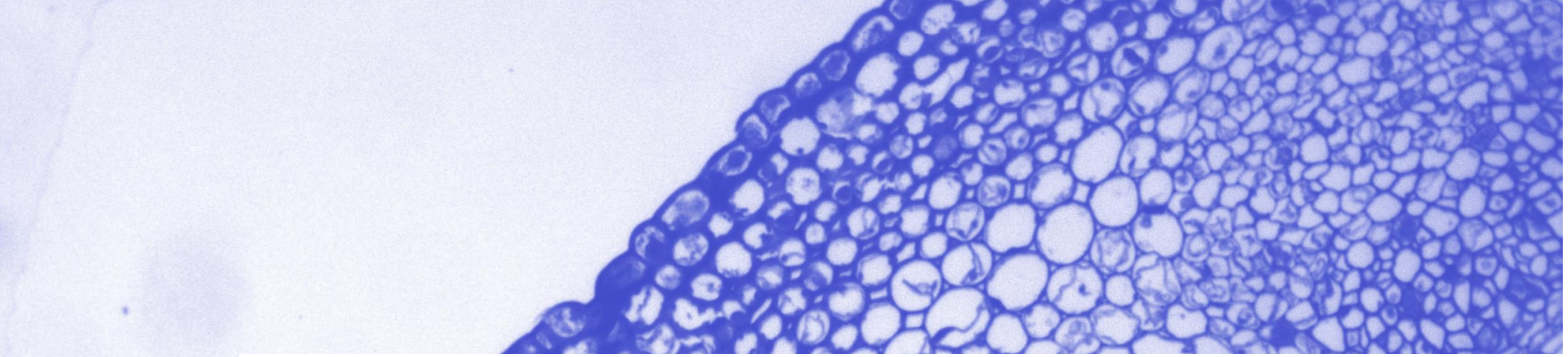
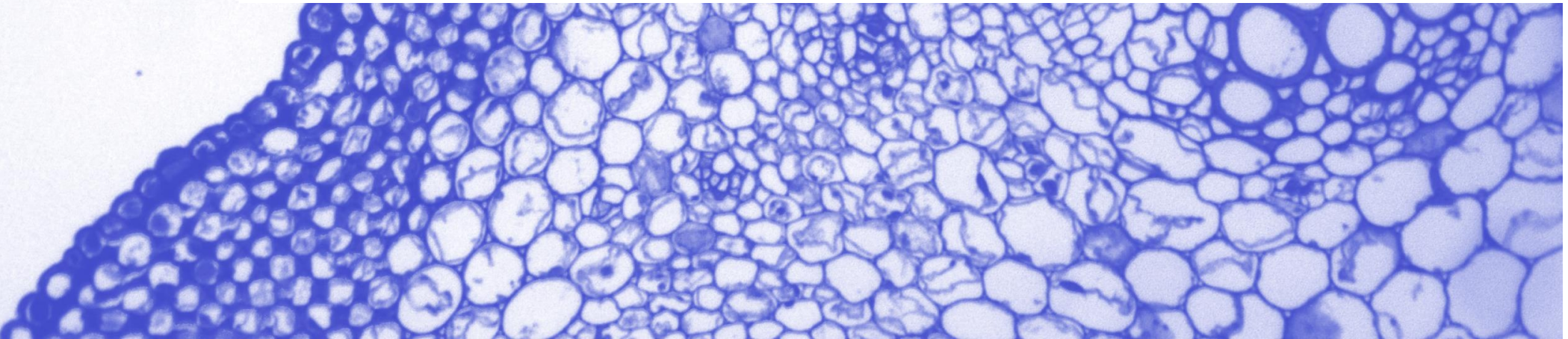


Gene, Cell, & RNA Therapy Landscape

Q2 2021 Quarterly Data Report

Q2 2021



American Society of Gene + Cell Therapy

Pharma Intelligence
Informa

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.

Informa Pharma Intelligence powers a full suite of analysis products – Datamonitor Healthcare™, Sitetrove™, Trialtrove™, Pharmaprojects™, Biomedtracker™, Scrip™, Pink Sheet™ and In Vivo™ – to deliver the data needed by the pharmaceutical and biomedical industry to make decisions and create real-world opportunities for growth.

With more than 400 analysts, journalists, and consultants keeping their fingers on the pulse of the industry, no key disease, clinical trial, drug approval or R&D project isn't covered through the breadth and depth of data available to customers. For more information visit pharmaintelligence.informa.com.

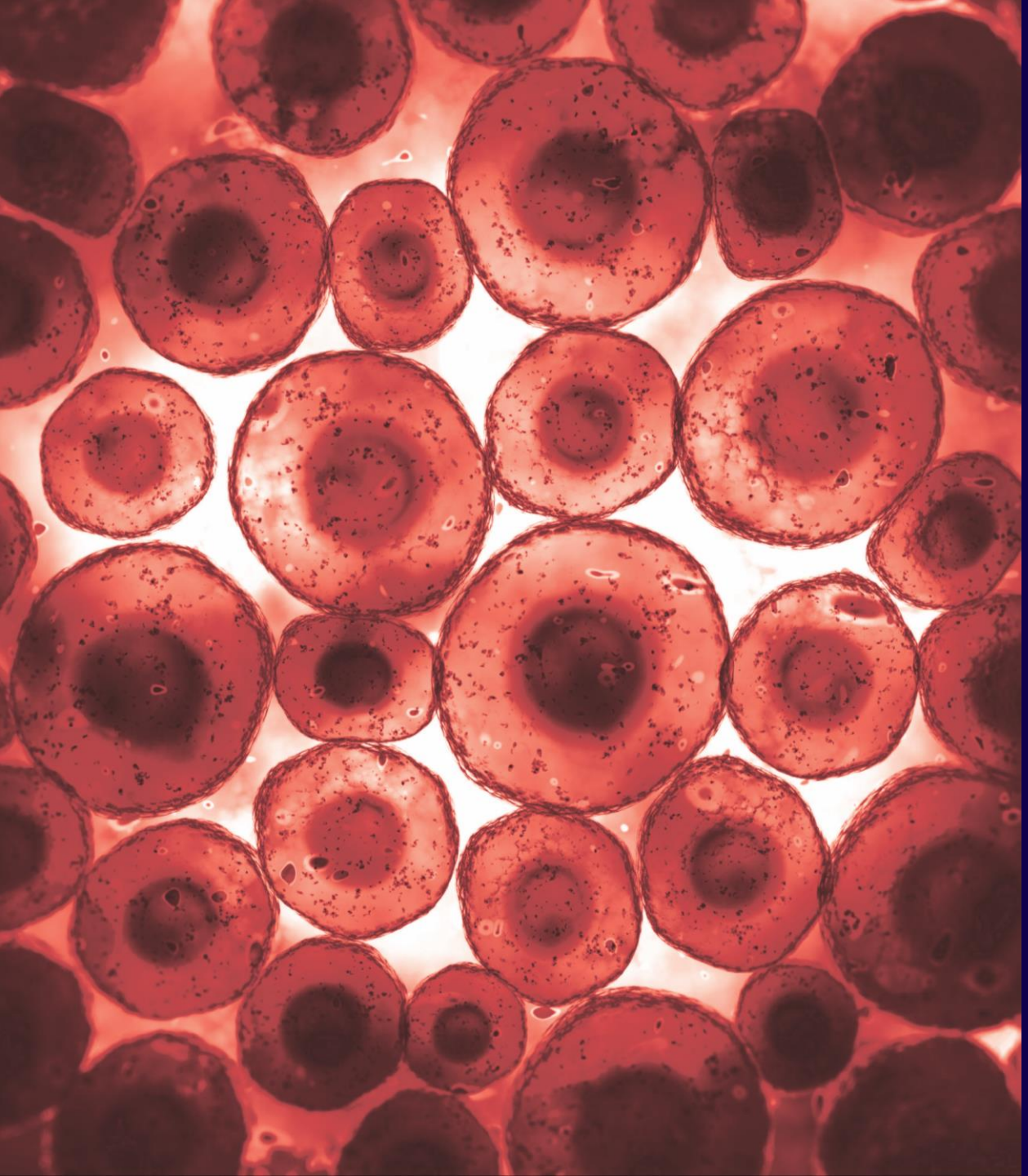


Table of contents

American Society of Gene + Cell Therapy

Introduction

ASGCT is pleased to provide the second in a quarterly report series with our data partner, Informa Pharma Intelligence. This series provides an iterative, detailed look at progress in the preclinical and clinical development landscape of gene and cell therapies globally, and should collectively tell a complete story of scientific achievement and clinical advancement.

Highlights in Q2 2021 include the approval of a new gene therapy in Japan, the expansion of gene therapy approvals to three new countries, continued growth in early-phase gene therapy development, and growth in studies using a herpes simplex virus.

The dollar value of start-up financing rebounded this quarter to an aggregate of $1.4 billion after a consecutive three-quarter decrease.

You will find new types of information in this quarter's report, as well, such as new clinical trials, key regulatory events, and listings of therapies in the preregistration phase this quarter, plus changes from Q2 2020 and noteworthy upcoming approval decisions.

ASGCT is excited to continue this series of landscape reports and to tell the story of this emerging technology as it translates to clinics and improves the lives of patients worldwide.

American Society of Gene + Cell Therapy

Key takeaways from Q2 2021

One new gene therapy was approved, and three previously-approved gene therapies were approved in additional countries/regions

- Delytact, a new genetically engineered oncolytic herpes simplex virus type 1, was approved in Japan for malignant glioma
- Yescarta gained approval in China, Zolgensma in South Korea, and Abecma in Canada

Oncology remains the most active therapeutic area of research (preclinical through preregistration)

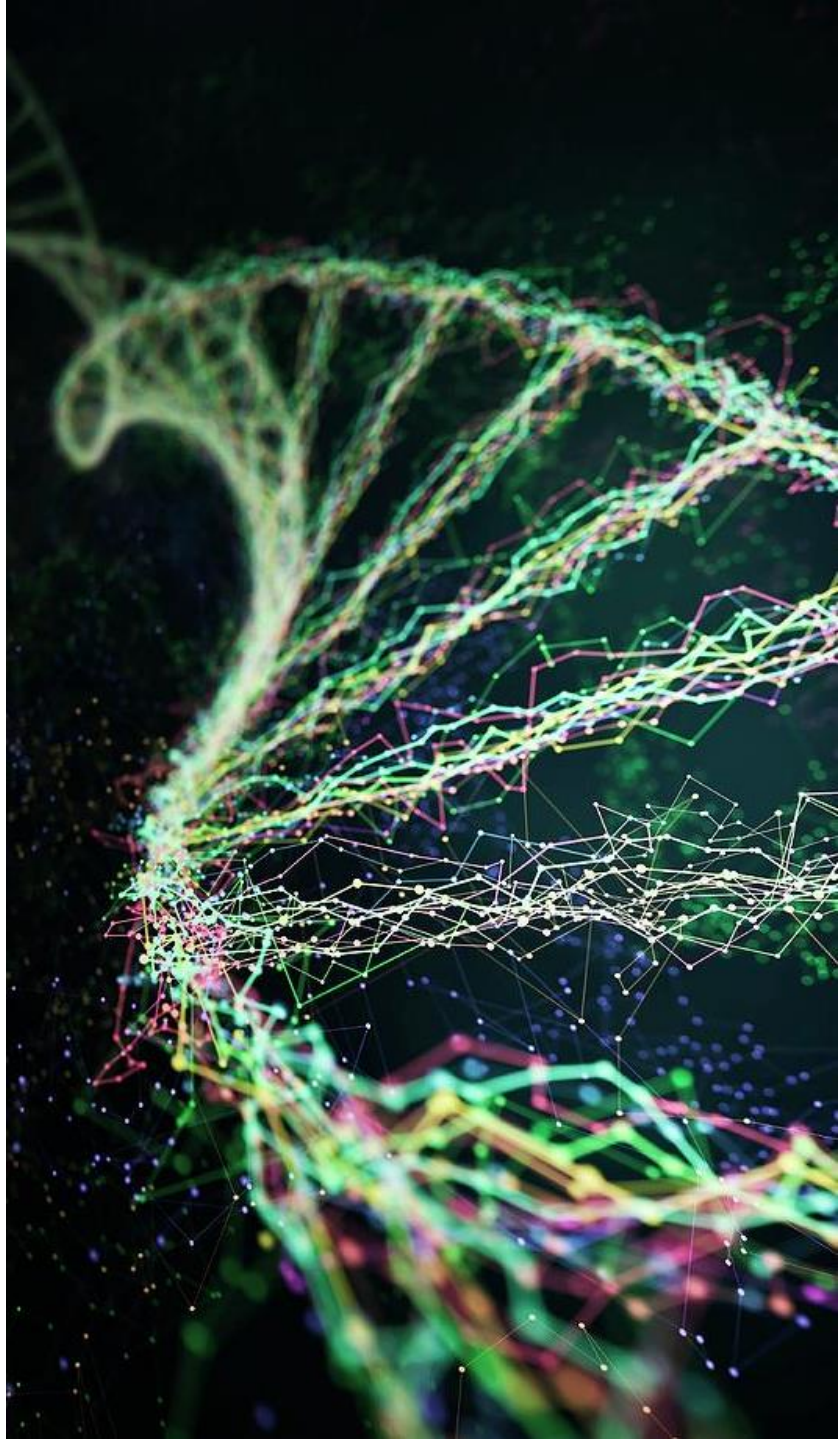
- More than 1,300 gene and cell therapy candidates are in development for oncology

Financing for start-ups showed a marked increase

- Seed and Series A financing volume nearly doubled in Q2, and the dollar value tripled, due to four $100M+ fundraisers

Overall dealmaking volume was down from Q1 but up from a year ago

- A total of 142 deals (financings, alliances, and acquisitions) were signed in Q2, down from 167 in Q1, but up from the 132 transactions in Q2 2020



Key highlights in Q2 2021

Q2 2021

American Society of Gene + Cell Therapy

Approved gene therapies as of Q2 2021

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, Australia	Amgen
Strimvelis	autologous CD34+ enriched cells	2016	Adenosine deaminase deficiency	EU	Orchard Therapeutics
Kymriah	tisagenlecleucel-t	2017	Acute lymphocytic leukemia; diffuse large B-cell lymphoma	US, EU, Japan, Australia, Canada, South Korea	Novartis
Luxturna	voretigene neparvovec	2017	Leber's congenital amaurosis; retinitis pigmentosa	US, EU, Australia, Canada	Spark Therapeutics (Roche)
Yescarta	axicabtagene ciloleucel	2017	Diffuse large B-cell lymphoma; non-Hodgkin's lymphoma; follicular lymphoma	US, EU, Japan, Canada, China	Kite Pharma (Gilead)
Collategene	beperminogene perplasmid	2019	Critical limb ischemia	Japan	AnGes
Zolgensma	onasemnogene abeparvovec	2019	Spinal muscular atrophy	US, EU, Japan, Australia, Canada, Brazil, Israel, Taiwan, South Korea	Novartis
Zynteglo	lentiviral beta-globin gene transfer	2019	Transfusion-dependent beta thalassemia	EU	bluebird bio
Tecartus	brexucabtagene autoleucel	2020	Mantel cell lymphoma	US, EU	Kite Pharma (Gilead)
Libmeldy	OTL-200	2020	Metachromatic Leukodystrophy	EU	Orchard Therapeutics
Breyanzi	lisocabtagene maraleucel	2021	Diffuse large B-cell lymphoma	US, Japan	Celgene (Bristol Myers Squibb)
Abecma	idecabtagene vicleucel	2021	Multiple myeloma	US, Canada	bluebird bio
Delytact	teserpaturev	2021	Malignant Glioma	Japan	Daiichi Sankyo

