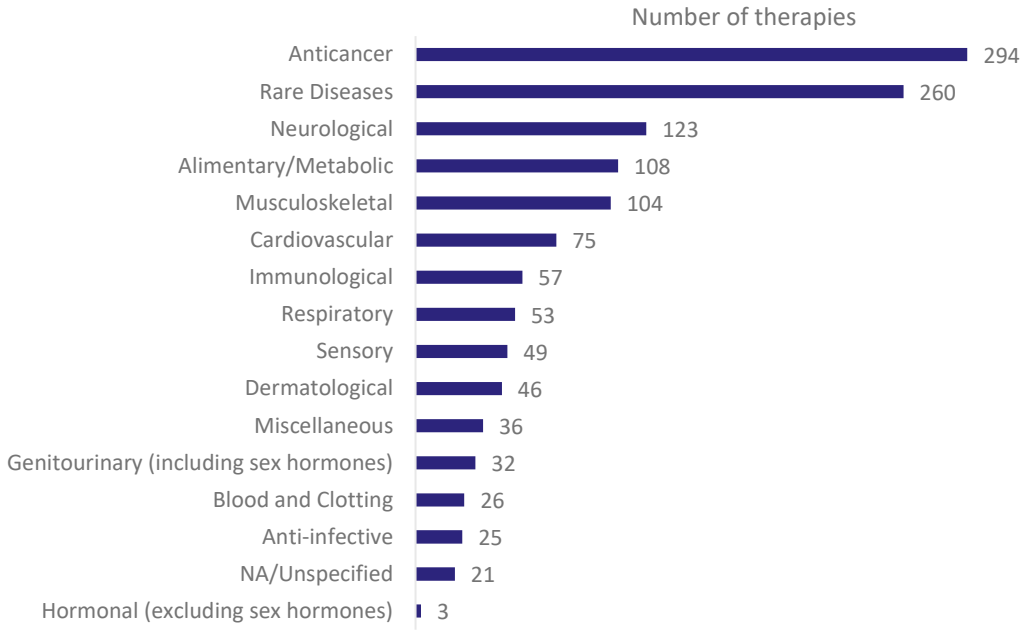
American Society of Gene + Cell Therapy

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, as found in the previous quarter





Source: Pharmaprojects| Citeline, October 2023

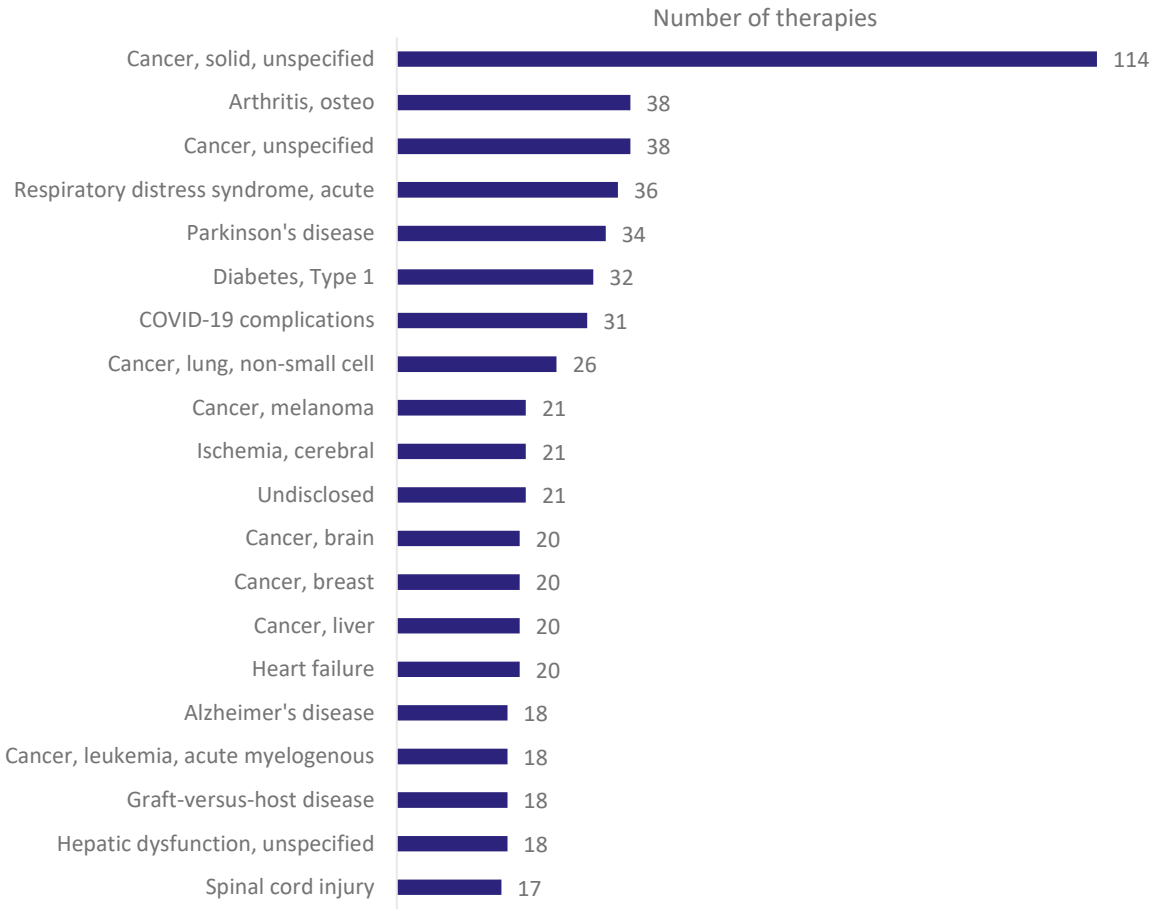
Note: Figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

Of the therapies for which indications are specified, for the first time in over a year, COVID-19 complications is not within the top three:

