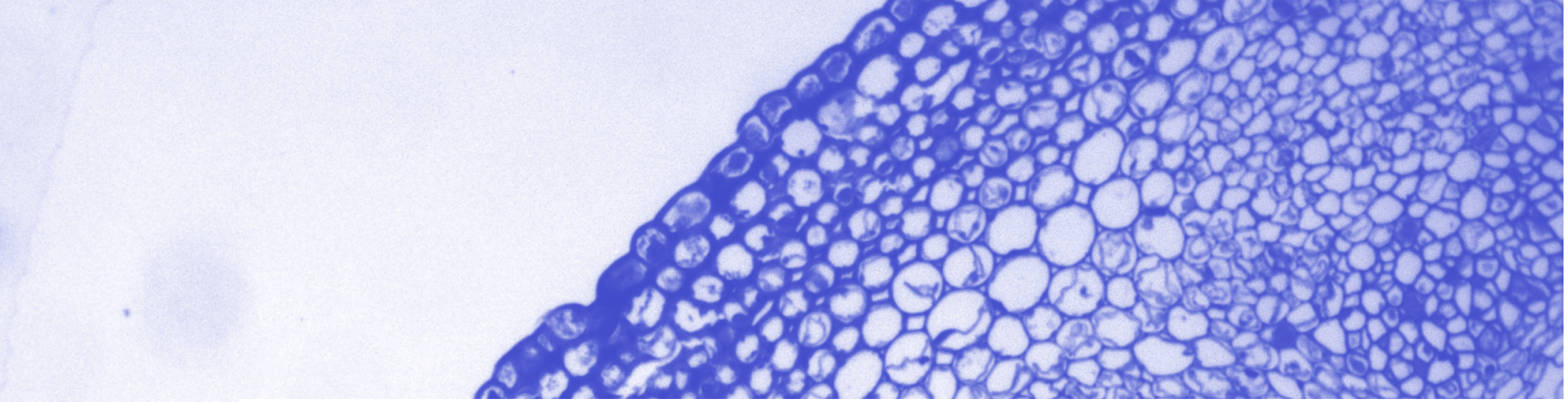
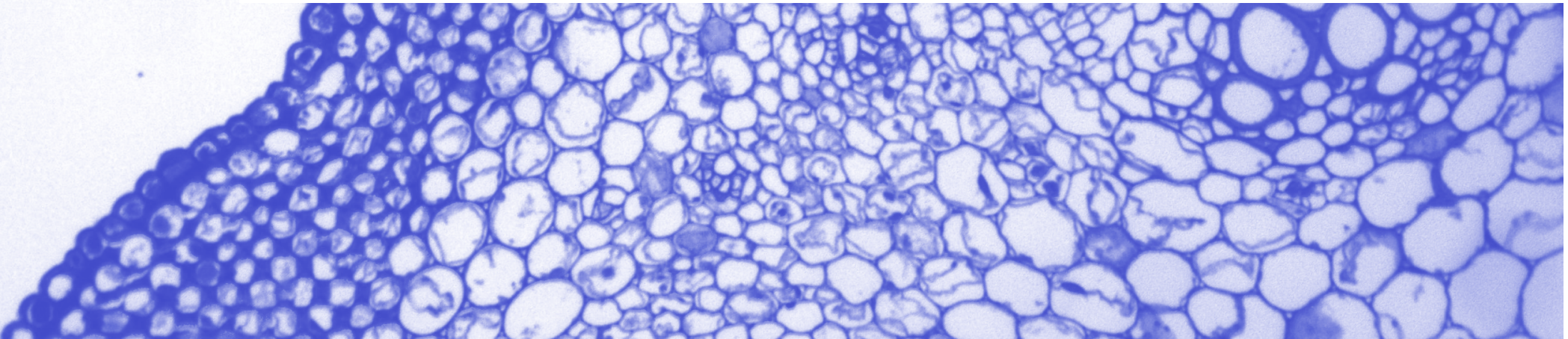


Gene, Cell, & RNA Therapy Landscape

Q3 2021 Quarterly Data Report

Q3 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.

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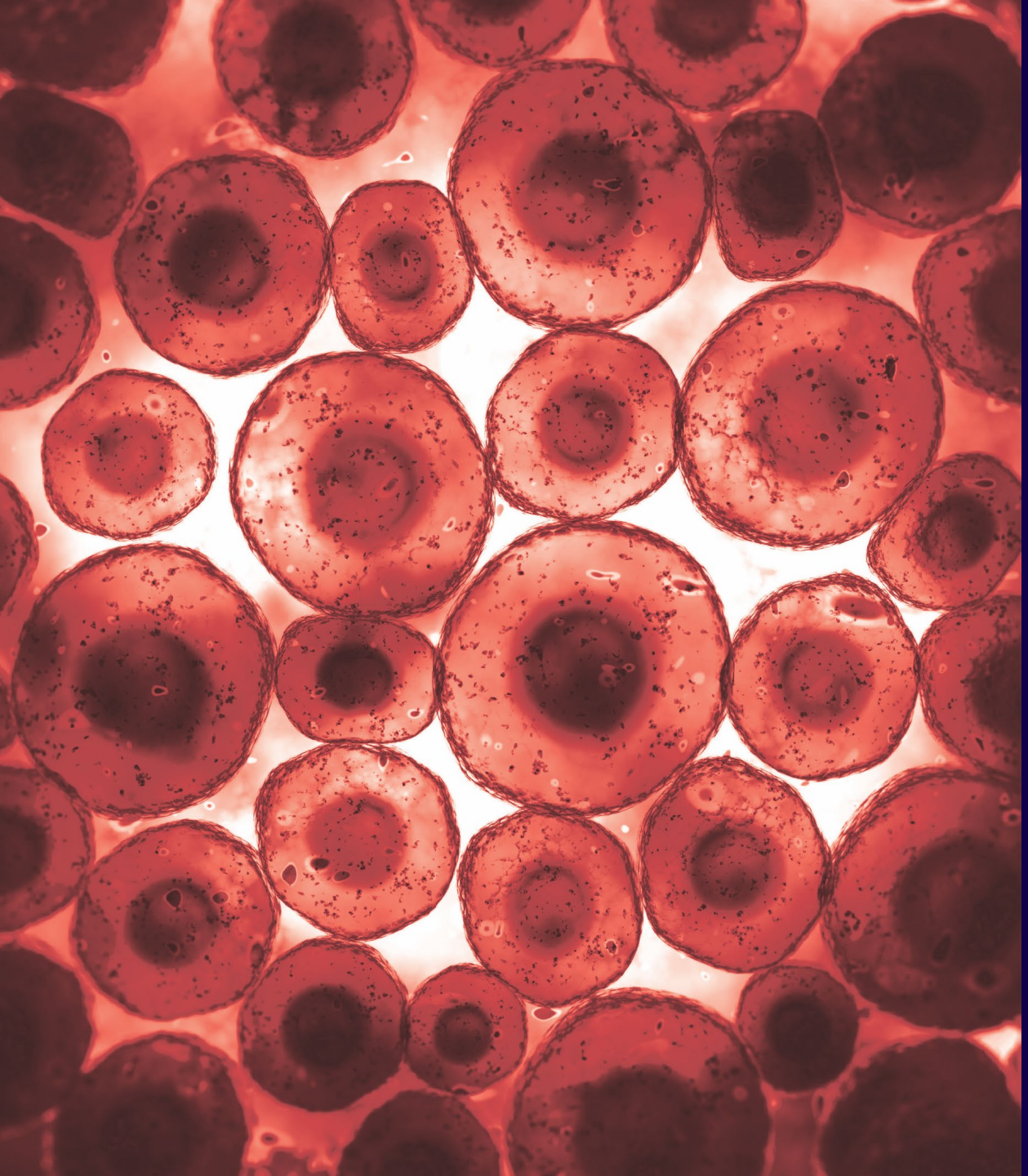

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American Society of Gene + Cell Therapy

Introduction

ASGCT welcomes you to the third in a quarterly report series with our data partner, Informa Pharma Intelligence. This series provides comprehensive details on the magnitude of development—3,366 gene and cell therapies in development globally from the preclinical through pre-registration stages—and changes in the breakdown of factors like modality and therapeutic area.