Source: Pharmaprojects | Informa, July 2021

Text highlighted in yellow represent new approvals during Q2 2021

American Society of Gene + Cell Therapy

Approved RNA therapies as of Q2 2021 (1/2)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Kynamro	mipomersen sodium	2013	Homozygous familial hypercholesterolaemia	US, Mexcio, Argentina, South Korea	Ionis Pharmaceuticals
Exondys 51	eteplirsen	2016	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Spinraza	nusinersen	2016	Muscular atrophy, spinal	US, EU, Canada, Japan, Brazil, Switzerland, Australia, South Korea, China, Argentina, Colombia, Taiwan,	Ionis Pharmaceuticals
Tegsedi	inotersen	2018	Amyloidosis, transthyretin-related hereditary	EU, Canada, US, Brazil	Ionis Pharmaceuticals
Onpattro	patisiran	2018	Amyloidosis, transthyretin-related hereditary	US, EU, Japan, Canada, Switzerland, Brazil, Taiwan	Alnylam
Vyondys 53	golodirsen	2019	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Waylivra	volanesorsen	2019	Hypertriglyceridaemia; Lipoprotein lipase deficiency	EU, UK	Ionis Pharmaceuticals
Comirnaty	tozinameran	2020	Infection, coronavirus, novel coronavirus prophylaxis	UK, Bahrain, Israel, Canada, US, Mexico, Kuwait, Singapore, Saudi Arabia, Chile, Switzerland, EU, Colombia, Philippines, Australia, Hong Kong, Peru, South Korea, New Zealand, Japan, Brazil, Sri Lanka, Vietnam, Thailand, Oman,	BioNTech

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

Source: Pharmaprojects | Informa, July 2021

Text highlighted in yellow represent new approvals during Q2 2021

American Society of Gene + Cell Therapy

Approved RNA therapies as of Q2 2021 (2/2)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
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	Moderna Therapeutics
Givlaari	givosiran	2020	Porphyria	US, EU, Canada, Switzerland	Alnylam
Oxlumo	lumasiran	2020	Hyperoxaluria	EU, US	Alnylam
Ampligen	rintatolimod	2020	Chronic fatigue syndrome	Argentina	AIM ImmunoTech
Viltepso	viltolarsen	2020	Dystrophy, Duchenne muscular	US, Japan	NS Pharma
Leqvio	inclisiran	2020	Atherosclerosis; Heterozygous familial hypercholesterolaemia; Hypercholesterolaemia; Homozygous familial hypercholesterolaemia	EU, UK	Alnylam
Amondys 45	casimersen	2021	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics

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

Source: Pharmaprojects | Informa, July 2021

Text highlighted in yellow represent new approvals during Q2 2021

American Society of Gene + Cell Therapy

Key highlights in Q2 2021

Brand Name	Generic Drug Name	Molecule type	Disease	Event Type	Event Date
Zynteglo	betibeglogene autotemcel	Viral Gene Therapy	Transfusion-dependent β-thalassemia	Withdrawal from German Market	Apr 20, 2021
Delytact	teserpaturev	Viral	Malignant glioma	Approval (Japan)	Jun 11, 2021
Roctavian	valoctocogene roxaparvovec	Viral Gene Therapy	Hemophilia A	MAA Submission (Europe)	Jun 28, 2021
N/A	ciltacabtagene autoleucel	Cellular*	Multiple myeloma	MAA Submission (Europe)	Apr 30, 2021
Abecma	idecabtagene vicleucel	Cellular*	Multiple myeloma	CHMP (European Panel) Results (Positive)	Jun 24, 2021
Skysona	elivaldogene autotemcel	Viral Gene Therapy	Cerebral adrenoleukodystrophy	CHMP (European Panel) Results (Positive)	May 20, 2021
N/A	ALLO-715	Cellular*	Multiple myeloma	Regenerative Medicine Advanced Therapy (RMAT) Designation	Apr 21, 2021
N/A	AK-OTOF	Viral Gene Therapy	Hearing loss	Rare Pediatric Disease (RPD) Designation	Apr 13, 2021
N/A	BBP-631	Viral Gene Therapy	Congenital Adrenal Hyperplasia (CAH)	Rare Pediatric Disease (RPD) Designation	May 14, 2021
N/A	LX-2006	Viral Gene Therapy	Friedreich's Ataxia	Rare Pediatric Disease (RPD) Designation	Jun 30, 2021

*These are genetically modified cell therapies (CAR-T therapies)

Source: Biomedtracker | Informa, July 2021

Gene therapy pipeline

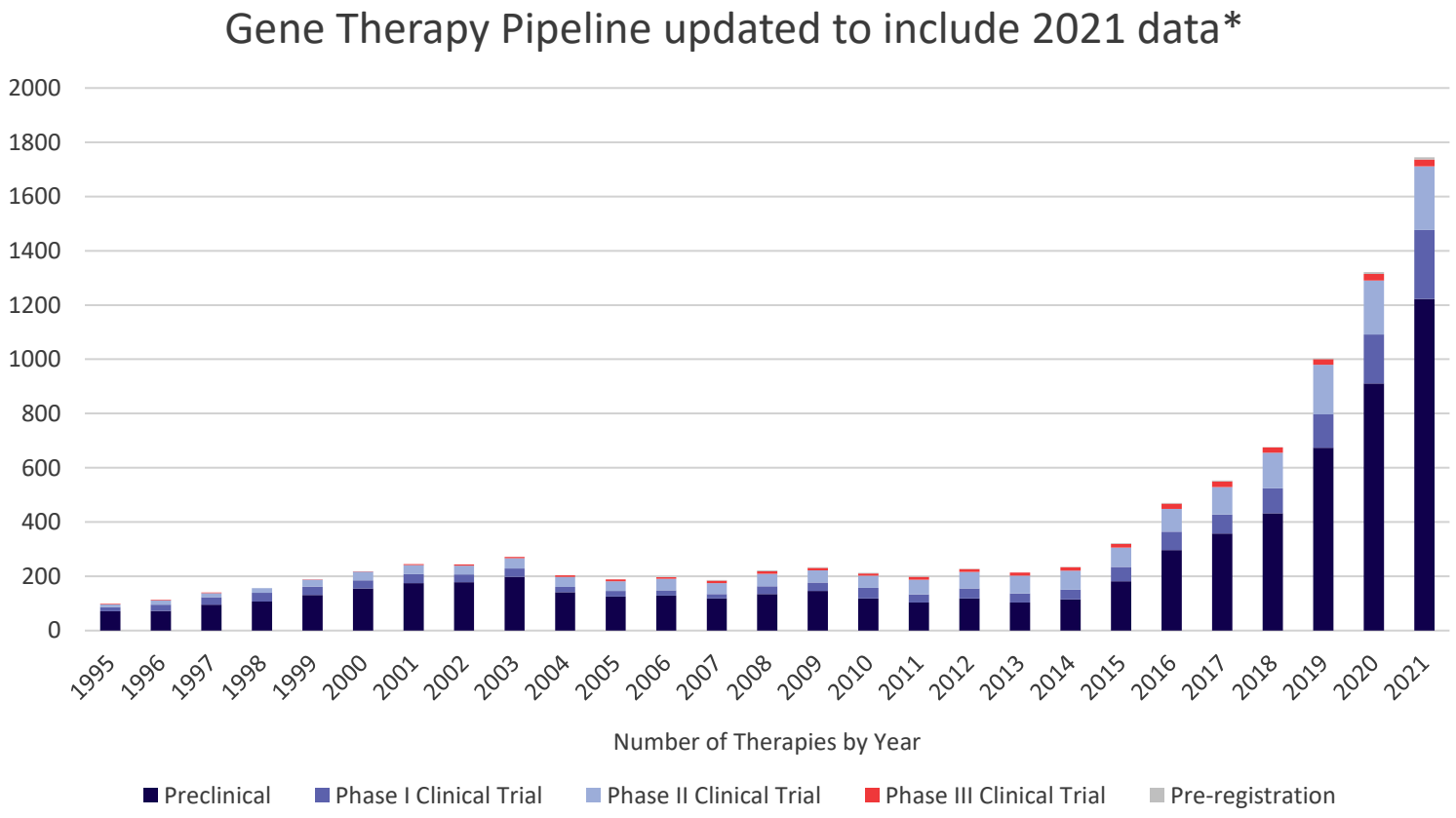
Gene therapy and genetically modified cell therapies

Q2 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline

- In May 2021, there were 1,745 therapies in development from preclinical through preregistration.
- Preclinical therapies account for the majority of the pipeline with 1,223 therapies in preclinical studies. This accounts for 70% of therapies in clinical development.



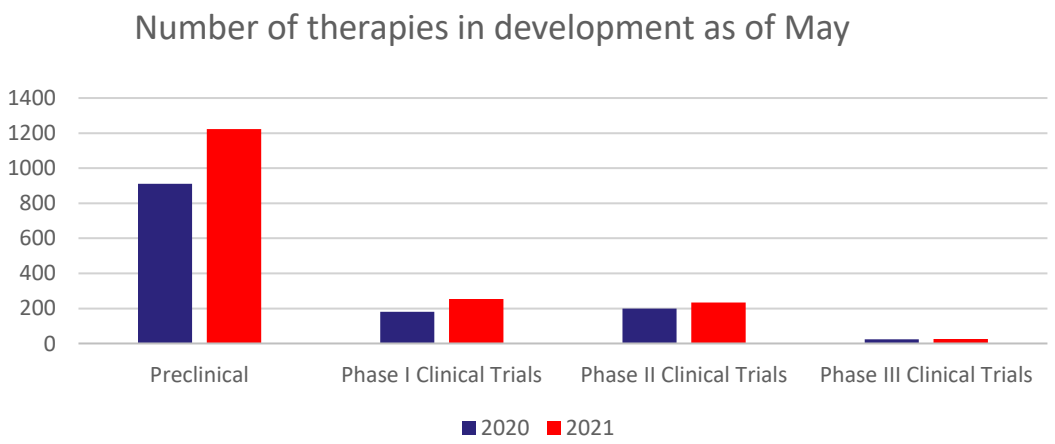
*These snapshots are taken every May to allow for year-on-year comparisons

Source: Pharmaprojects | Informa, May 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline – 2020 vs 2021

- When comparing preclinical development between 2020 and 2021, there was a significant increase in the number of therapies in preclinical development with 911 in 2020 and 1,223 therapies in 2021
- There was a significant increase in Phase I clinical trials in 2021 (from 180 therapies in 2020 vs 254 therapies in 2021)



Global Status as of May	Number of Therapies	
	2020	2021
Preclinical	911	1,223
Phase I Clinical Trial	180	254
Phase II Clinical Trial	199	234
Phase III Clinical Trial	24	26
Pre-registration	7	8
Total number of therapies (preclinical to pre-registration)	**1,321**	**1,745**
Total number of therapies in the clinic	**410**	**522**

Source: Pharmaprojects | Informa, May 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline – Q1 vs Q2 2021

- Over the course of the second quarter, the largest growth was a 9 percent increase in the number of therapies in preclinical development
- The number of Phase III therapies remained the same, and there is one less therapy in pre-registration with the approval of Delytact
- Therapies currently in preregistration:
  - valoctocogene roxaparvovec (Biomarin)
  - lenadogene nolparvovec (Genethon, GenSight Biologics)
  - elivaldogene autotemcel (Bluebird Bio)
  - nadofaragene firadenovec (Ferring, FKD Therapeutics, Trizell)
  - relmacabtagene autoleucel (JW Therapeutics)
  - ciltacabtagene autoleucel (Johnson & Johnson)
  - eladocagene exuparvovec (PTC Therapeutics)

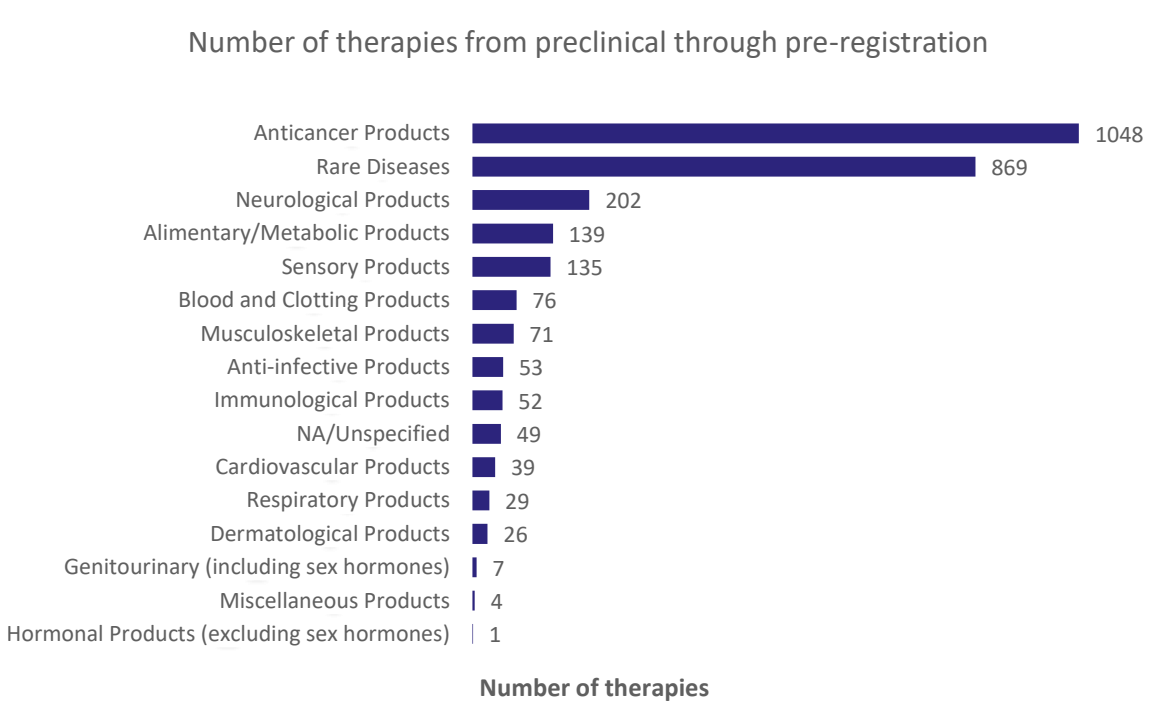
Global Status	April 2021	July 2021
Preclinical	1,190	1,296
Phase I Clinical Trials	225	269
Phase II Clinical Trials	231	236
Phase III Clinical Trials	27	27
Pre-registration	8	7
Total	**1,711**	**1,835**