1. Osteoarthritis
2. Acute respiratory distress syndrome
3. Parkinson’s disease



Source: Pharmaprojects| Citeline, October 2023

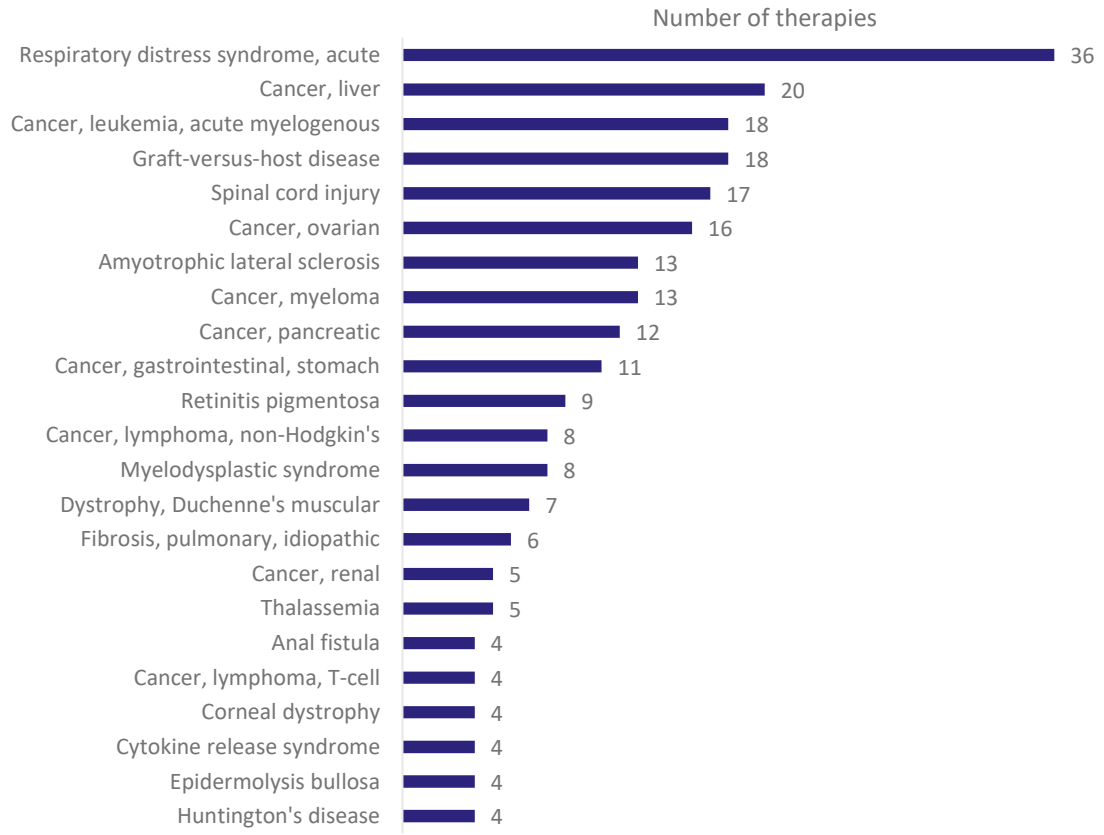
Note: Figures based on indications in pipeline development only for each therapy

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



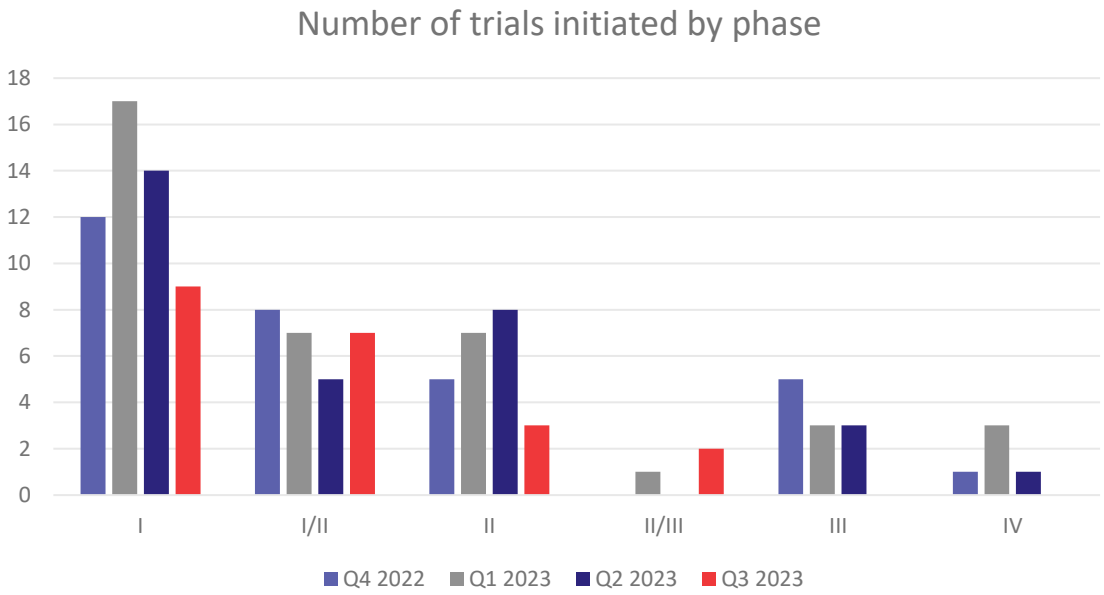
Source: Pharmaprojects| Citeline, October 2023

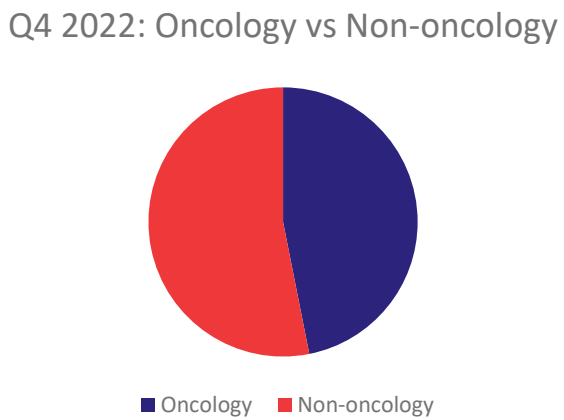
Note: Figures based on indications in pipeline development only for each therapy