Highlights in Q3 2021 include the approvals of two new gene therapies in the European Union (EU) and China, the expansion of two gene therapy approvals to new regions (South Korea and the EU), continued growth in gene therapy research, and growth in the RNA therapeutic space of studies of anti-infective prophylactic vaccines.

New this quarter, the report provides a spotlight on a therapeutic area—non-oncology indications—to provide a deeper dive into a segment of the pipeline. On the gene therapy side, slightly over half of rare disease development is for non-oncology diseases (445 therapies).

Reflective of the continued innovation in the field, 22 companies raised nearly a billion dollars in start-up financing (seed or Series A financing) this quarter.

ASGCT is pleased to provide this rich data resource on the dynamic development leading to the clinical application of genetic and cellular therapies to alleviate human disease.

Key takeaways from Q3 2021

Two new gene therapies were approved

- Skysona, a gene therapy consisting of CD34+ hematopoietic stem cells transduced with a lentiviral vector encoding ABCD1 cDNA, was approved for adrenoleukodystrophy in the EU
- Relma-cel, a CD19-directed CAR T-cell therapy, was approved for diffuse large B-cell lymphoma in China

The majority of gene, cell, and RNA therapies in development globally for rare diseases are for non-oncology indications

- Amyotrophic lateral sclerosis is in the top five non-oncology rare diseases for all three categories of therapy
- The majority of gene therapies in development for non-oncology rare diseases are for neurological or blood disorders
- For non-oncology rare diseases, 323 gene therapies are in preclinical development while 127 gene therapies are in phase I through pre-registration

Start-up financing was down from Q2, but up from a year ago

- 22 companies raised seed or Series A financing totaling $907.9 million in Q3, down 37% from Q2 (which featured three $200 million+ rounds)
- Q3 2021's dollar value outpaced all other previous quarters in the last year, except Q2 2021

Key highlights in Q3 2021

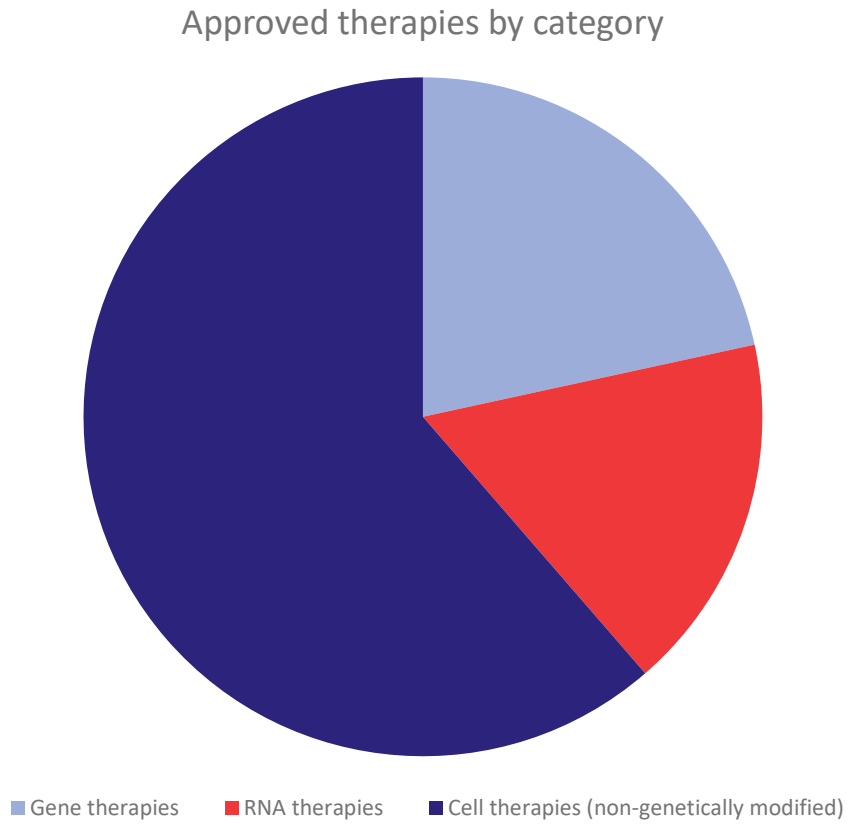
Q3 2021

American Society of Gene + Cell Therapy

Approved gene, cell, and RNA therapies

Globally, for clinical use, there are:

- 19 gene therapies approved (including genetically modified cell therapies)
- 15 RNA therapies approved
- 54 non-genetically modified cell therapies approved



Source: Pharmaprojects | Informa, October 2021

American Society of Gene + Cell Therapy

Approved gene therapies as of Q3 2021 (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	US, EU, UK Japan, Australia, Canada, South Korea	Novartis
Luxturna	voretigene neparvovec	2017	Leber's congenital amaurosis; retinitis pigmentosa	US, EU, UK, Australia, Canada, South Korea	Spark Therapeutics (Roche)
Yescarta	axicabtagene ciloleucel	2017	Diffuse large B-cell lymphoma; non-Hodgkin's lymphoma; follicular lymphoma	US, EU, UK, Japan, Canada, China	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	lentiviral beta-globin gene transfer	2019	Transfusion-dependent beta thalassemia	EU, UK	Bluebird Bio
Tecartus	brexucabtagene autoleucel	2020	Mantel cell lymphoma	US, EU	Kite Pharma (Gilead)
Libmeldy	OTL-200	2020	Metachromatic Leukodystrophy	EU, UK	Orchard Therapeutics
Breyanzi	lisocabtagene maraleucel	2021	Diffuse large B-cell lymphoma; follicular lymphoma	US, Japan	Celgene (Bristol Myers Squibb)

Source: Pharmaprojects | Informa, October 2021

Text highlighted in yellow represent new approvals during Q3 2021

Approved gene therapies as of Q3 2021 (2/2)

Product name	Generic name	Year first approved	Disease(s)	Locations approved	Originator company
Abecma	idecabtagene vicleucel	2021	Multiple myeloma	US, Canada, EU	bluebird bio
Delytact	teserpaturev	2021	Malignant Glioma	Japan	Daiichi Sankyo
Skysona	elivaldogene autotemcel	2021	Adrenoleukodystrophy	EU	bluebird bio
Relma-cel	relmacabtagene autoleucel	2021	Diffuse large B-cell lymphoma	China	JW Therapeutics