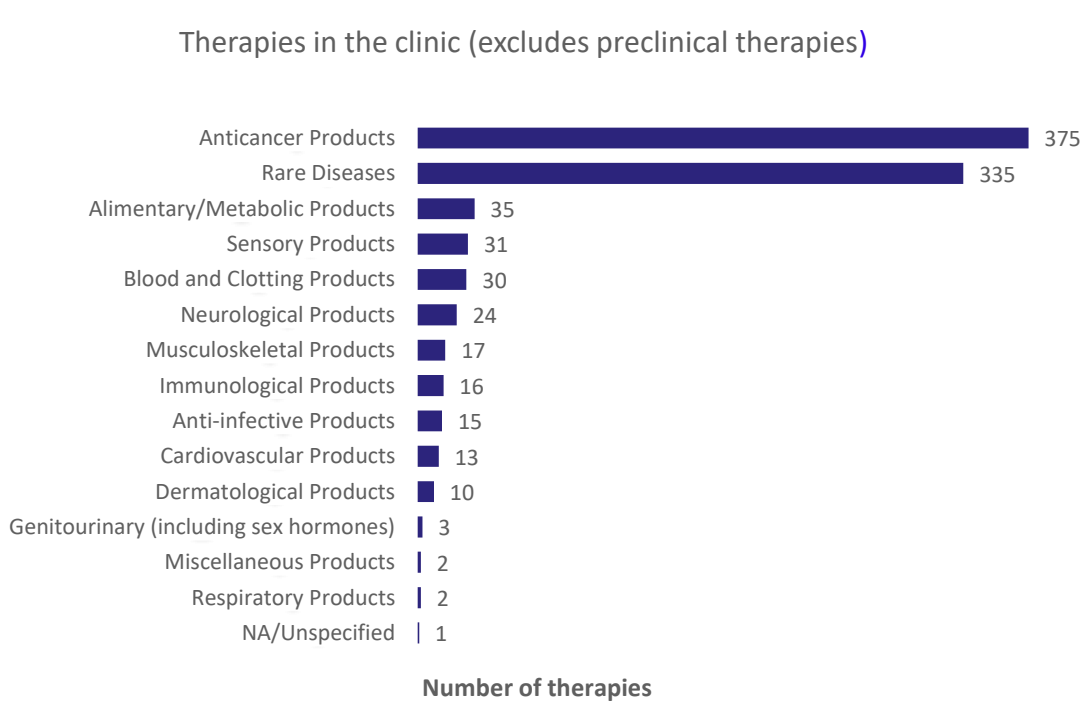
Source: Pharmaprojects | Informa, May 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: Most commonly targeted therapeutic areas

- The top 2 therapeutic areas targeted by gene therapies from preclinical through pre-registration are oncology and rare diseases. Rare diseases includes oncology rare diseases
- The focus on oncology and rare diseases remains for therapies in clinical development



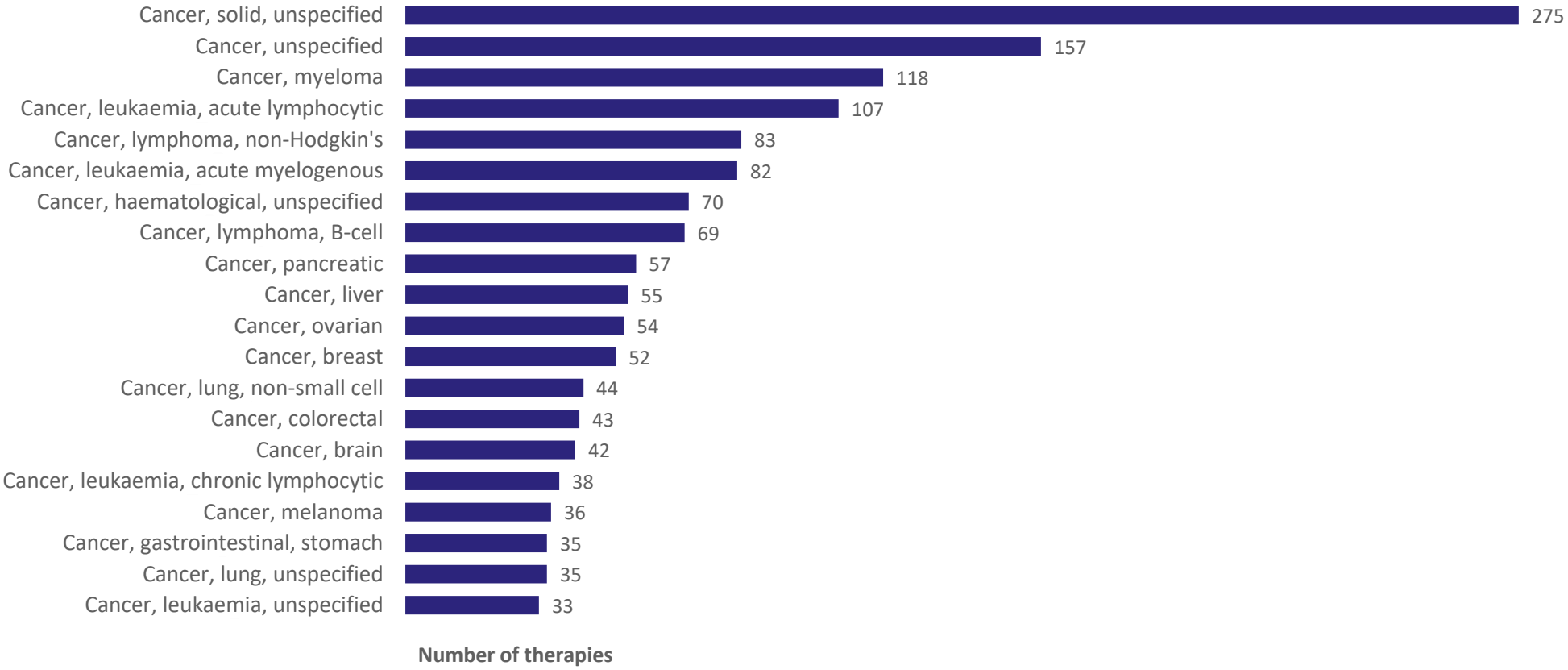


Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common oncology diseases targeted

- From preclinical through pre-registration, 1,048 therapies are being developed for oncology
- Multiple myeloma and acute lymphocytic leukemia (ALL) remain the top two specified oncology indications
- Non-Hodgkin's lymphoma is now the third most common indication (acute myelogenous leukemia in Q1)

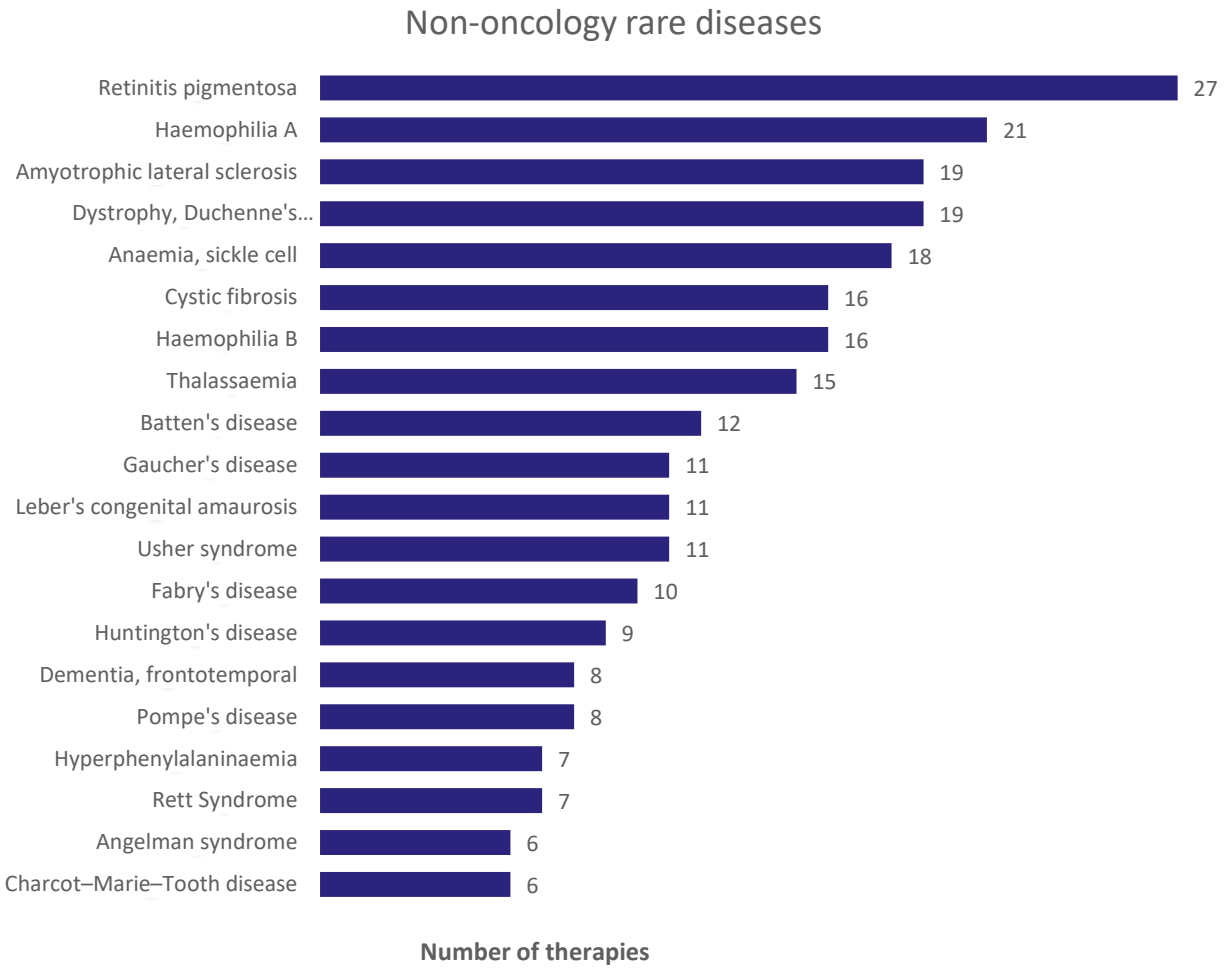


Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common non-oncology rare diseases targeted

- There are 869 therapies in development for rare diseases from preclinical through pre-registration. This number includes oncology rare diseases. There are 435 therapies for non-oncology rare diseases in development
- Retinitis pigmentosa, Hemophilia A, amyotrophic lateral sclerosis (ALS), Duchenne’s muscular dystrophy (DMD), and sickle cell anemia make up the top 5 non-oncology rare diseases most targeted by gene therapies

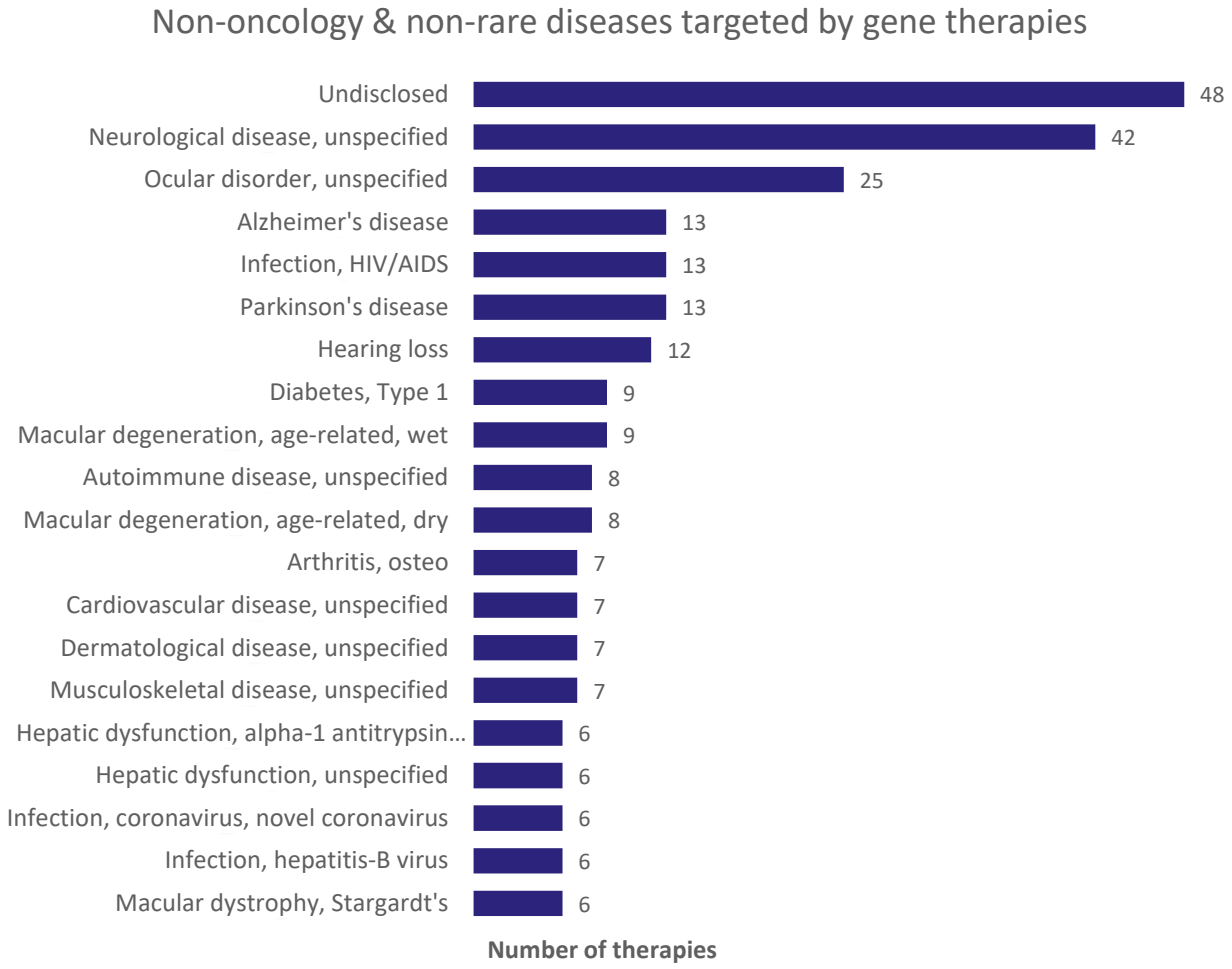


Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common additional diseases targeted

- From preclinical through pre-registration, there are 356 therapies that are in development for diseases outside of oncology or rare diseases
- Of diseases that are not oncology or rare diseases that are disclosed: neurological diseases, ocular disorders, Alzheimer's disease, HIV/AIDs, and Parkinson's Disease make up the 5 diseases most targeted by gene therapies