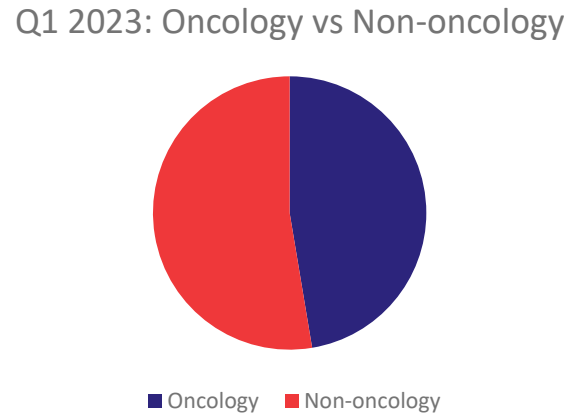
American Society of Gene + Cell Therapy

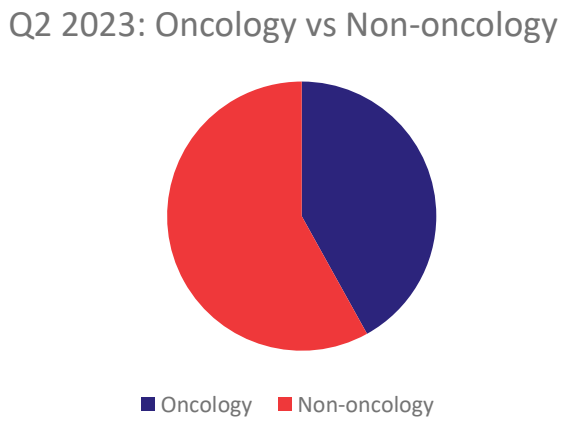
Non-genetically modified cell therapy trial activity

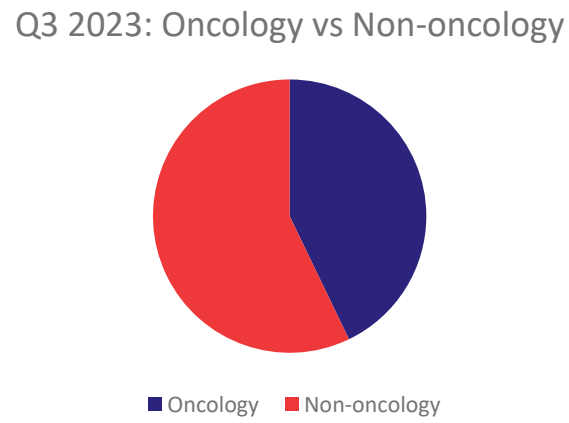
- 21 trials were initiated for non-genetically modified cell therapies in Q3 2023, 10 less than the previous quarter
- Of these 21, 57% are for non-oncology indications, a decrease of one percentage point from Q2 2023