Source: Pharmaprojects | Informa, October 2021

Text highlighted in yellow represent new approvals during Q3 2021

American Society of Gene + Cell Therapy

Approved RNA therapies as of Q3 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, UK, Canada, Japan, Brazil, Switzerland, Australia, South Korea, China, Argentina, Colombia, Taiwan, Turkey	Ionis Pharmaceuticals
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	Alnylam
Vyondys 53	golodirsen	2019	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Waylivra	volanesorsen	2019	Hypertriglyceridemia; Lipoprotein lipase deficiency	EU, UK, Brazil	Ionis Pharmaceuticals
Comirnaty	tozinameran	2020	Infection, coronavirus, novel coronavirus prophylaxis	UK, Bahrain, Israel, Canada, US, Rwanda, Serbia, United Arab Emirates, Macao, 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, October 2021

Text highlighted in yellow represent new approvals during Q3 2021

Approved RNA therapies as of Q3 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, Mexico, Australia, Nigeria	Moderna Therapeutics
Givlaari	givosiran	2020	Porphyria	US, EU, UK, Canada, Switzerland, Brazil, Israel, Japan	Alnylam
Oxlumo	lumasiran	2020	Hyperoxaluria	EU, UK, US, Brazil	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 hypercholesterolemia; Hypercholesterolemia; Homozygous familial hypercholesterolemia	EU, UK, Australia, Canada, Israel	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, October 2021

Text highlighted in yellow represent new approvals during Q3 2021

Key highlights in Q3 2021

Below are select noteworthy events that happened in Q3 2021

Brand Name	Generic Drug Name	Molecule type	Disease	Event Type	Event Date
Viralym-M	N/A	Cellular	Antiviral - Other Treatments	Orphan Drug Designation (U.S.)	09/29/2021
TSHA-101	N/A	Viral Gene Therapy	GM2 Gangliosidoses (Tay-Sachs Disease, Sandhoff Disease, AB Variant)	Orphan Drug Designation (Europe)	09/29/2021
DB-OTO	N/A	Viral Gene Therapy	Hearing Loss - General	Rare Pediatric Disease (RPD) Designation and Orphan Drug Designation (U.S)	09/09/2021
Lumevoq	N/A	Viral Gene Therapy	Leber's Hereditary Optic Neuropathy (LHON) (Ophthalmology)	Promising Innovative Medicine Designation (U.K.)	09/06/2021
Relma-cel	relmacabtagene autoleucel	Cellular*	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	Approval (Emerging Markets)	09/06/2021
Waylivra	volanesorsen	Antisense	Familial Chylomicronemia Syndrome (FCS)/Lipoprotein Lipase Deficiency (LPLD)	Approval (Emerging Markets)	08/23/2021
Givlaari	givosiran	siRNA/RNAi	Porphyria	Approval (Japan)	08/03/2021
ARO-AAT	N/A	siRNA/RNAi	Alpha-1 Antitrypsin Deficiency (A1AD or AATD)	Breakthrough Therapy Designation (U.S.)	07/29/2021
LX1004	N/A	Other Nucleic Acid	Neuronal Ceroid Lipofuscinosis (NCL)	Rare Pediatric Disease (RPD) Designation	07/28/2021
Skysona	elivaldogene autotemcel	Viral Gene Therapy	Adrenoleukodystrophy	Approval (Europe)	07/21/2021
TSHA-105	N/A	Viral Gene Therapy	Seizure Disorders (Epilepsy)	Orphan Drug Designation (Europe)	07/19/2021
Roctavian	valoctocogene roxaparvovec	Viral Gene Therapy	Hemophilia A	European Filing Accepted	07/15/2021

*This is a genetically modified cell therapy (CAR-T therapy)

Source: Biomedtracker | Informa, October 2021

Pipeline overview

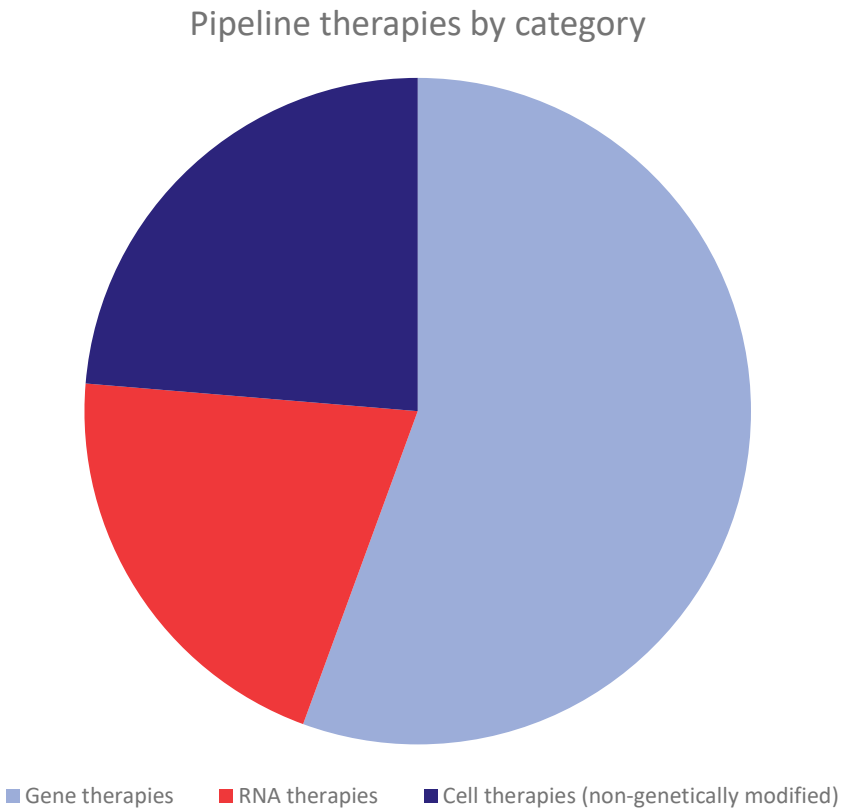
Q3 2021

American Society of Gene + Cell Therapy

Pipeline of gene, cell, and RNA therapies

3,366 therapies are in development, ranging from preclinical through pre-registration

- 1,890 gene therapies (including genetically-modified cell therapies such as CAR T-cell therapies) are in development, accounting for 56% of gene, cell, and RNA therapies
- 805 non-genetically modified cell therapies are in development, accounting for 24% of gene, cell, and RNA therapies



Source: Pharmaprojects| Informa, October 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q3 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: 2021 quarterly comparison