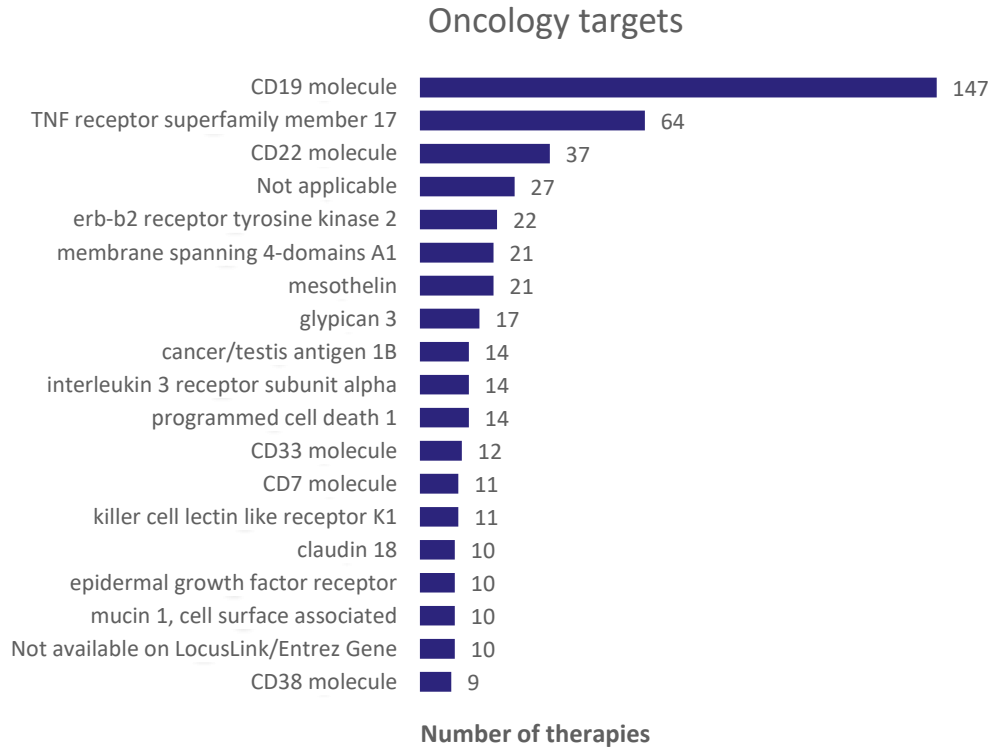
Source: Pharmaprojects | Informa, July 2021

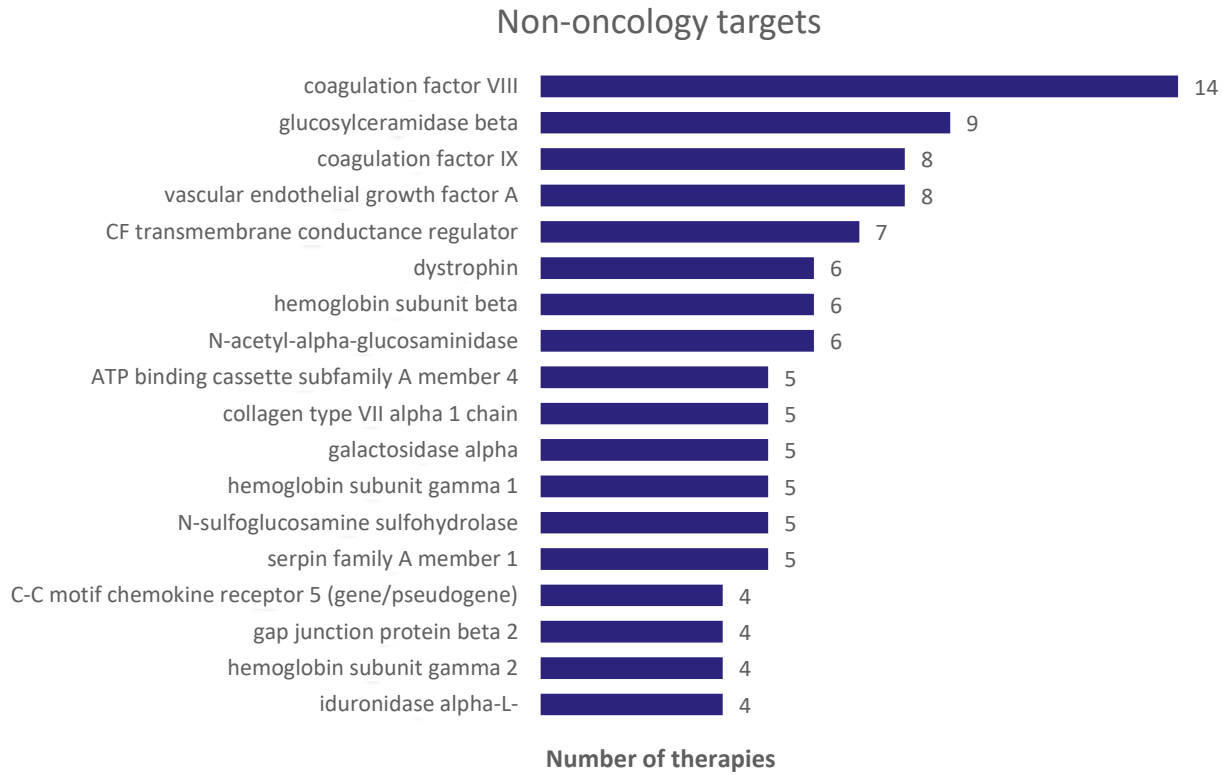
American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common targets

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

- CD19 and B-cell maturation antigen (BCMA), also known as TNF receptor superfamily member 17, remain the most common targets for oncology indications
- Coagulation factor VIII is the most common target for non-oncology indications



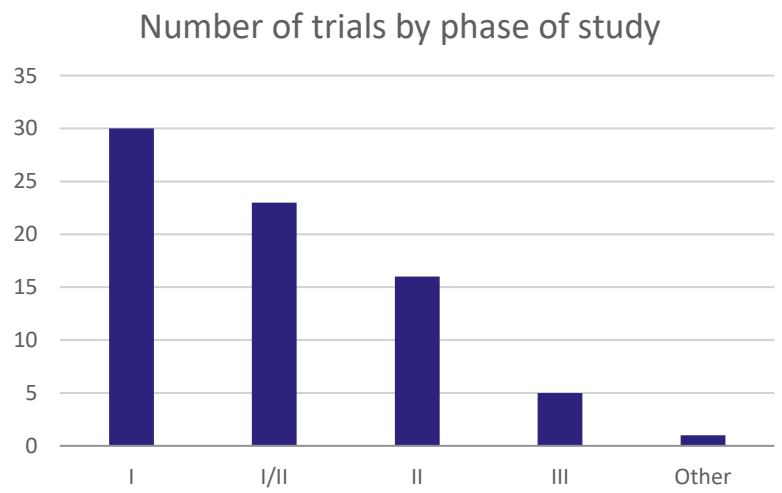


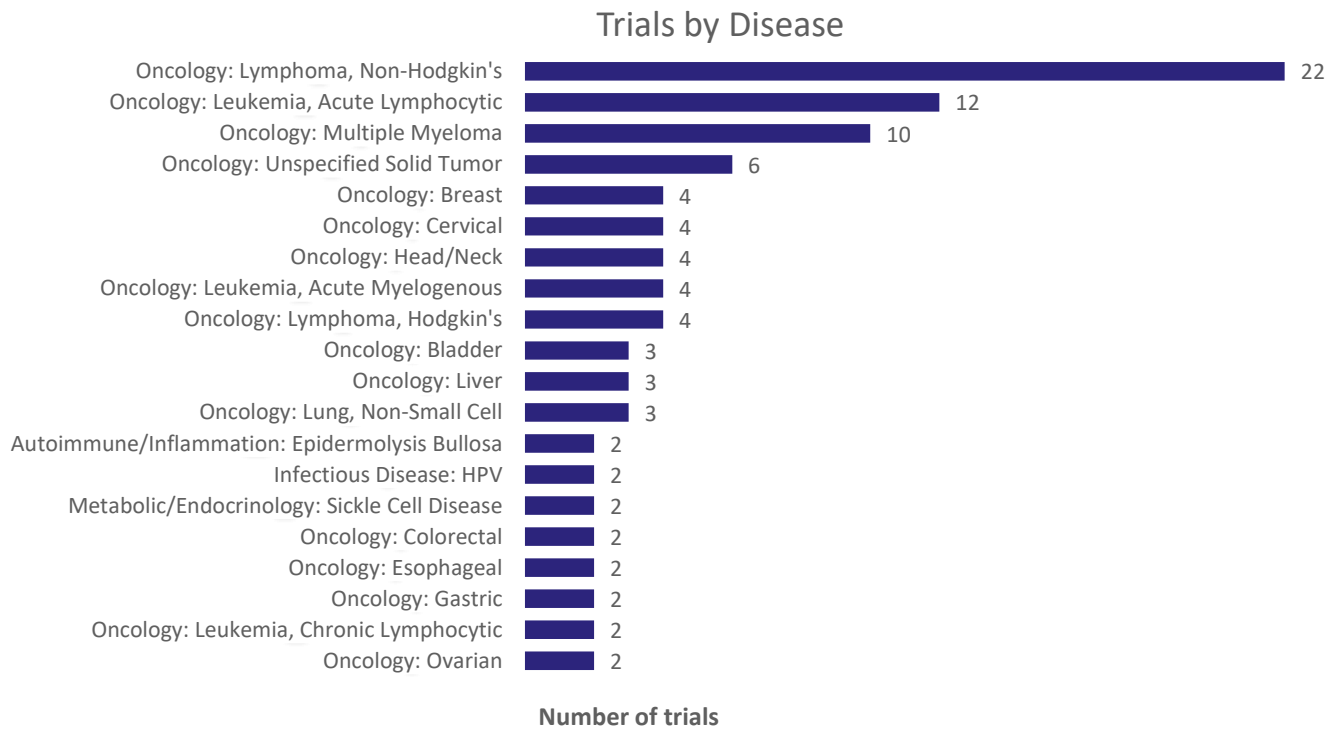
Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

Gene therapy clinical trial activity in 2021

- A total of 75 clinical trials were initiated in 2021 so far
- The top 10 diseases for trial starts in 2021 were all for oncology with the top 3 being the blood cancers non-Hodgkin's lymphoma (NHL), acute lymphocytic leukemia (ALL), and multiple myeloma



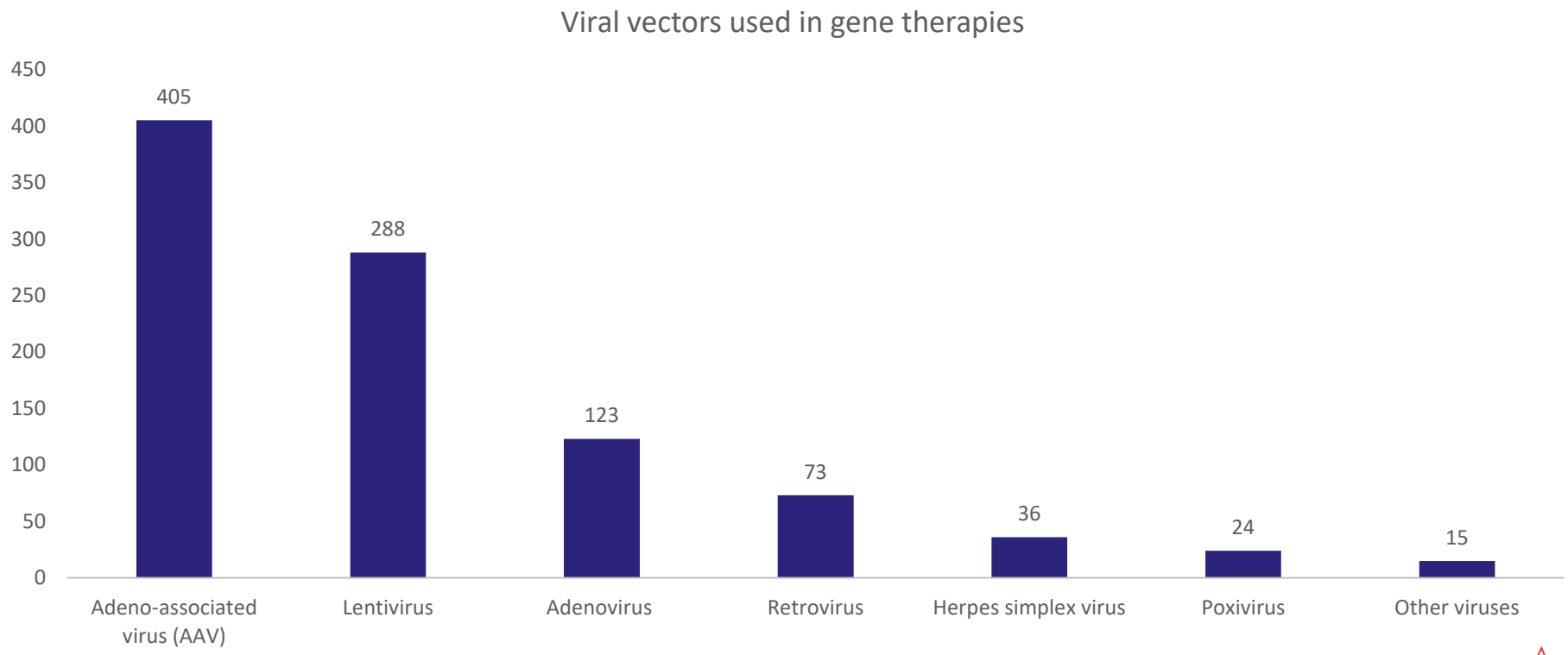


Source: Trialtrove | Informa, July 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: Most commonly used vectors

- 89% of gene therapies in development use viral vectors for delivery
- Adeno-associated virus (AAV) and lentivirus remain most common viral vectors used in development
- The largest quarterly growth: 33 percent increase in studies using a herpes simplex virus