Source: Trialtrove| Citeline, October 2023

American Society of Gene + Cell Therapy

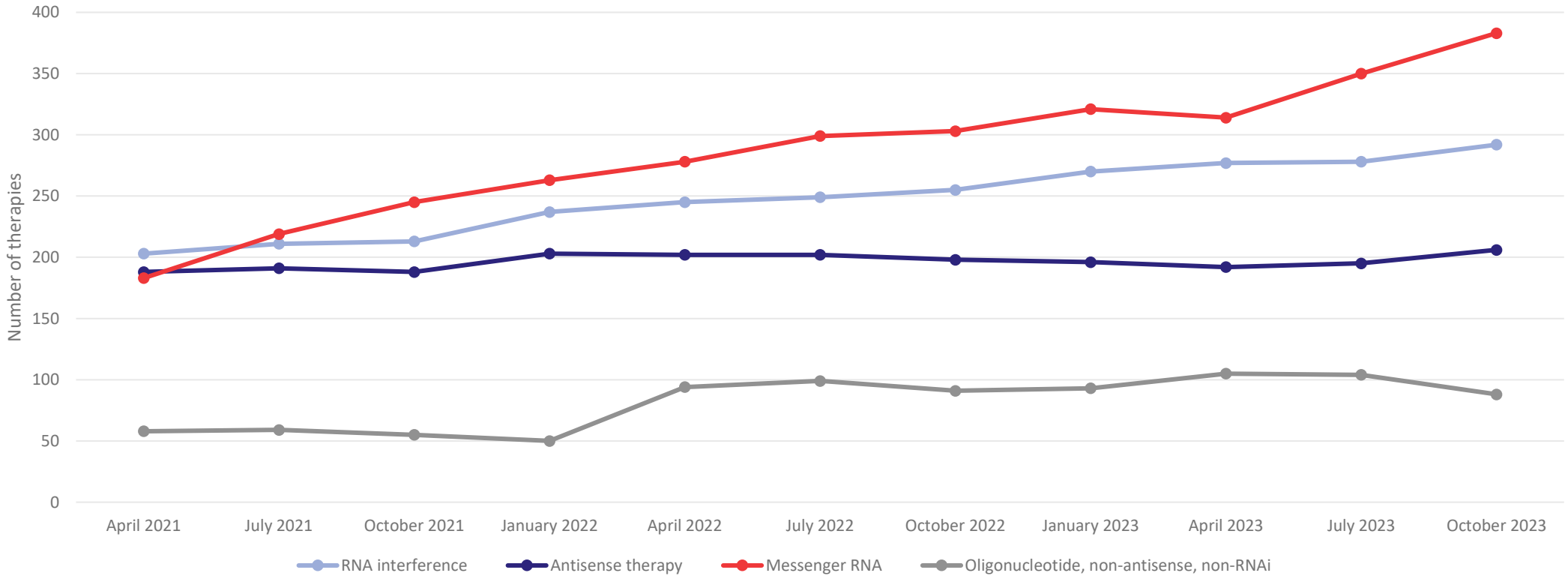
RNA therapy pipeline

Q3 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

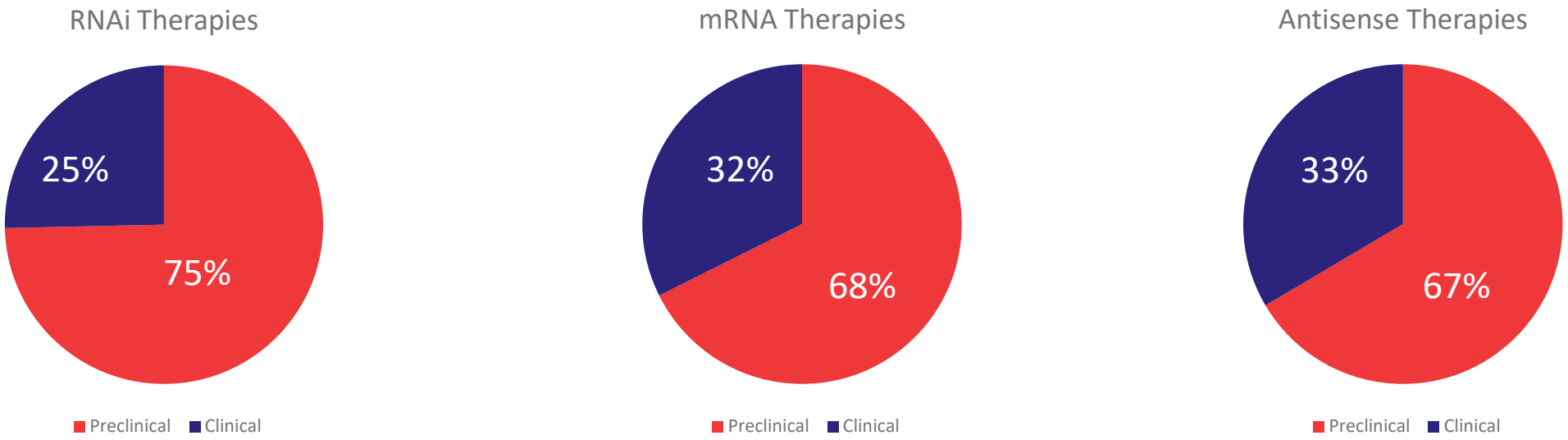


Source: Pharmaprojects| Citeline, October 2023

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 75%, 68%, and 67% of their respective pipelines

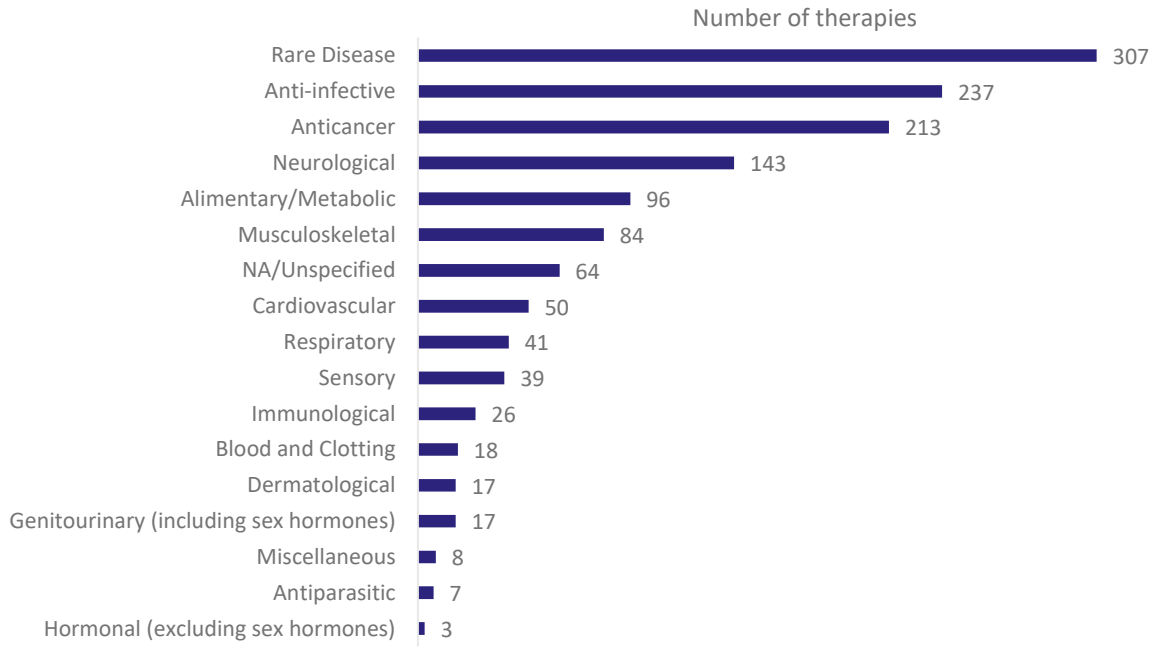


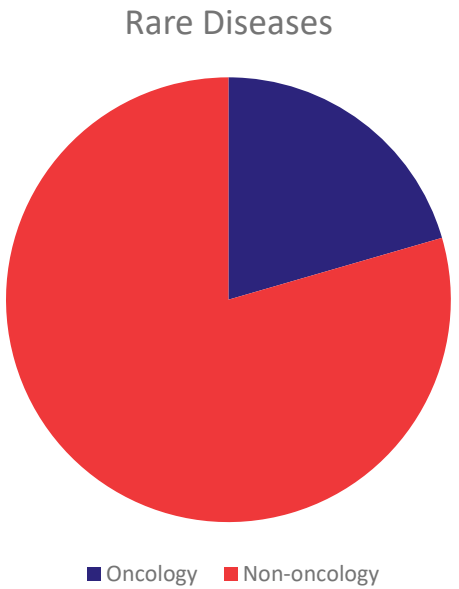
Source: Pharmaprojects| Citeline, October 2023

RNA therapies: Most commonly targeted therapeutic areas

Of the 976 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 remain 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 81%