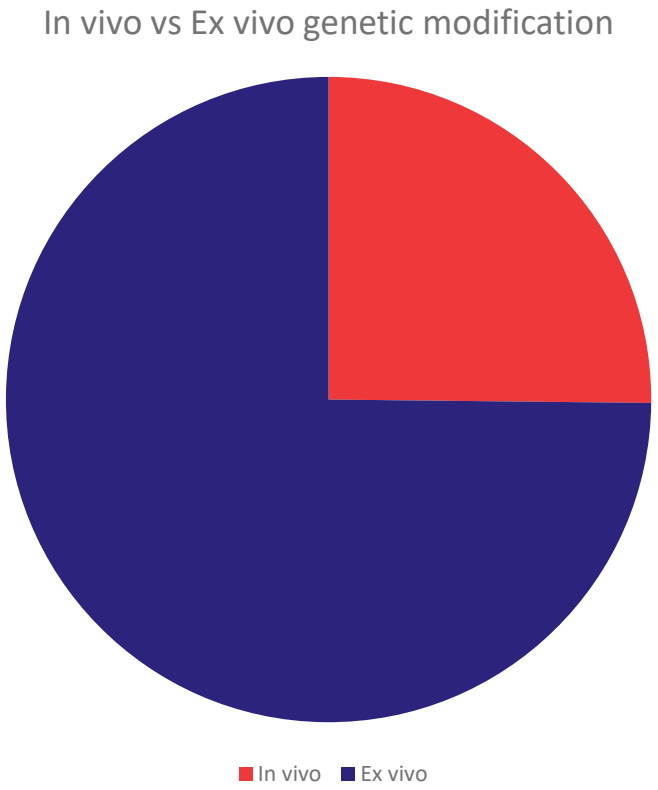
- The greatest percentage growth since Q2 is seen in Phase III development, which has increased by 7%
- Therapies in preclinical development have seen a more modest growth of 4%, after growth in Q2
- The number of gene therapies in pre-registration has decreased by two therapies, due to new approvals.
- Therapies currently in pre-registration:
  - valoctocogene roxaparvovec (Biomarin)
    - In the EU and UK
  - lenadogene nolparvovec (Genethon, GenSight Biologics)
    - In the EU and UK
  - nadofaragene firadenovec (Ferring, FKD Therapeutics, Trizell)
    - In the US
  - ciltacabtagene autoleucel (Johnson & Johnson, Legend Biotech)
    - In the EU, UK, Brazil, and US
  - eladocagene exuparvovec (PTC Therapeutics)
    - In the EU and UK

Global Status	April 2021	July 2021	October 2021
Preclinical	1,190	1,296	1,353
Phase I	225	269	264
Phase II	231	236	239
Phase III	27	27	29
Pre-registration	8	7	5
Total	**1,711**	**1,835**	**1,890**

Source: Pharmaprojects| Informa, October 2021

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

- The majority of gene therapies in preclinical development through pre-registration use e*x vivo* genetic modification
- In 25% of gene therapies, the genetic modification occurs *in vivo*

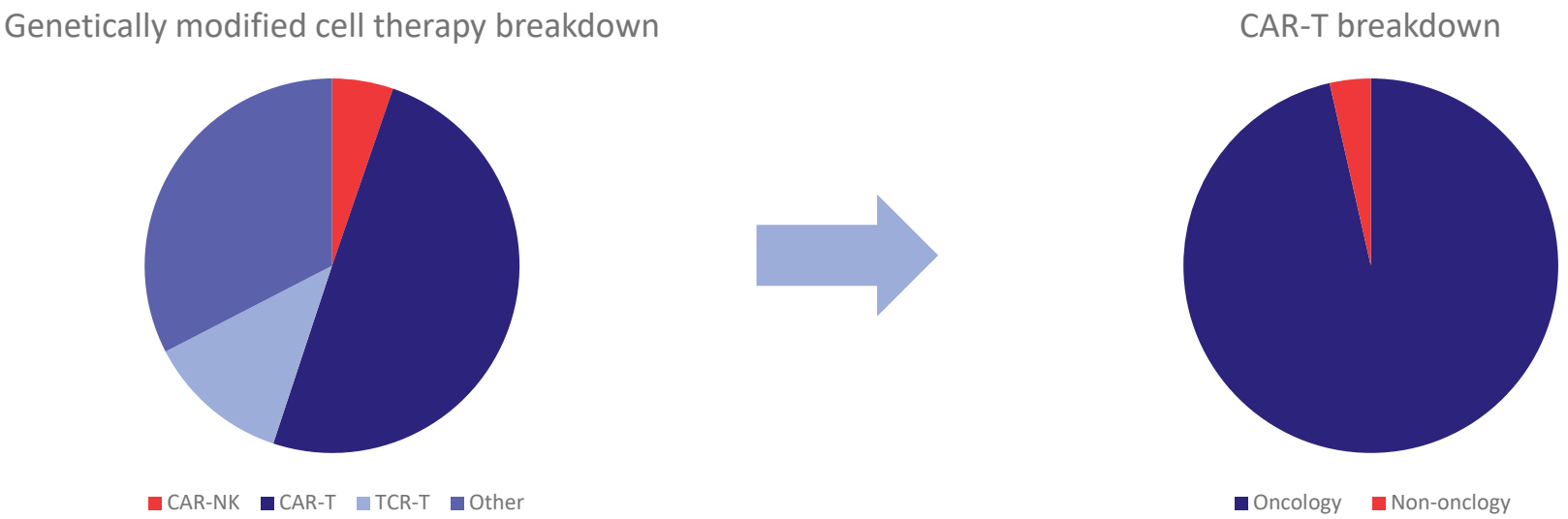


Source: Cell and Gene Therapy dashboard | Informa, October 2021

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 50%, followed by the “other” category, which includes a list of much less common technologies, including CAR-M, TAC T-cell therapy, and CAAR-T
- Of the CAR T-cell therapies, 98% are in development for cancer indications. The remaining non-oncology indications include HIV/AIDs, myelodysplastic syndrome, and autoimmune disease (unspecified)