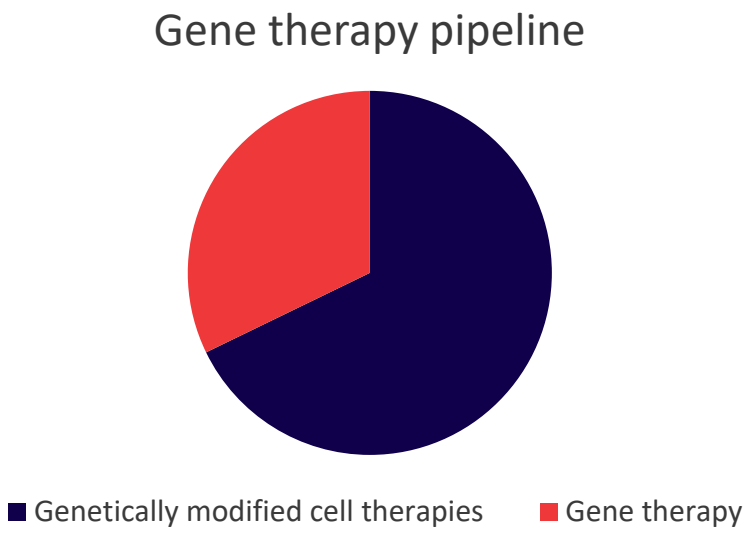


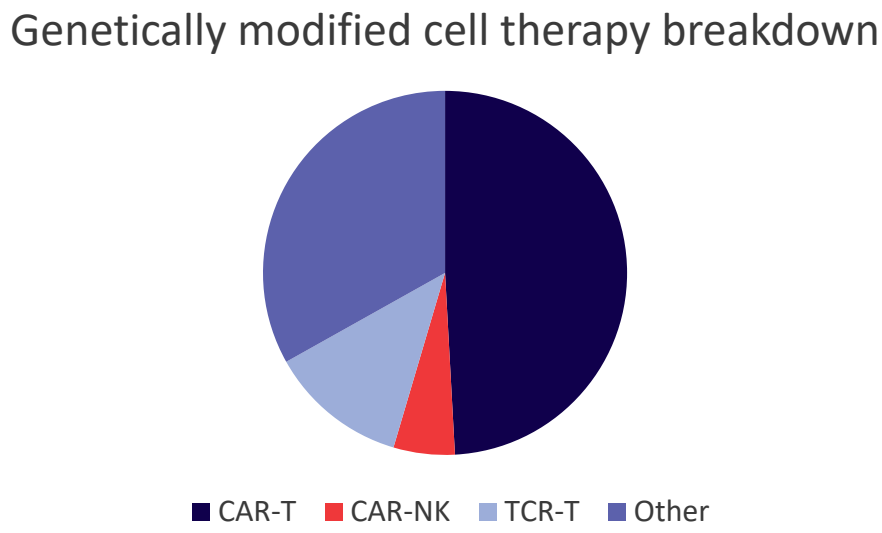
Source: Cell and Gene Therapy dashboard | Informa, July 2021

American Society of Gene + Cell Therapy

Gene therapy breakdown: CAR Ts dominate pipeline

- Of the gene therapies in development, 68% are genetically modified cell therapies
- Chimeric Antigen Receptor T cells (CAR Ts) represent 49% while T cell receptor T cells (TCR Ts) account for 12% of the genetically modified cell therapies in development





Source: Cell and Gene Therapy dashboard | Informa, July 2021

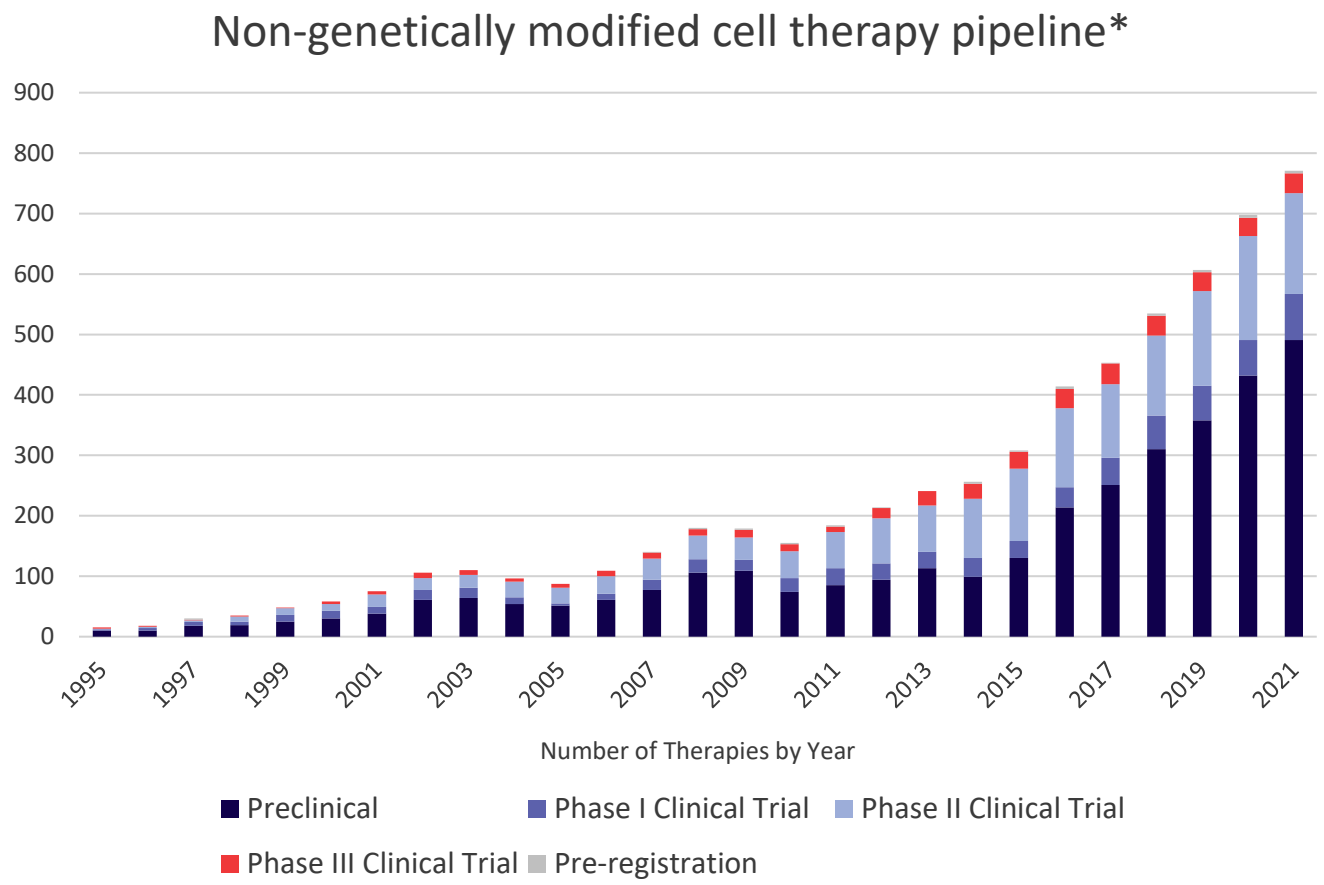
Non-genetically modified cell therapy pipeline

Q2 2021

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline

- In May 2021, there were 771 therapies in development (preclinical through pre-registration):
  - 64% of candidates are in preclinical development
  - There were 33 therapies in Phase III clinical studies
  - There are 4 therapies in pre-registration (undergoing regulatory review):
    - Gliovac (Epitopoietic Research)
    - Astrostem (K-StemCell/Nature Cell)
    - Donislecel (CellTrans)
    - RVT-802 (Enzyvant Sciences/Sinovant Sciences)



*These are snapshots taken every May to allow for year-on-year comparisons

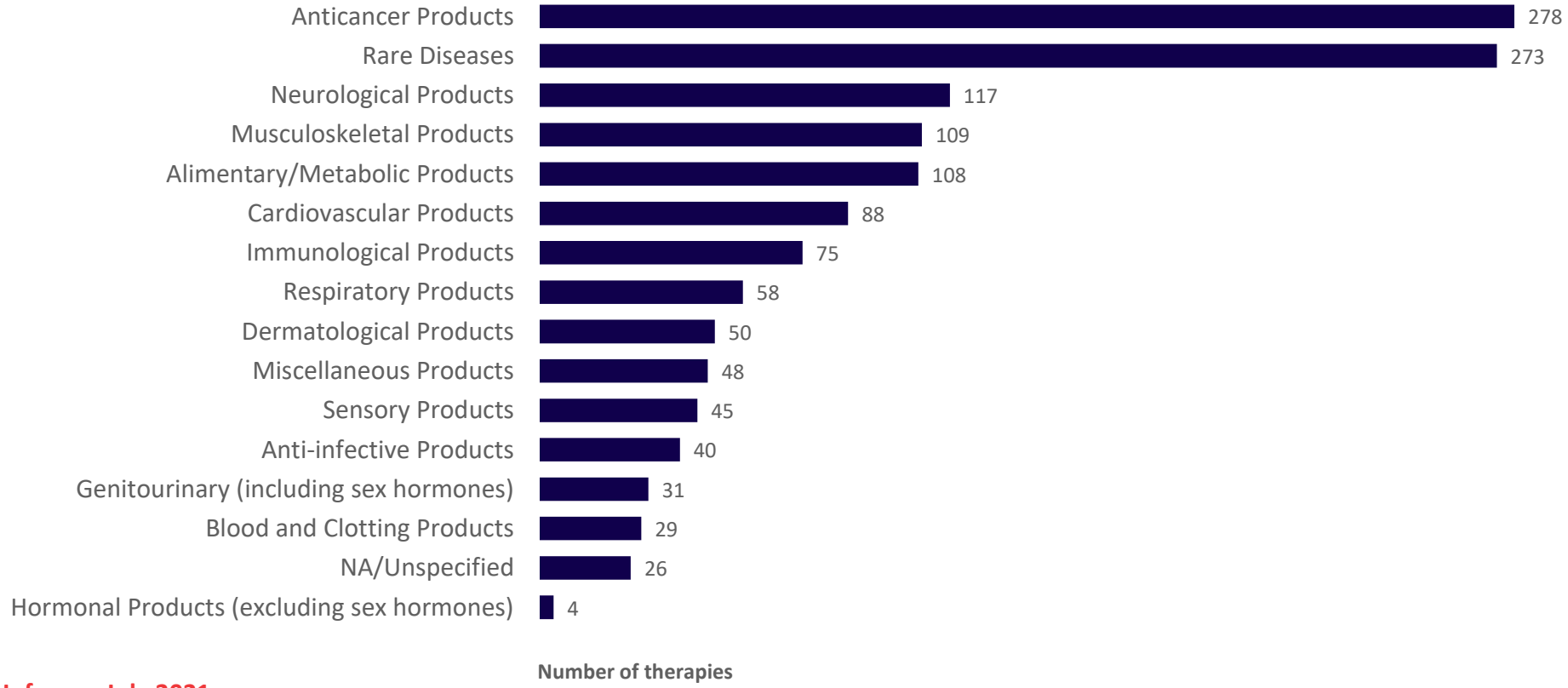
Source: Pharmaprojects | Informa, May 2021

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):

- Similar to gene therapy, oncology and rare diseases are the most targeted therapeutic areas for non-genetically modified cell therapies (rare diseases includes oncology rare diseases).

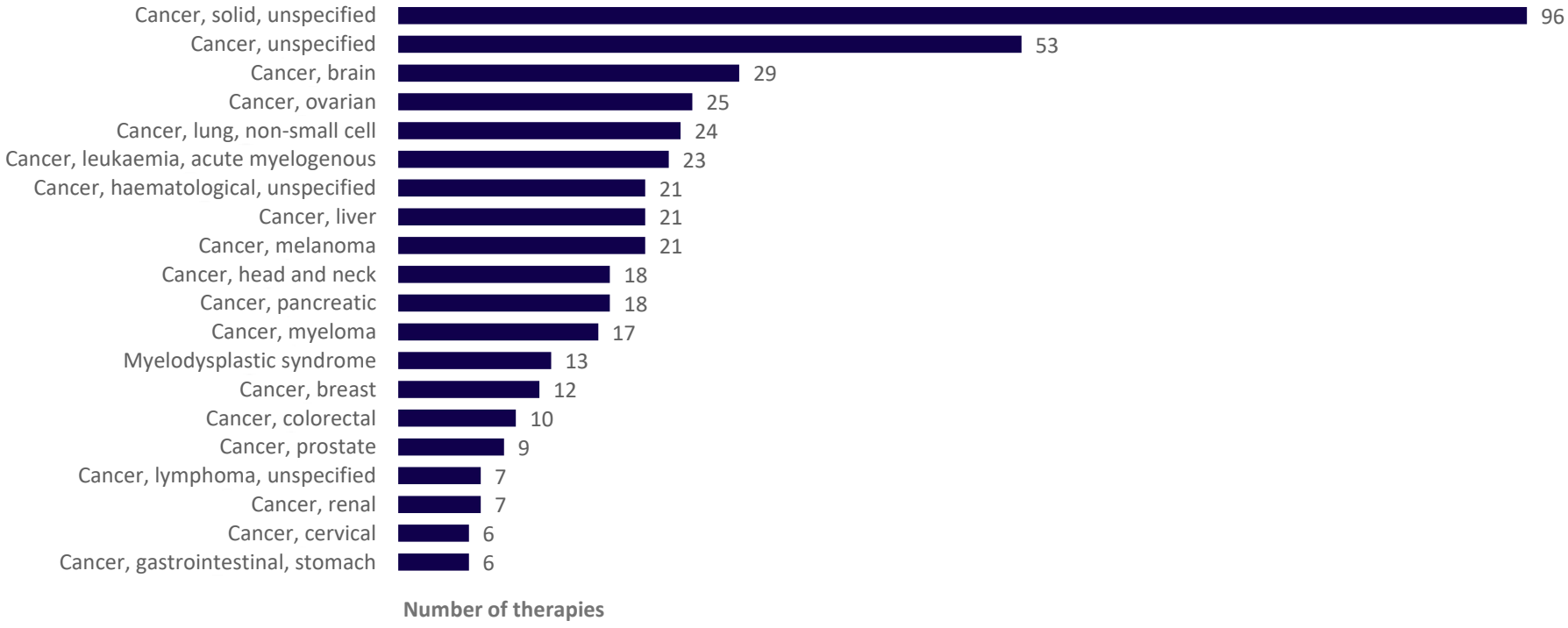


Source: Pharmaprojects | Informa, July 2021

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

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

- Of the diseases in which indications are specified, the top three indications are brain cancer, ovarian cancer and non-small cell lung cancer