Source: Pharmaprojects| Citeline, October 2023

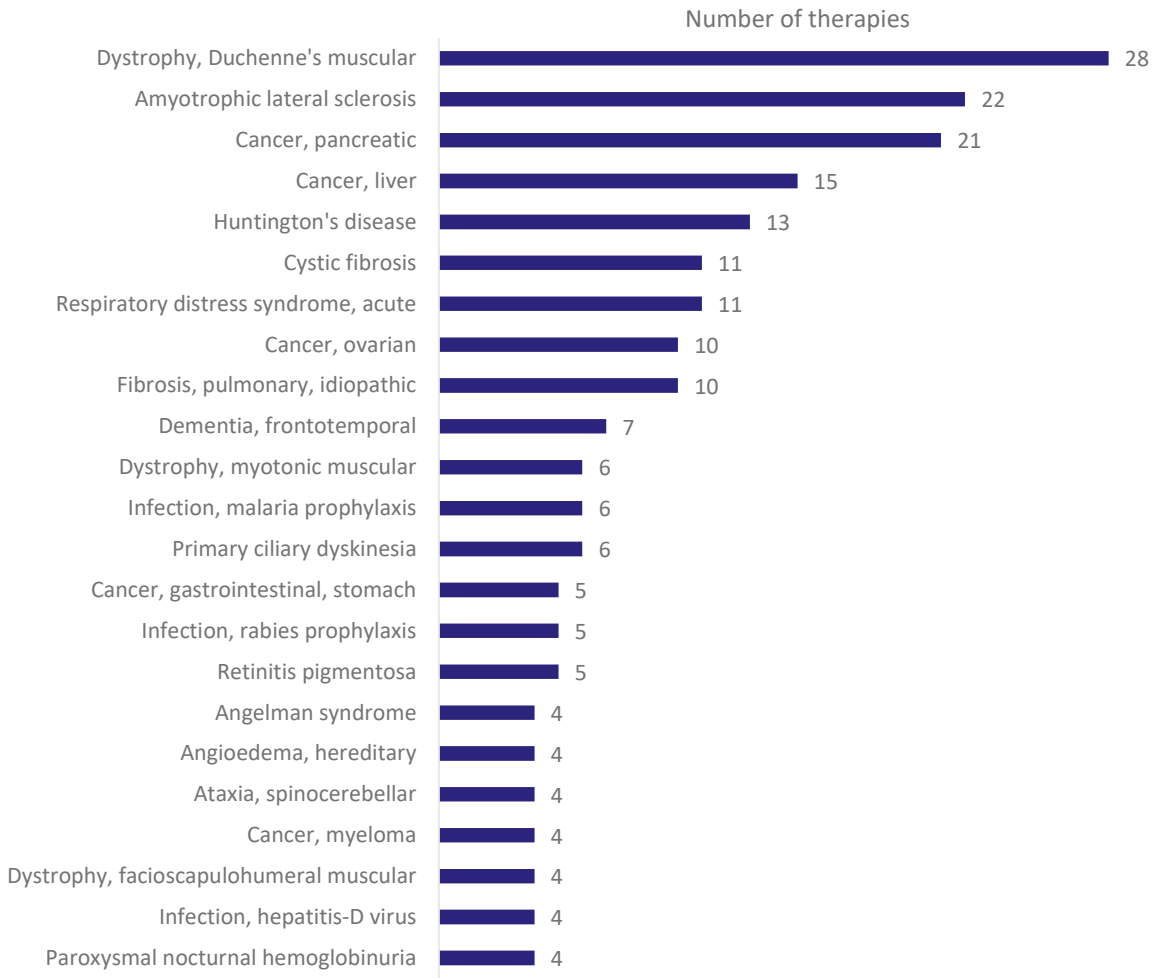
Note: Figures based on indications in pipeline development only for each therapy

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



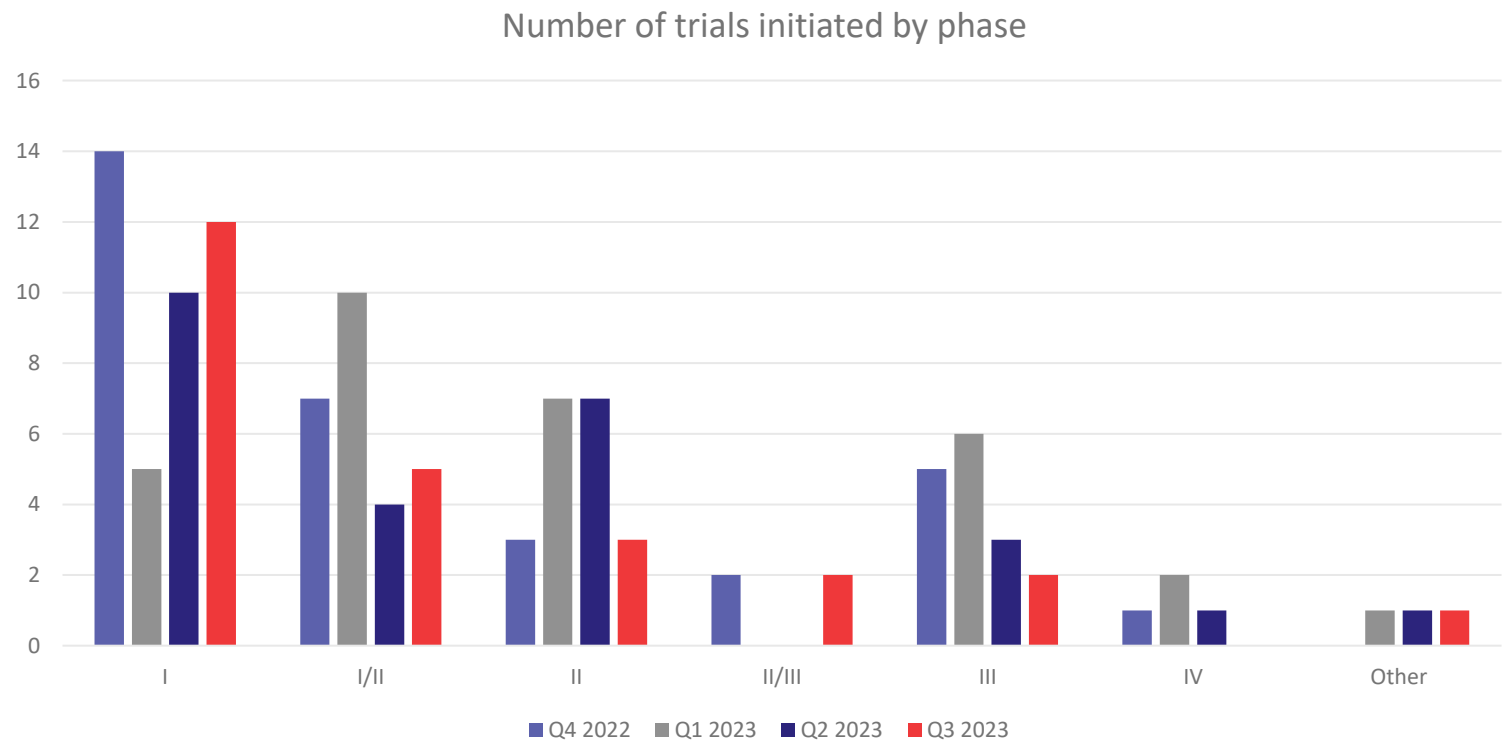
Source: Pharmaprojects| Citeline, October 2023