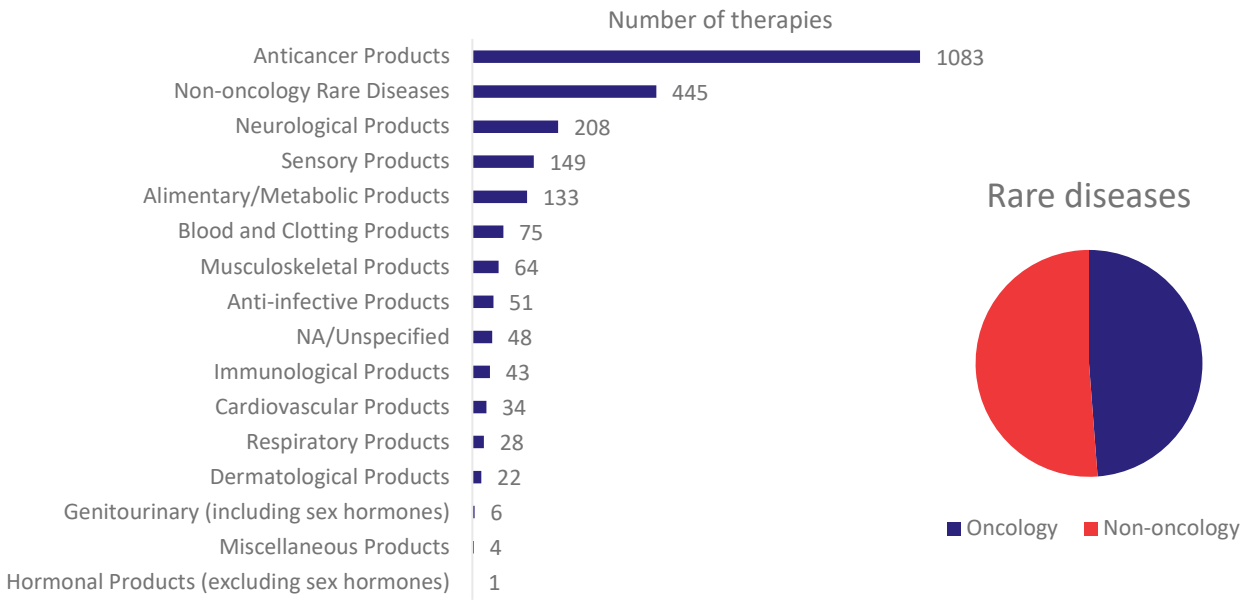


Source: Cell and Gene Therapy dashboard | Informa, October 2021

Gene therapy pipeline: Most commonly targeted therapeutic areas

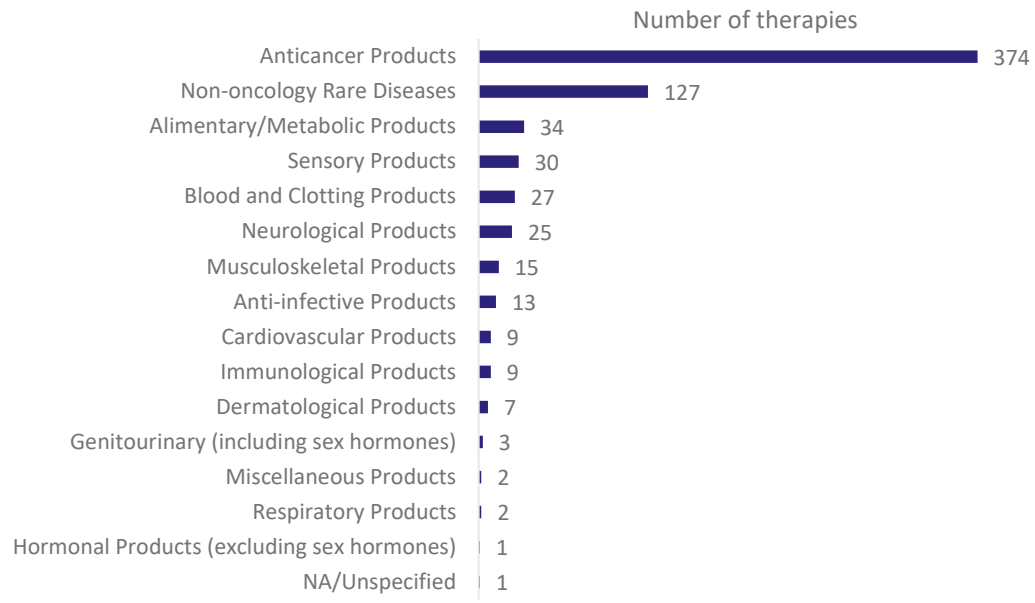
- Anticancer therapies and therapies for rare diseases remain the top areas of development in both the pipeline (preclinical to pre-registration) and in the clinic (phase I to pre-registration) specifically
- Of all the gene therapies in pipeline development for rare diseases, 51% are in development for non-oncology indications

Number of therapies from preclinical through pre-registration



Rare diseases

Therapies in the clinic (excludes preclinical development)



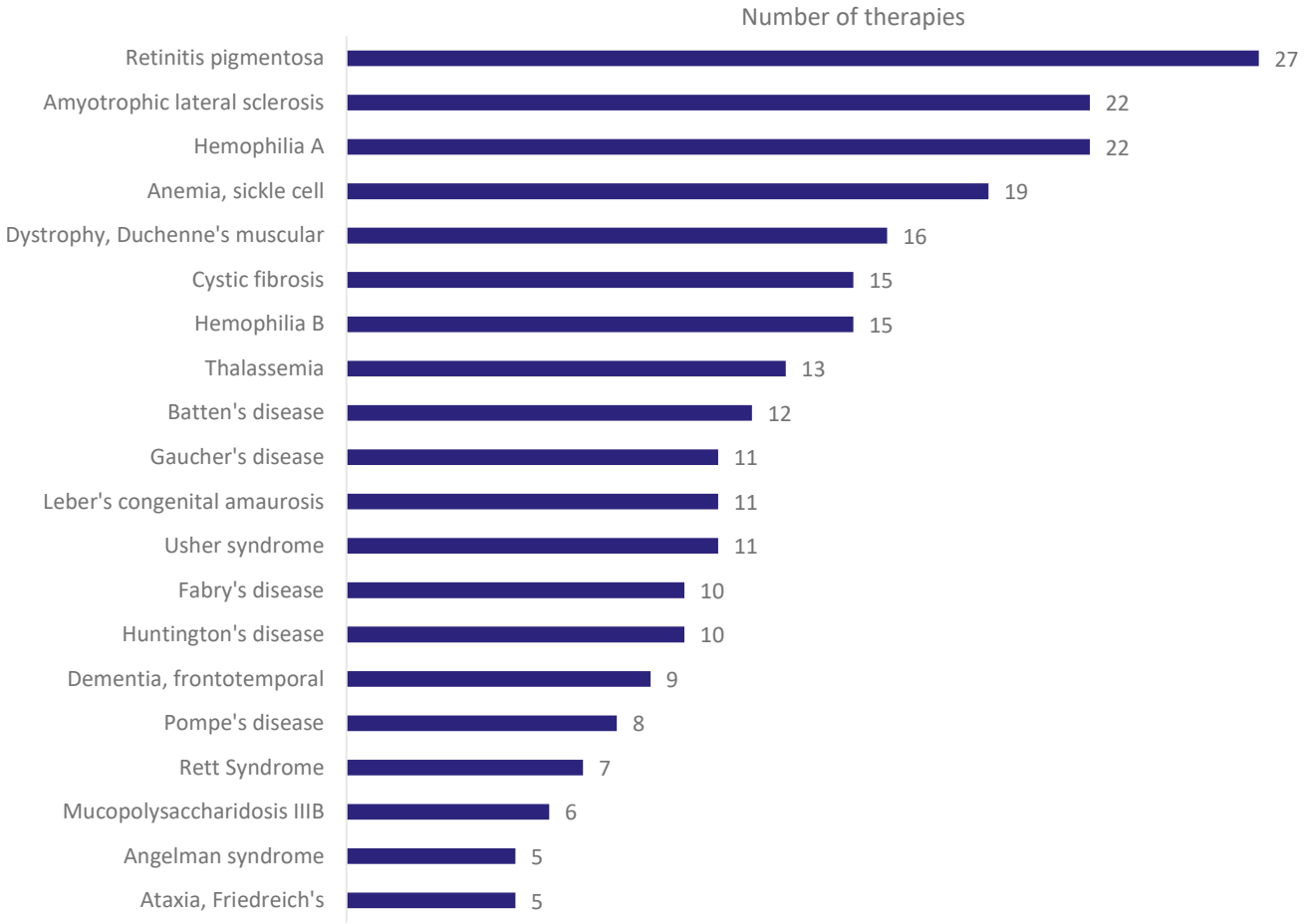
Source: Pharmaprojects| Informa, October 2021

*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

- Of the 445 gene therapies in preclinical to pre-registration stages of development for non-oncology rare diseases, the majority of the top 20 indications are neurological or blood disorders
- As found in Q2, the top 5 non-oncology rare diseases for which gene therapies are being developed are:
  - retinitis pigmentosa
  - amyotrophic lateral sclerosis (ALS)
  - hemophilia A
  - Duchenne’s muscular dystrophy (DMD)
  - sickle cell anemia