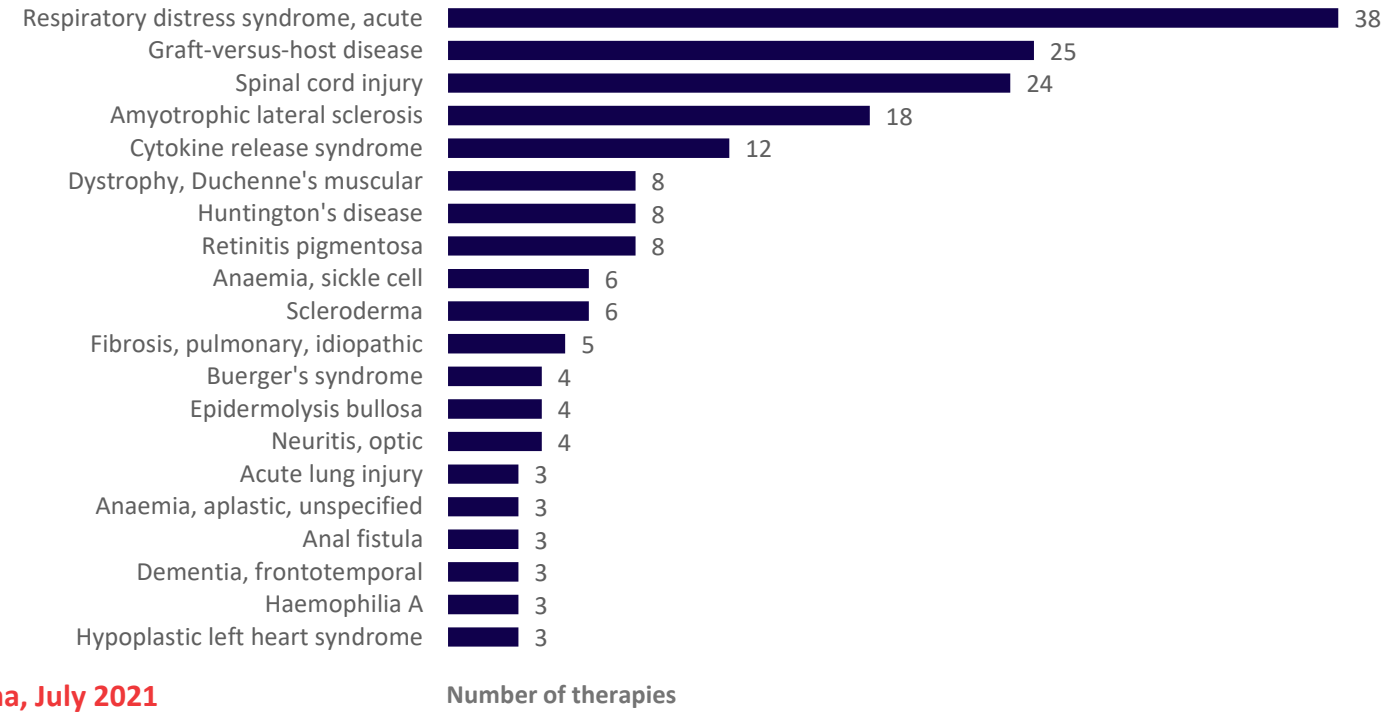
Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

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

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

- Rare diseases: second most targeted therapeutic category for non-genetically modified cell therapies
- Of the non-oncology rare diseases being targeted, the top 3 are respiratory distress syndrome (ARDS), graft-versus-host disease (GVHD), and spinal cord injury

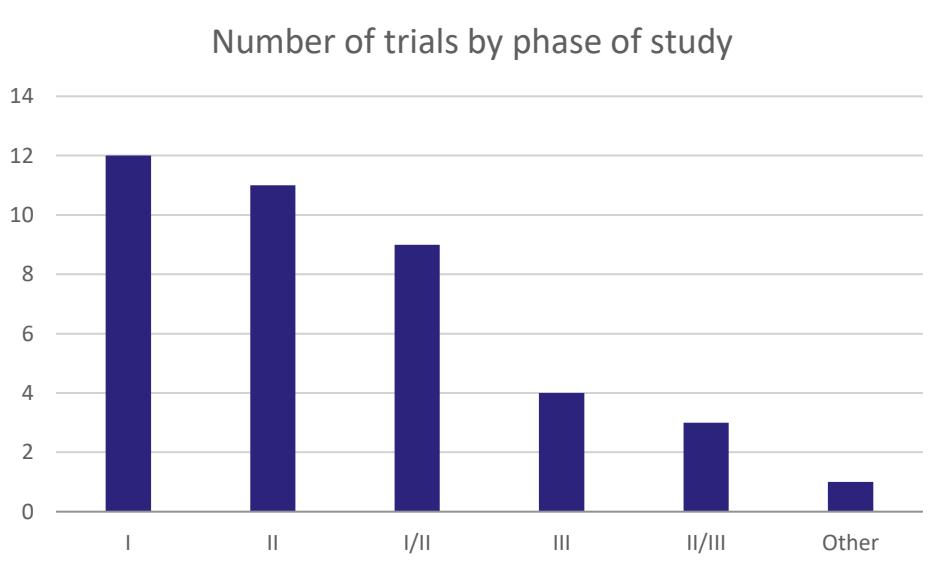


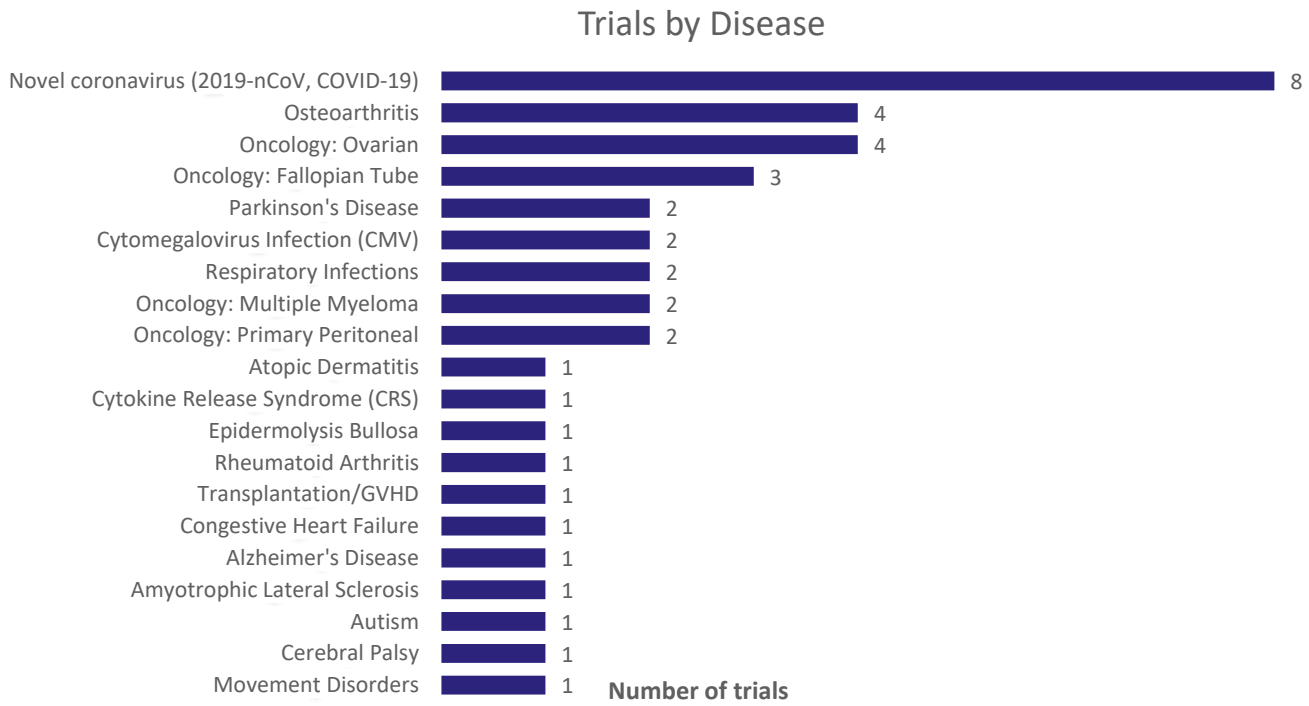
Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy trial activity in 2021

- A total of 40 clinical trials were initiated in 2021 so far
- The top four diseases for trial starts in 2021 were for COVID-19 infections, osteoarthritis, ovarian cancer, fallopian tube cancer and Parkinson's disease





Source: Trialtrove | Informa, July 2021

American Society of Gene + Cell Therapy

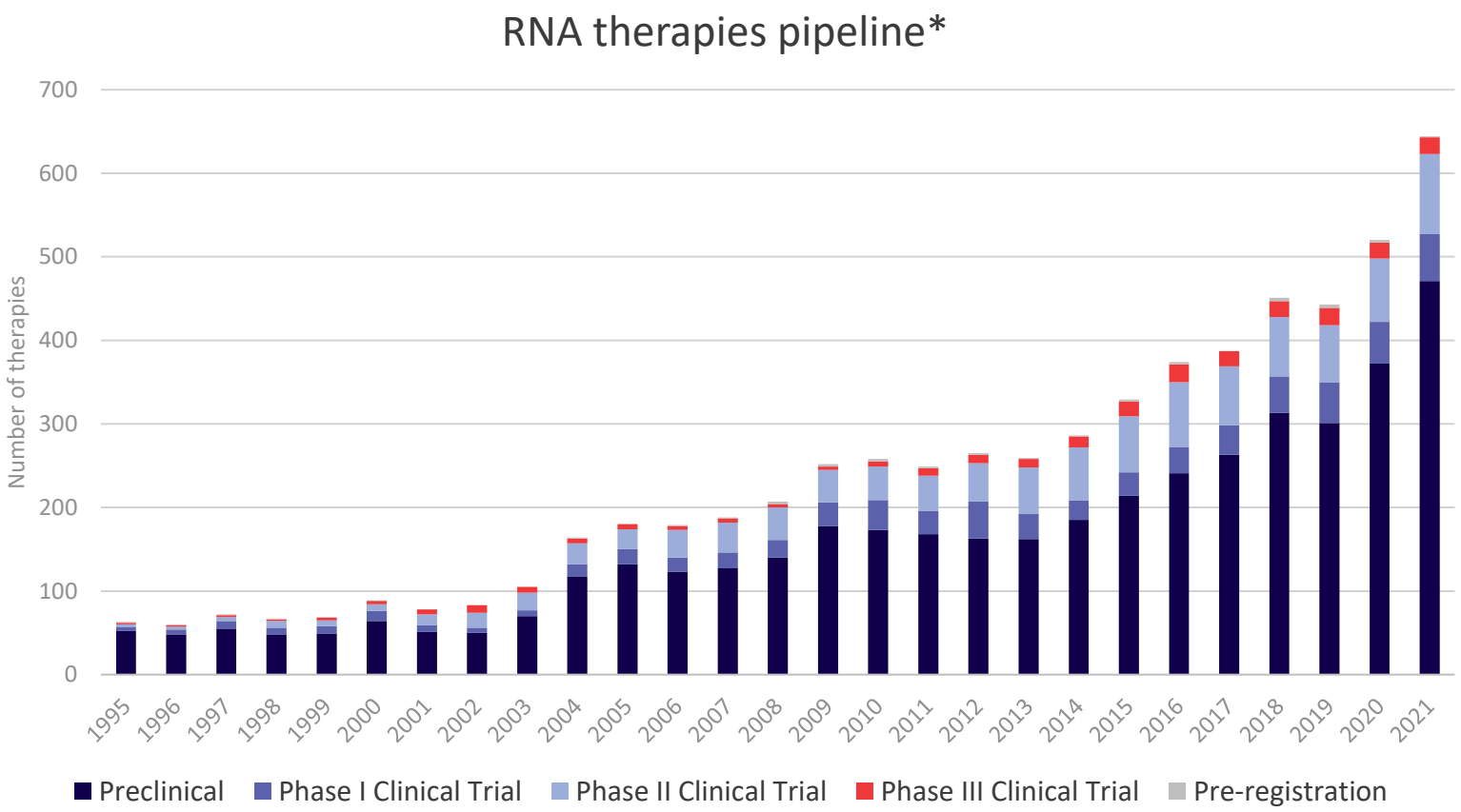
RNA therapy pipeline

Q2 2021

American Society of Gene + Cell Therapy

RNA therapies pipeline

- In 2021:
  - More than 600 therapies were in development (from preclinical to pre-registration stage), with 73% of therapies in preclinical development
  - 20 therapies were in Phase III clinical studies
  - 1 therapy in pre-registration (vutrisiran, Alnylam)



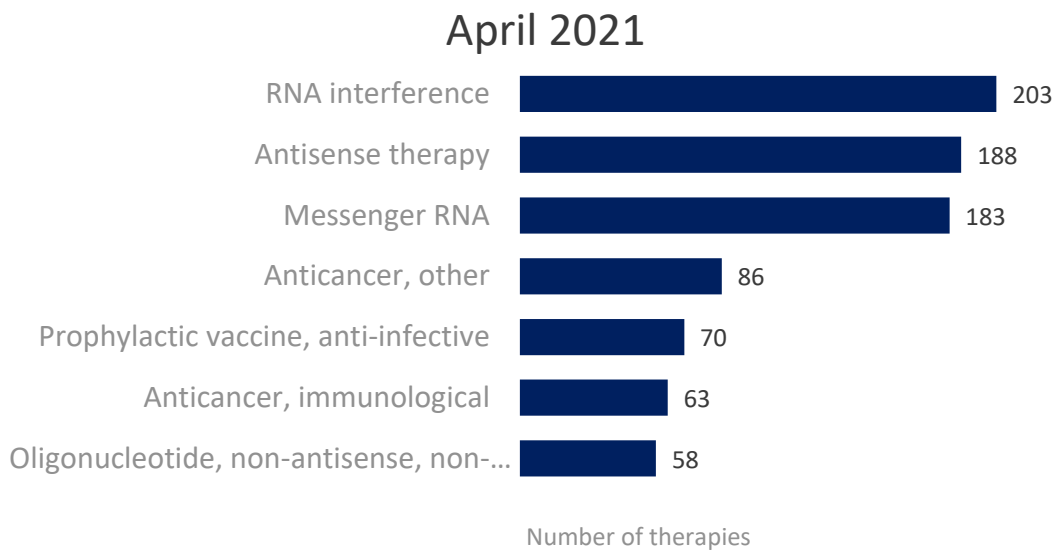
*These are snapshots are taken every May to allow for year-on-year comparisons

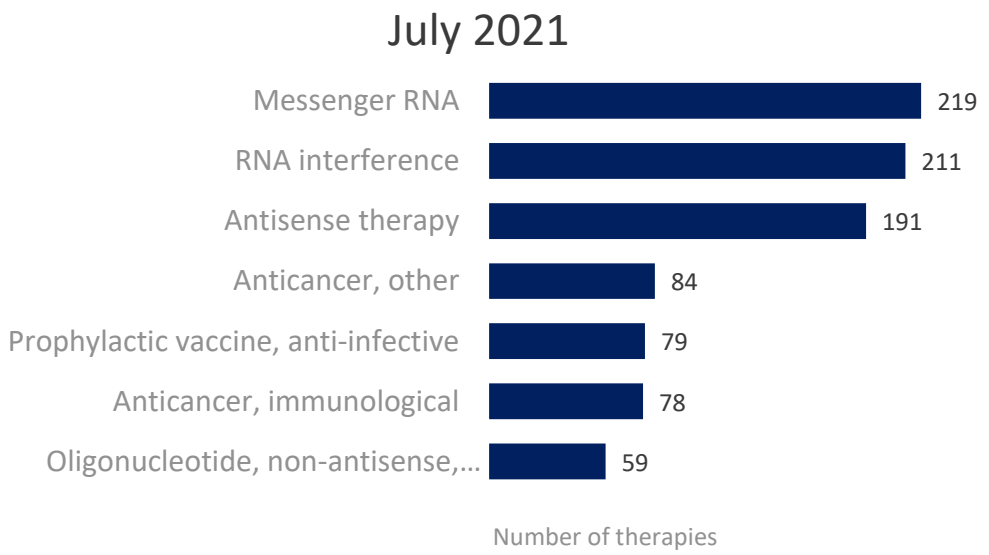
Source: Pharmaprojects | Informa, May 2021

American Society of Gene + Cell Therapy

RNA therapy pipeline: Most common modalities

- Between Q1 and Q2 2021, messenger RNA therapeutics overtook RNA interference (RNAi) and antisense oligonucleotides to become the most common modality in development (preclinical through pre-registration