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

American Society of Gene + Cell Therapy

RNA therapy pipeline: Clinical trial activity

- 25 RNA trials were initiated in Q3 2023, compared to 26 in Q2 2023, 80% of which were for non-oncology indications



Source: Trialtrove| Citeline, October 2023

American Society of Gene + Cell Therapy

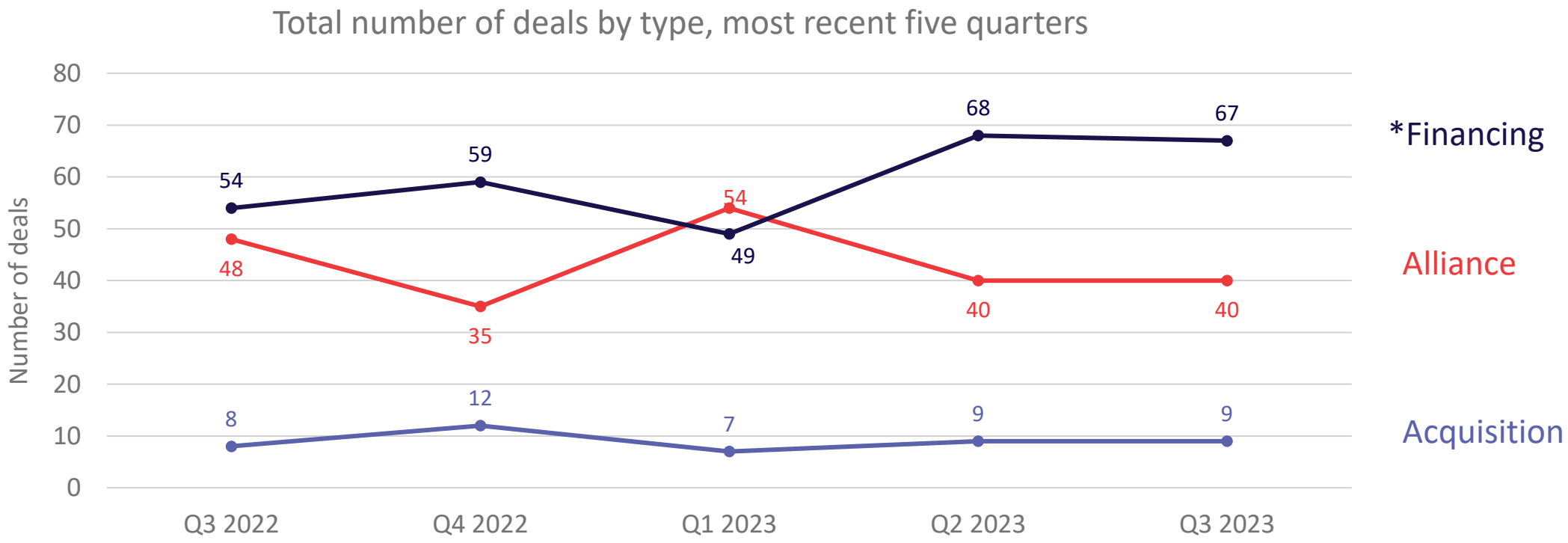
Overview of dealmaking for gene, cell, and RNA therapy companies

Q3 2023

American Society of Gene + Cell Therapy

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

- Total financings, alliances, and acquisitions amounted to 116 transactions in Q3 2023, remaining virtually flat from the previous quarter's 117 aggregate
- Q3 2023's deal activity represented a 5% increase over the 110 deals signed in the same quarter a year ago
- In the last year, financing volume has seen the biggest jump, with 54 completed in Q3 2022 vs. 67 in Q3 2023 (+24%)



Source: Biomedtracker| Citeline, BioSciDB| Evaluate, October 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

Q3 2023 acquisitions in gene, cell, and RNA therapy

- Acquisition volume remained steady in Q3 2023 with nine deals, the same number as in Q2 2023 and just slightly ahead of the eight transactions done in Q3 2022
- In the current quarter's largest deal, Novartis paid $500 million up front plus up to $500 million in earn-outs for DTx Pharma, which has the proprietary Fatty Acid Ligand Conjugated OligoNucleotide (FALCON) technology to improve delivery of RNA medicines
- In a stock exchange deal worth $485 million, Quince acquired EryDel and its *ex vivo* red blood cell platform for treating ataxia-telangiectasia