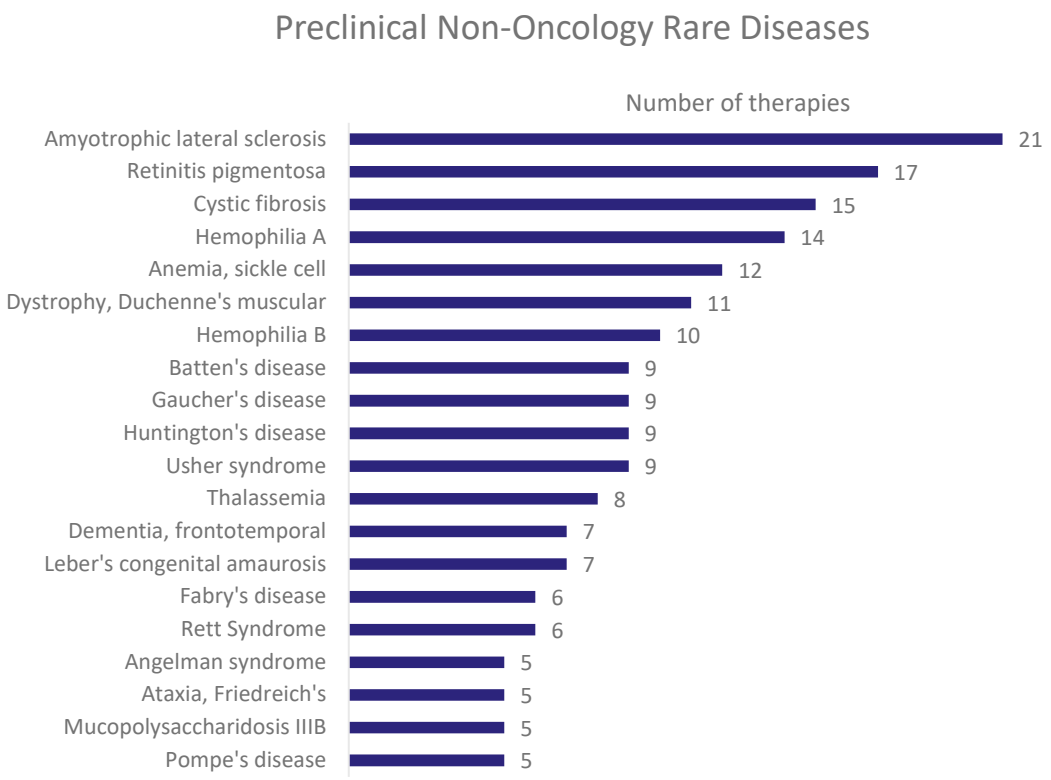
Source: Pharmaprojects| Informa, October 2021

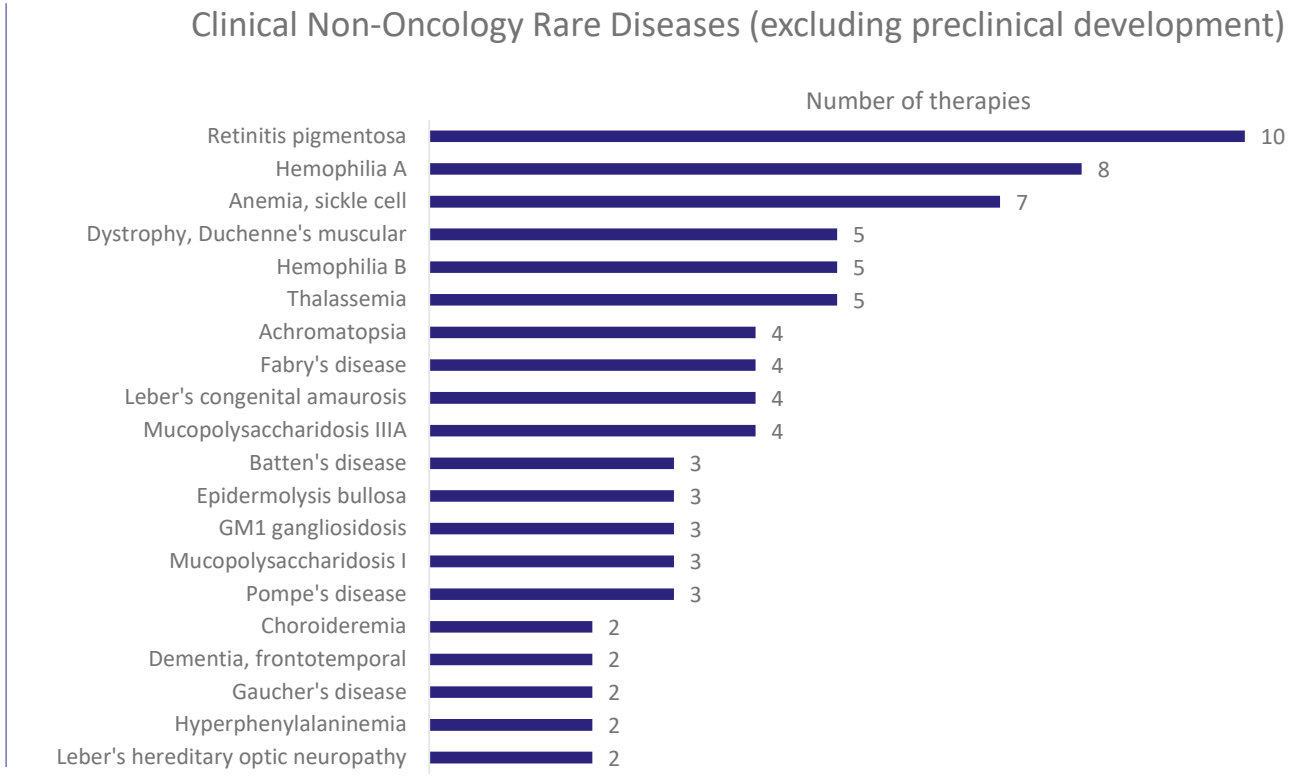
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

Non-oncology rare diseases: Preclinical vs clinical

- The majority of development for each indication remains at the preclinical stage
- For non-oncology rare diseases, 323 gene therapies are in preclinical development while 127 gene therapies are in phase I to pre-registration





Source: Pharmaprojects| Informa, October 2021

*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

Top 5 non-oncology rare diseases: Deep dive into late-stage therapies

	Latest-stage therapies			
	Phase II	**Phase III**	**Pre-registration**	**Approved**

Retinitis pigmentosa		• AAV2/5-hRKp.RPGR (Johnson & Johnson, MeiraGTx)
		  • Phase III in the US
				• voretigene neparvovec (Spark Therapeutics, Novartis)
				  • Approved in the US, EU, UK, Australia, Canada, South Korea

Amyotrophic lateral sclerosis	• donaperminogene seltoplasmid (Reyon Pharmaceutical, Helixmith) • Phase II in the US			

Hemophilia A		• giroctocogene fitelparvovec (Pfizer, Sangamo Therapeutics)
		  • Phase III in Japan, South Korea, Taiwan, Turkey, US
		• SPK-FVIII AAV (Spark Therapeutics)
		  • Phase III in the US
			• valoctocogene roxaparvovec (BioMarin)
			  • Pre-registration in the EU and UK	