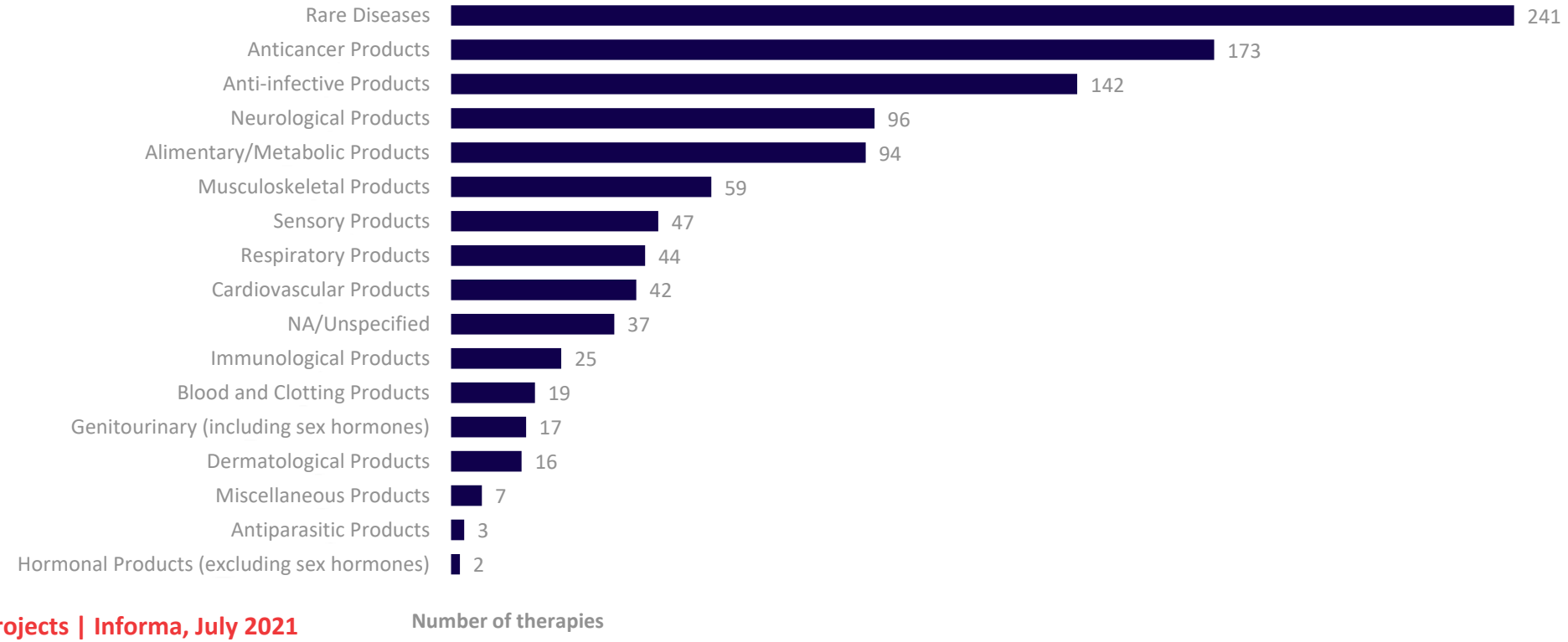
Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

RNA therapies: Most common diseases targeted

Of the 692 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Oncology and rare diseases are the top 2 therapeutic areas being targeted. However, unlike gene therapies and non-genetically modified cell therapies, the top therapeutic area being targeted by RNA therapeutics is for rare diseases (please note that rare oncology diseases are included in the rare diseases therapeutic category)

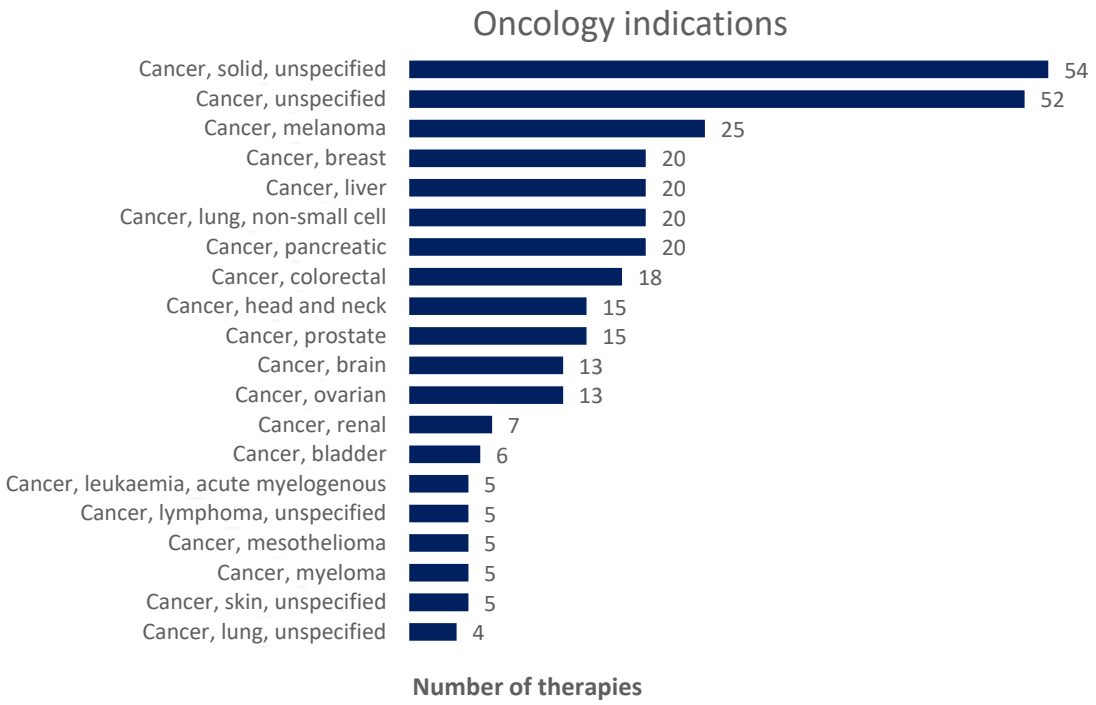


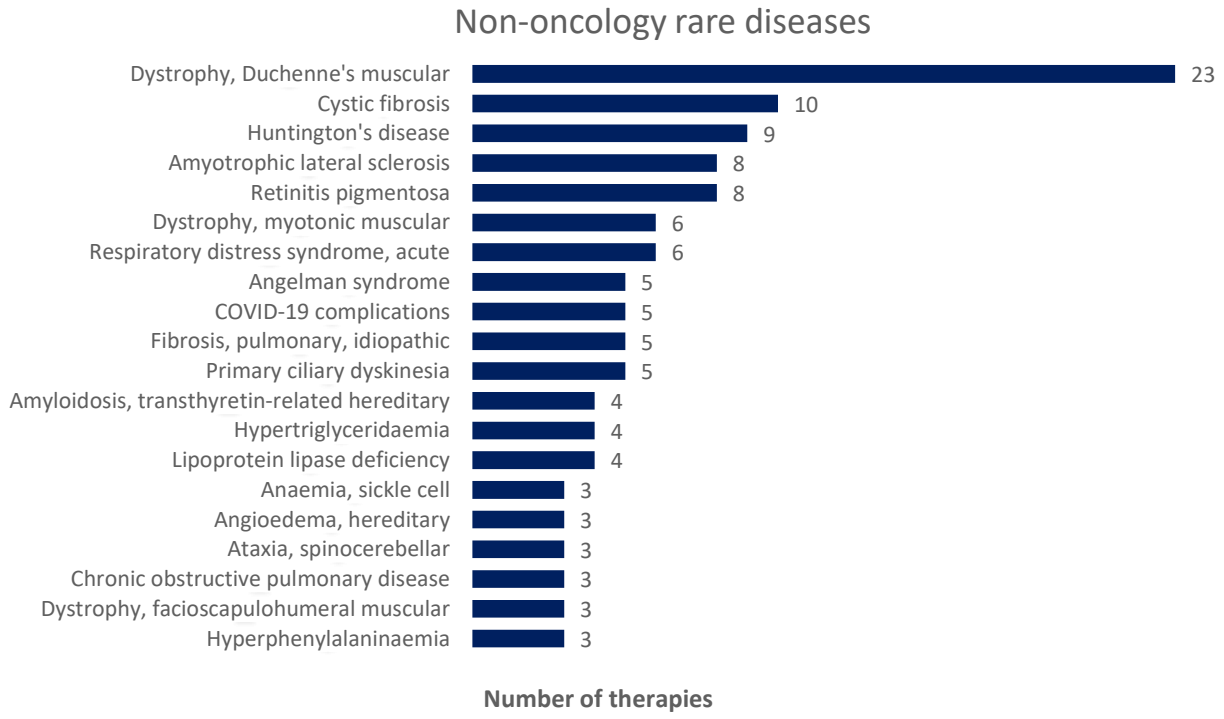
Source: Pharmaprojects | Informa, July 2021

RNA therapies: Most common diseases targeted

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

- Top oncology indications targeted are solid tumors with the top 5 (where specified) being melanoma, breast cancer, liver cancer, non-small cell lung cancer (NSCLC), and pancreatic cancer
- For non-oncology rare diseases, Duchenne's muscular dystrophy, cystic fibrosis, Huntington's disease, amyotrophic lateral sclerosis (ALS), and retinitis pigmentosa are the top 5 targeted diseases



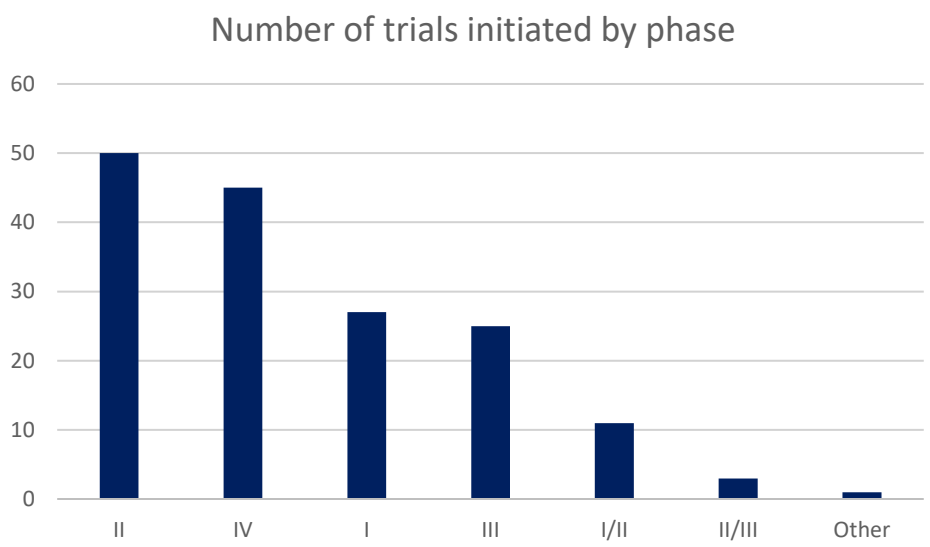


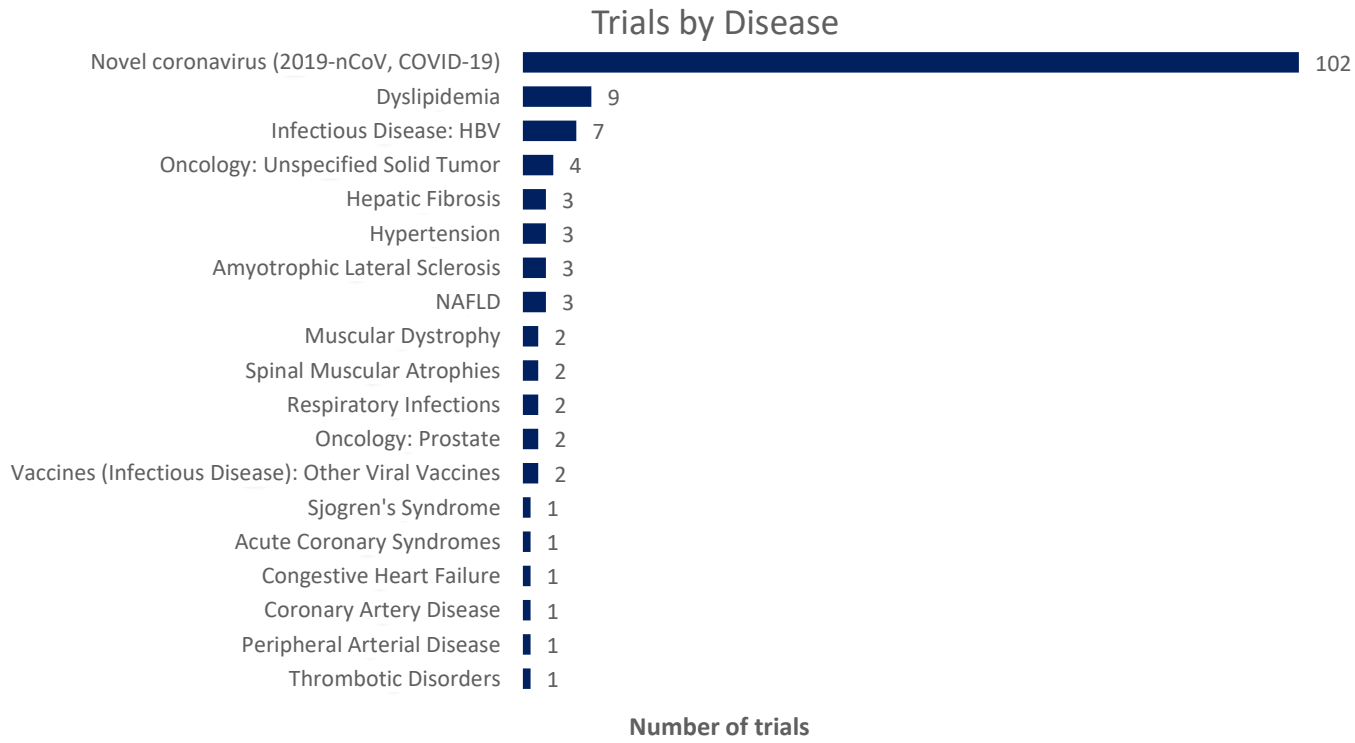
Source: Pharmaprojects | Informa, July 2021

American Society of Gene + Cell Therapy

RNA therapy pipeline: Clinical trial activity

- 162 RNA therapy trials were initiated in the first 6 months of 2021
- Trials evaluating vaccines for COVID-19 infections predominate but there are also trials initiated for dyslipidemia and hepatitis B infections