Deal Date	Deal Title	Potential Deal Value (USD $)
14 July 2023	Korro Bio and Frequency Therapeutics Announce Merger Agreement	Undisclosed
17 July 2023	Novartis Acquires DTx Pharma for up to $1B	1,000,000,000
18 July 2023	Neurogene and Neoleukin Enter Merger Agreement	Undisclosed
24 July 2023	Quince Therapeutics to Acquire EryDel SpA	485,000,000
9 August 2023	Regeneron to Acquire Decibel Therapeutics	213,000,000
17 August 2023	Bruker to Acquire PhenomeX in All-Cash Transaction	108,000,000
30 August 2023	Serina Therapeutics to Become Publicly Traded via Business Combination with AgeX Therapeutics	Undisclosed
6 September 2023	Kriya Acquires Tramontane Therapeutics	Undisclosed
18 September 2023	Ligand's Pelican Subsidiary Merges with Primordial Genetics to Form Primrose Bio	Undisclosed

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

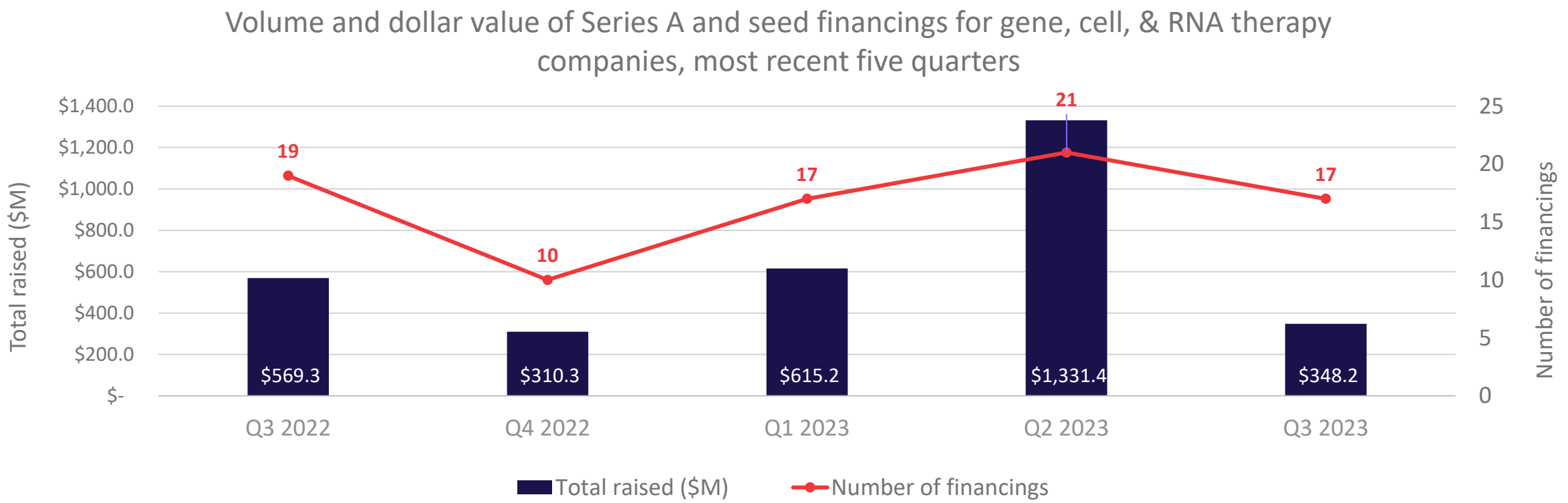
Start-up funding for gene, cell, and RNA therapy companies

Q3 2023

American Society of Gene + Cell Therapy

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

- At 17 transactions, the volume of seed and Series A financings was down 15% in Q3 2023 compared with Q2 2023
- Aggregate dollar value saw a much steeper decrease of 73%, declining to $348.2 million; Q2 2023 had featured five $100 million-plus financings, whereas Q3 2023 had none that met that criterion
- Q3 2023's figures also represented decreases in volume (-11%) and value (-39%) versus the same quarter one year ago



Source: Biomedtracker| Citeline, October 2023

American Society of Gene + Cell Therapy

Q3 2023 start-up financing for gene, cell, and RNA therapy companies (1/2)

Deal Date	Deal Title	Modality Type	Company Location	Academic Source	Potential Deal Value ($M)
12 July 2023	Tenpoint Therapeutics Launches with $70M Series A Financing	Engineered cell therapy	United Kingdom, Cambridge	Moorfields Eye Hospital; University College London Institute of Ophthalmology; Institut de la Vision in Paris; University of Washington	70
13 July 2023	CoJourney Raised $20M in Series A Financing	Contract manufacturing	United States, Pennsylvania, Philadelphia	Undisclosed	30
18 July 2023	Verismo Raises $17M in Second Pre-Series A Round	KIR-CAR-T	United States, Pennsylvania, Philadelphia	University of Pennsylvania	17
25 July 2023	NK:IO Raises £1.2M Seed Funding	NK cell therapy	United Kingdom, London	Imperial College London	1.5
26 July 2023	Kincell Bio Launches with $36M in Financing	Contract manufacturing	United States, North Carolina, Raleigh	n/a, spun out of Inceptor Bio's CMC, manufacturing, and quality organizations	36
03 August 2023	Amber Bio Launches with $26M in Seed Funding	Multi-kilobase gene editing	United States, California, San Francisco	Broad Institute; University of California, Berkeley	26
24 August 2023	ExcepGen Emerges from Stealth with $4M Funding Round	mRNA therapeutics	United States, California, San Francisco	University of Oxford	4
29 August 2023	Epigenic Therapeutics Raises $32M Series A Financing	Gene modulation therapy through epigenome regulation	China, Shanghai	Undisclosed	32
30 August 2023	Mercury Bio Raises $2M in Seed Round	RNA therapeutics delivery	United States, New Mexico, Santa Fe	Undisclosed	2

Source: Biomedtracker| Citeline, October 2023

Q3 2023 start-up financing for gene, cell, and RNA therapy companies (2/2)