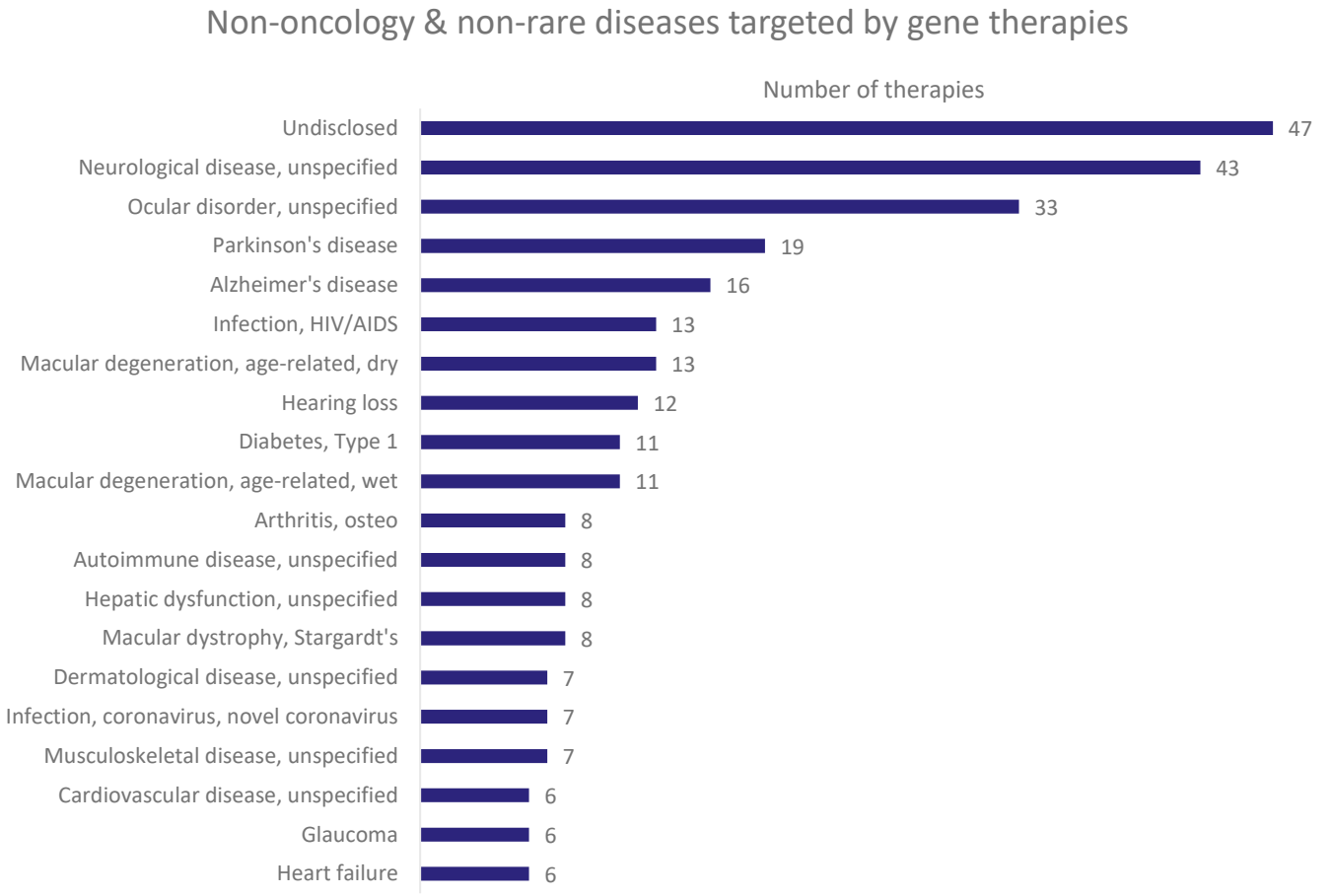
Anemia, sickle cell		• betibeglogene autotemcel (bluebird bio) • Phase III in the US		

Dystrophy, Duchenne's muscular		• fordadistrogene movaparvovec (Pfizer)
		  • Phase III in the UK and US
		• delandistrogene moxeparvovec (Sarepta Therapeutics)
		  • Phase III in the US		

Source: Pharmaprojects| Informa, October 2021

Gene therapy pipeline: Most common additional diseases targeted

- There are 412 therapies that are in preclinical development through pre-registration for diseases outside of oncology or rare diseases
- Neurological diseases, ocular disorders, Parkinson's disease, Alzheimer's disease and HIV/AIDs remain the five top non-oncology, non-rare diseases targeted by gene therapies



Source: Pharmaprojects| Informa, October 2021

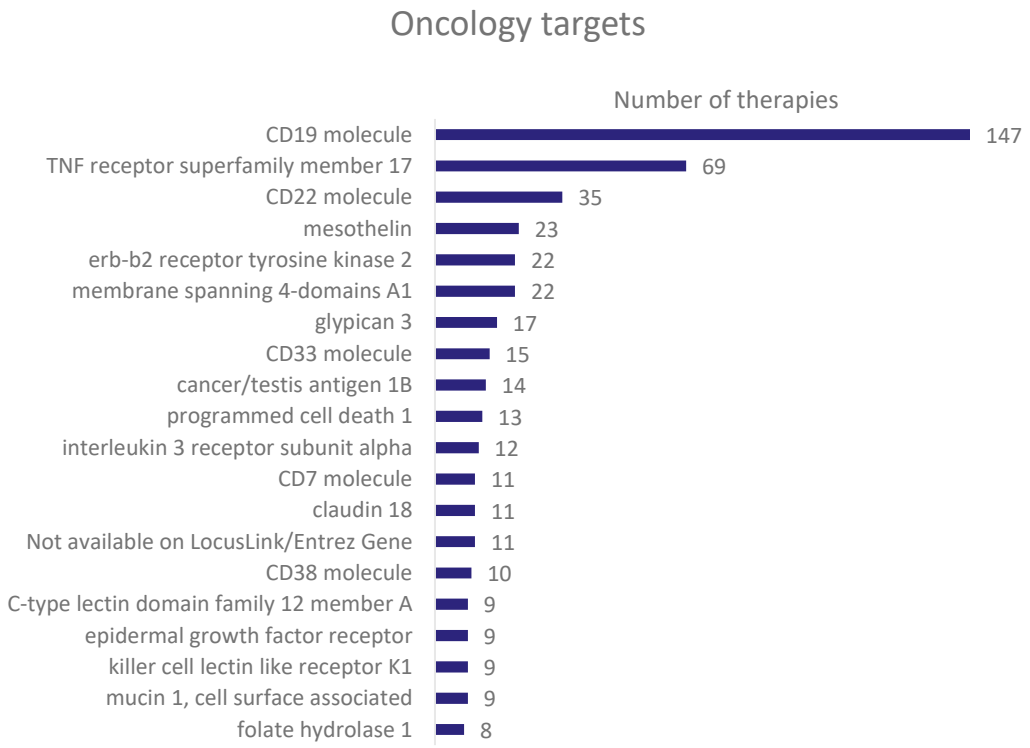
*figures based on indications in pipeline development only for each therapy