Source: Trialtrove | Informa, July 2021

American Society of Gene + Cell Therapy

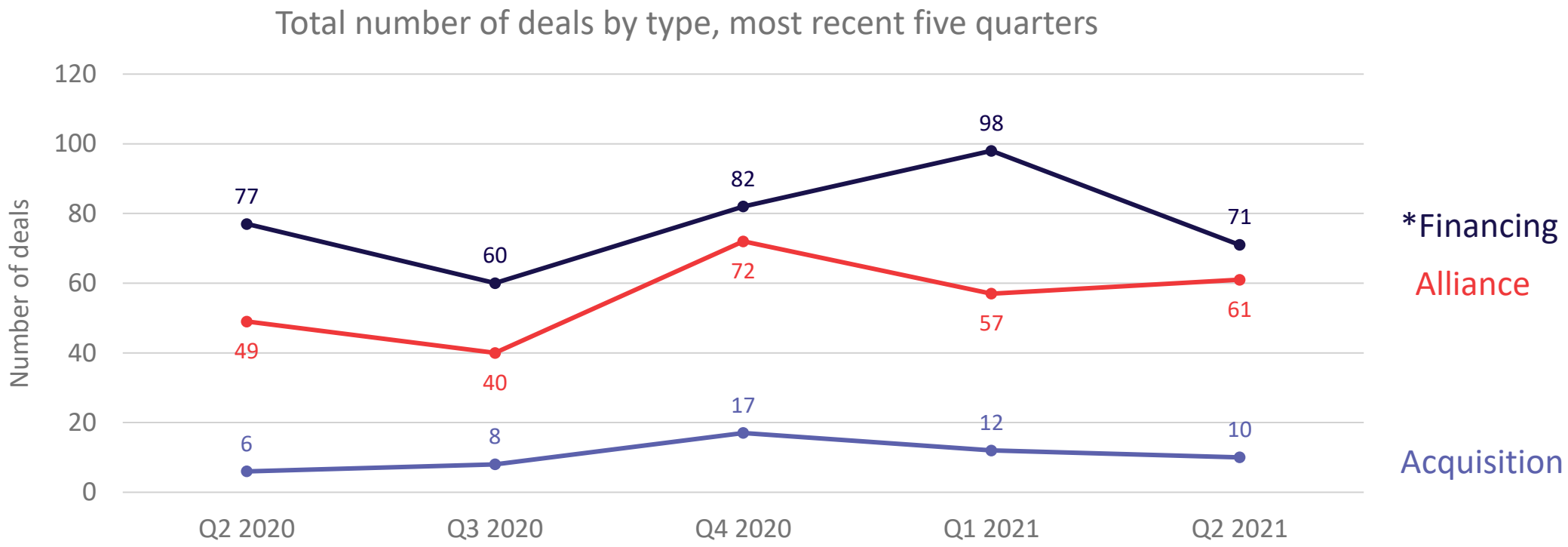
Overview of dealmaking for gene, cell, and RNA therapy companies

Q2 2021

American Society of Gene + Cell Therapy

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

- The gene, cell, & RNA industry has seen a greater volume of alliances, plus a slight uptick in acquisitions in Q2 2021 vs one year ago
- Biggest decrease in Q2 2021 was seen in financings, with >20 fewer transactions done in Q2 than in Q1, and this was mainly attributable to fewer follow-on public offerings



Source: Biomedtracker | Informa, July 2021

*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 2021 acquisitions in gene, cell, & RNA therapy

Deal Date	Deal Title	Potential Deal Value (USD)
04/09/2021	Sanofi Acquires Tidal Therapeutics	470,000,000
04/20/2021	SparingVision Acquires GAMUT Therapeutics	Undisclosed
05/04/2021	Athenex Acquires Kuur Therapeutics to Expand Cell Therapy Development with Off-the-Shelf Engineered CAR-NKT Platform	185,000,000
05/17/2021	Charles River Laboratories to Acquire Vigene Biosciences to Enhance Gene Therapy Capabilities	350,000,000
06/01/2021	Auris Medical Acquires RNA Therapeutics Company Trasir, Changes Name and Strategic Focus	Undisclosed
06/14/2021	Brooklyn ImmunoTherapeutics Executes Letter of Intent to Acquire Novellus Therapeutics	125,000,000
06/14/2021	Avalon GloboCare to Acquire SenlangBio in All Stock Transaction	Undisclosed
06/22/2021	uniQure to Acquire Corlieve Therapeutics and Advance its Gene Therapy Program to Treat Temporal Lobe Epilepsy	298,300,000
06/30/2021	Scopus BioPharma Expands Immunotherapy Pipeline with Acquisition of Olimmune	Undisclosed
06/17/2021	Danaher Pays $9.6B for Aldevron, Manufacturer of High-Quality Plasmid DNA, mRNA, and Proteins	9,600,000,000

Source: Biomedtracker | Informa, July 2021

American Society of Gene + Cell Therapy

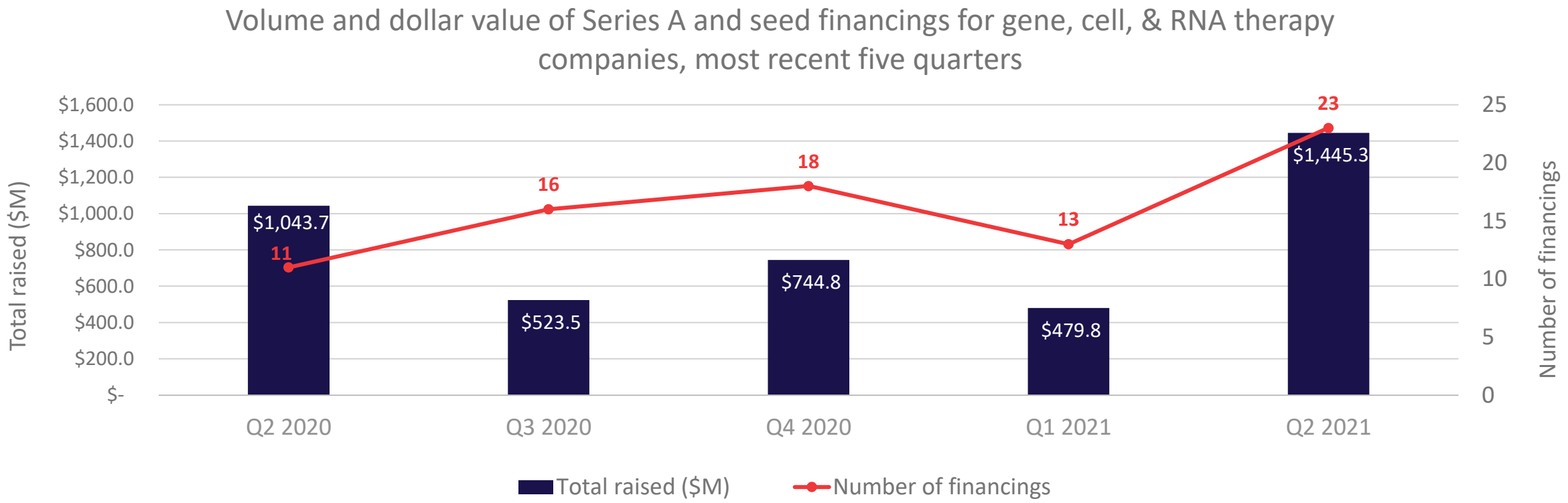
Start-up funding for gene, cell, & RNA therapy companies

Q2 2021

American Society of Gene + Cell Therapy

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

- 23 companies raised seed or Series A financing in Q2 2021, reaching an aggregate $1.4 billion
- Nearly 75% (17/23) of biotechs are based in the US (mainly Massachusetts and California), the rest in Europe and Asia
- Top financing ($250M) was done by a new company created by Intellia, Cellex (and subsidiary GEMoaB), and Blackstone to develop allogeneic universal CAR-T therapies based on Intellia's CRISPR/Cas9 platform and CEMoaB's switchable, universal CAR T-cell platforms



Source: Biomedtracker | Informa, July 2021

American Society of Gene + Cell Therapy

Q2 2021 start-up financing for gene, cell, & RNA therapy companies (1/2)

Deal Date	Deal Title	Company Location	Academic Source	Potential Deal Value (USD)
04/07/2021	Shoreline Biosciences Announces $43M Early Round To Advance Pipeline	United States, California, San Diego	University of California, San Diego	43,000,000
04/19/2021	Rejuvenate Bio Raises over $10M in Series A financing	United States, California, San Diego	Harvard University: Harvard Medical School and Wyss Institute	10,000,000
04/20/2021	Code Biotherapeutics Launches with $10M in Seed Financing	United States, Pennsylvania, Hatfield	Undisclosed	10,000,000
04/29/2021	Capsida Biotherapeutics Debuts with $50M Series A Round	United States, California, Newbury Park	California Institute of Technology: Tianqiao and Chrissy Chen Institute for Neuroscience	50,000,000
04/30/2021	Treeline Biosciences Launches with $211M Series A Round	United States, Connecticut, Stamford	Undisclosed	211,669,568
05/05/2021	Isolere Bio Closes $7M in Seed Funding	United States, North Carolina, Durham	Duke University	7,000,000
05/06/2021	Dyno Therapeutics Closes $100M Series A Round	United States, Massachusetts, Cambridge	Harvard University: Harvard Medical School and Wyss Institute	100,000,000
05/10/2021	Gennao Bio Closes $40M Series A Financing to Develop Pipeline of Targeted Nucleic Acid Therapeutics	United States, New York, New York	Yale University	40,000,000
05/11/2021	Appia Bio Launches With $52M Series A Financing	United States, California, Los Angeles	University of California, Los Angeles	52,000,000
05/18/2021	G2 Bio Companies Launch with $200M to Develop Transformative Genetic-Based Therapies	United States, Pennsylvania, Philadelphia	University of Pennsylvania: Gene Therapy Program	200,000,000
05/18/2021	Vedere Bio II Launches with $77M Series A Financing to Develop Ocular Gene Therapies	United States	University of California, Berkeley; University of Pennsylvania: School of Veterinary Medicine	77,000,000
05/20/2021	HAYA Therapeutics Completes CHF 18M Seed Financing To Advance Anti-fibrotic Therapies Targeting Long Non-coding RNAs	Switzerland, Vaud	Lausanne University Hospital	19,985,500
05/27/2021	miRecule Inc. Closes $5.7M Seed Funding	United States, Maryland, Gaithersburg	National Institutes of Health: BioHealth Innovation	5,700,000

Source: Biomedtracker | Informa, July 2021

American Society of Gene + Cell Therapy

Q2 2021 start-up financing for gene, cell, & RNA therapy companies (2/2)

Deal Date	Deal Title	Company Location	Academic Source	Potential Deal Value (USD)
06/09/2021	Alcyone Therapeutics Launches with $23M to Advance Gene Therapies for CNS Disorders	United States, Massachusetts, Lowell	Nationwide Children's Hospital: Abigail Wexner Research Institute	23,000,000
06/15/2021	VectorY Raises $37.58M in Seed Financing	Netherlands, Amsterdam	Undisclosed	37,582,695
06/16/2021	Mnemo Therapeutics Announces $90M Series A to Accelerate Next Generation Integrated CAR-T and Epigenetic Targeting Platform	France, Paris	Institut Curie; Memorial Sloan Kettering Cancer Center	90,000,000
06/16/2021	Ochre Bio Closes $9.6M Seed Financing	United Kingdom, Oxford	Working in collaboration with Oxford University	9,600,000
06/18/2021	Nuevocor Closes $24M Series A Financing to Advance Novel Gene Therapies for Cardiomyopathies	Singapore	Agency for Science, Technology and Research (A*STAR)	24,000,000
6/22/2021	Unnamed autologous/allogeneic CAR-T company launched with $250M from Blackstone Life Sciences, Intellia Therapeutics, and Cellex Cell Professionals	United States, Massachusetts, Cambridge	n/a – founded around pooled resources from GEMoaB GmbH (Cellex's parent company) and Intellia	250,000,000
06/23/2021	Abata Therapeutics Launches with $95M Series A Funding	United States, Massachusetts, Cambridge	Co-founders are from Harvard Medical School, Massachusetts Institute of Technology, and University Hospital of Zurich	95,000,000
06/23/2021	Vita Therapeutics Raises $32M in Series A Financing	United States, Maryland, Baltimore	Johns Hopkins University; Kennedy Krieger Institute	32,000,000
06/23/2021	Strand Therapeutics Raises $52M via Oversubscribed Series A Round	United States, Massachusetts, Cambridge	MIT Synthetic Biology Center	52,000,000
06/24/2021	OliX' subsidiary mCureX Therapeutics Raises ₩6.5B in Pre-Series A Investment	Korea (South)	n/a – subsidiary of OliX Pharmaceuticals	5,738,860

Source: Biomedtracker | Informa, July 2021

American Society of Gene + Cell Therapy

Notable Q2 2021 start-up gene, cell, & RNA therapy companies

Company details	Academic source	Financing type/amount raised	Lead investor(s)	Therapy areas of interest
T-cell engineering EnfiniT platform technology, including identification of antigens with greater tumor specificity and development of next-generation CAR-T therapies	Institut Curie; Memorial Sloan Kettering Cancer Center	Series A; $90M	Casdin Capital, Sofinnova Partners, and an undisclosed investor	Oncology
CapsidMap platform, which designs AAV vectors using artificial intelligence	Harvard University: Harvard Medical School and Wyss Institute	Series A/$100M	Andreessen Horowitz	Liver, muscle, eye, central nervous system, lung, heart and kidney diseases
DiscoverHAYA platform to discover tissue and cell-specific long non-coding RNA drug candidates	Lausanne University Hospital	Seed/$20M	Broadview Ventures	Fibrosis and conditions related to aging

Source: Biomedtracker | Informa, July 2021; company websites

American Society of Gene + Cell Therapy

Upcoming catalysts

Q2 2021

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward looking events) that are expected in Q3 2021

Therapy	Generic Name	Disease	Catalyst	Catalyst Date
Skysona	elivaldogene autotemcel, Lenti-D	Cerebral adrenoleukodystrophy	European Approval Decision	May 21 - Sep 30, 2021
Yescarta	axicabtagene ciloleucel	Marginal cell lymphoma	FDA Approval Decision	Jun 18 - Sep 30, 2021
Abecma	idecabtagene vicleucel	Multiple myeloma	European Approval Decision	Jun 24 - Aug 30, 2021

Source: Biomedtracker | Informa, July 2021

Appendix

Methodology, sources, & glossary of key terms

Q2 2021

American Society of Gene + Cell Therapy

Methodology: Sources and scope of therapies

Sources for all data come from Informa Pharma Intelligence

Pipeline and trial data

- Data derived from **Citeline (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

Glossary of Key Terms

Therapy Type Definitions

Gene therapy is the introduction, removal, or change in genetic material—specifically DNA or RNA—into the cells of a patient to treat a specific 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.

American Society of Gene + Cell Therapy

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

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

Ly Nguyen-Jatkoe, PhD
Executive Director, Americas
Informa Pharma Custom Intelligence

Betsy Foss-Campbell, MA
Director of Policy and Advocacy
American Society of Gene + Cell Therapy

Amanda Micklus, MSc
Senior Pharma Consultant
Informa Pharma Custom Intelligence

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

Doro Shin, MPH
Senior Director, Content Marketing
Informa Pharma Intelligence

American Society of Gene + Cell Therapy

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

Pharma Intelligence
Informa

Contact: pharma@informa.com