Deal Date	Deal Title	Modality Type	Company Location	Academic Source	Potential Deal Value ($M)
01 September 2023	Innovac Therapeutics Completes $18M Series Pre-A Financing	mRNA vaccines	United States, Massachusetts, Cambridge	Undisclosed	18
06 September 2023	Rejuvenation Technologies Gets $10.6M in Seed Round	mRNA therapeutics	United States, California, Mountain View	Stanford University	10.6
07 September 2023	BlueWhale Bio Secures $18M in Seed Funding	Contract manufacturing	United States, Pennsylvania, Philadelphia	University of Pennsylvania	18
14 September 2023	AlveoGene Completes Seed Round	Gene therapy	United Kingdom, Oxford	Harrington Discovery Institute at University Hospitals; Old College Capital (University of Edinburgh's venture investment fund); UK Respiratory Gene Therapy Consortium	Undisclosed
18 September 2023	Broken String Biosciences Raises $15M Series A Financing	Technology for assessing off-target gene editing events	United Kingdom, Cambridge	Cardiff University	15
19 September 2023	AIRNA Raises $30M in Initial Financing	RNA editing therapeutics	United States, Massachusetts, Cambridge	Stanford University; University of Tübingen	30
21 September 2023	JURA Bio Brings in $16.1M in Seed Financing	Cell therapy	United States, Massachusetts, Cambridge	Massachusetts Institute of Technology	16.1
27 September 2023	CellFE Closes $22M Series A Financing	Microfluidics-based cell engineering	United States, California, Alameda	UC Berkeley; Georgia Tech	22

Source: Biomedtracker| Citeline, October 2023

Notable Q3 2023 start-up gene, cell, and RNA therapy companies

	Company details	Academic source	Financing type/amount raised	Lead investor(s)	Therapy areas of interest
tenpoint THERAPEUTICS	Vision-restoring engineered cell-based therapeutics and *in vivo* reprogramming	Moorfields Eye Hospital; University College London Institute of Ophthalmology; Institut de la Vision in Paris; University of Washington	Series A/$70M	F-Prime and Sofinnova Partners (founding investors)	Degenerative ocular diseases
kincell	Early-stage immune cell therapy CDMO	n/a, spun out of Inceptor Bio's CMC, manufacturing and quality organizations	Initial funding/$36M	Kineticos Ventures	n/a
EPIGENIC 益杰立科	Next-generation gene modulation therapies based on epigenome regulation and editing	Undisclosed	Series A/$32M	Qiming Venture Partners and OrbiMed	Chronic/prevalent diseases

Source: Biomedtracker| Citeline, October 2023

Upcoming catalysts

Q3 2023

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward-looking events) expected in Q4 2023

Therapy	Generic Name	Disease	Catalyst	Catalyst Date
Onpattro	patisiran	Transthyretin Amyloid Cardiomyopathy (ATTR-CM, Wild Type Or Hereditary)	PDUFA for sNDA/sBLA	6 Oct 2023 - 6 Oct 2023
AT-132	resamirigene bilparvovec	X-linked Myotubular Myopathy	Meeting with FDA	31 Jul 2023 - 31 Oct 2023
Exa-cel	exagamglogene autotemcel	Thalassemia	FDA Advisory Panel Meeting	1 Aug 2023 - 31 Oct 2023
OTL-200	atidarsagene autotemcel	Metachromatic Leukodystrophy	Approval (Europe) - Individual Country	23 Aug 2023 - 31 Oct 2023
Exa-cel	exagamglogene autotemcel	Sickle Cell Anemia	FDA Advisory Panel Meeting	1 Aug 2023 - 31 Oct 2023
DCR-PHXC	nedosiran	Hyperoxaluria	PDUFA/Approval Decision (US)	12 Sep 2023 - 31 Oct 2023
Oxlumo	lumasiran	Hyperoxaluria	Supplemental Approval (Europe)	18 Aug 2023 - 31 Oct 2023
Honedra	autologous CD34+ cells	Buerger's Disease	Approval Decision (Japan)	23 Aug 2023 - 30 Nov 2023
NurOwn	autologous bone marrow-derived mesenchymal stem cells	Amyotrophic Lateral Sclerosis (ALS)	PDUFA/Approval Decision (US)	8 Dec 2023 - 8 Dec 2023
Exa-cel	exagamglogene autotemcel	Sickle Cell Anemia	PDUFA/Approval Decision (US)	8 Dec 2023 - 8 Dec 2023
Lovo-cel	lovotibeglogene autotemcel	Sickle Cell Anemia	PDUFA/Approval Decision (US)	20 Dec 2023 - 20 Dec 2023
Eplontersen	eplontersen	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)	PDUFA/Approval Decision (US)	22 Dec 2023 - 22 Dec 2023
Exa-cel	exagamglogene autotemcel	Thalassemia; Sickle Cell Anemia	Approval Decision (UK)	27 Sep 2023 - 31 Dec 2023
Leqvio	inclisiran	Dyslipidemia / Hypercholesterolemia	Approval Decision (Japan)	1 Jul 2023 - 31 Dec 2023
QALSODY	tofersen	Amyotrophic Lateral Sclerosis (ALS)	CHMP (European Panel) Results	1 Oct 2023 - 31 Dec 2023
HPC-Cord Blood Therapy	umbilical cord blood mononuclear stem cell therapy	Ischemic Stroke	PDUFA/Approval Decision (US)	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 (European Panel) Results	1 Sep 2023 - 31 Mar 2024
Vyjuvek	beremagene geperpavec	Epidermolysis Bullosa	CHMP (European Panel) Results	1 Sep 2023 - 31 Mar 2024
Exa-cel	exagamglogene autotemcel	Thalassemia	CHMP (European Panel) Results	1 Sep 2023 - 31 Mar 2024
Exa-cel	exagamglogene autotemcel	Thalassemia; Sickle Cell Anemia	Approval Decision (Europe)	1 Nov 2023 - 31 May 2024
QALSODY	tofersen	Amyotrophic Lateral Sclerosis (ALS)	Approval Decision (Europe)	1 Nov 2023 - 31 May 2024

Source: Biomedtracker| Citeline, October 2023

Appendix

Methodology, sources, and glossary of key terms

Q3 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 (eg, 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 (eg, 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

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

Shardha Millington
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

American Society of Gene + Cell Therapy

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

Contact:
clientservices@citeline.com