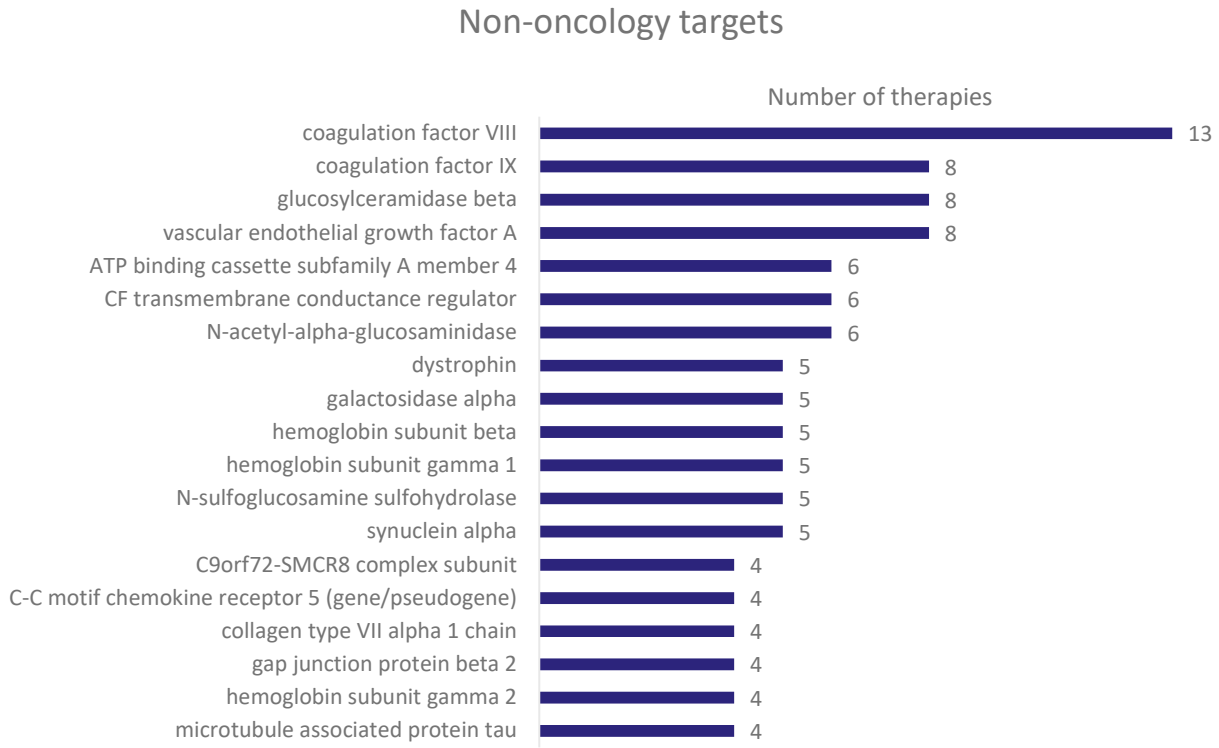
American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common targets

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

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



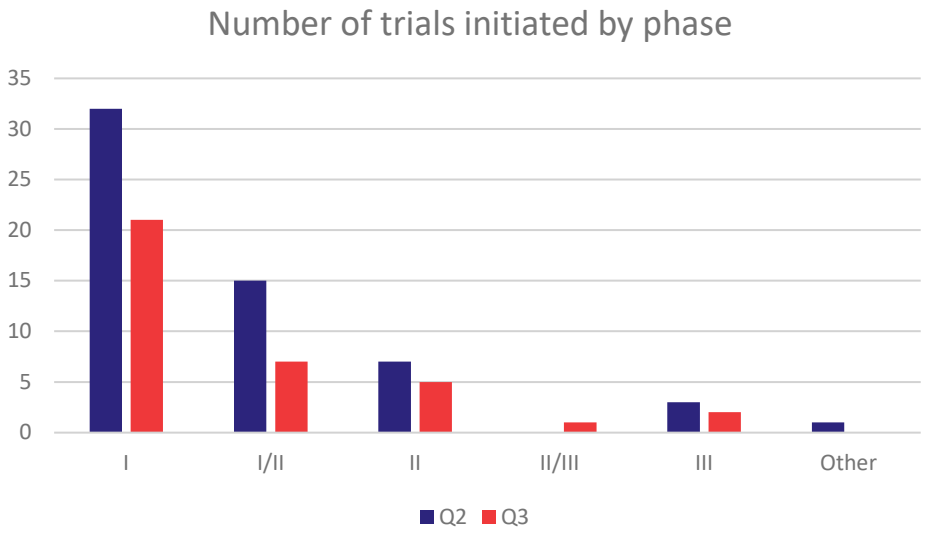


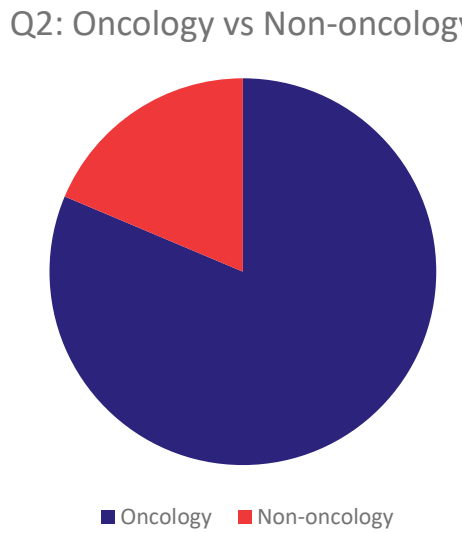
Source: Pharmaprojects| Informa, October 2021

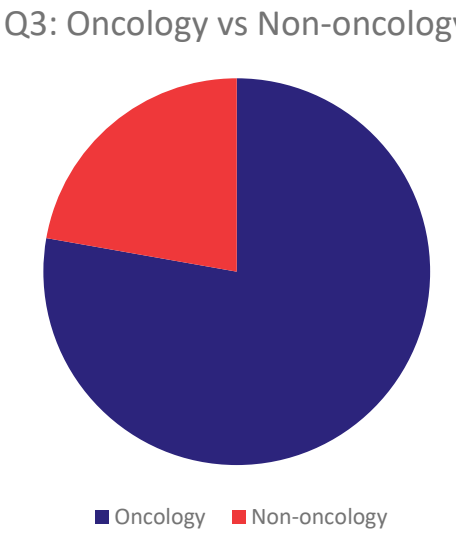
American Society of Gene + Cell Therapy

Gene therapy clinical trial activity in 2021

- 36 trials were initiated in Q3 for gene therapies, compared to 58 in Q2
- The number of trials initiated in Q3 for therapies for non-oncology diseases increased slightly from 19% to 22% from Q2







Source: Trialtrove| Informa, October 2021

American Society of Gene + Cell Therapy

Non-genetically modified cell therapy pipeline

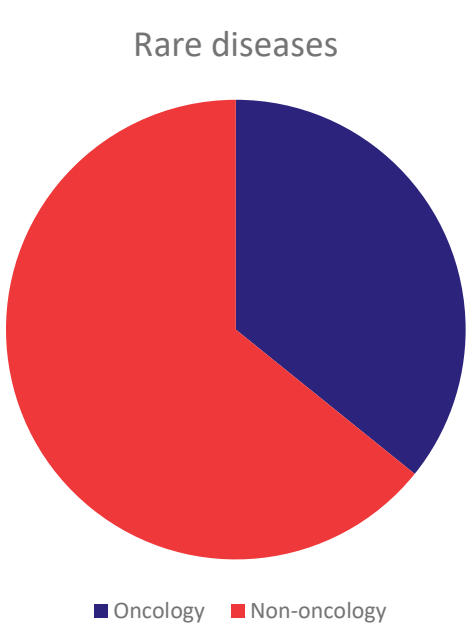
Q3 2021

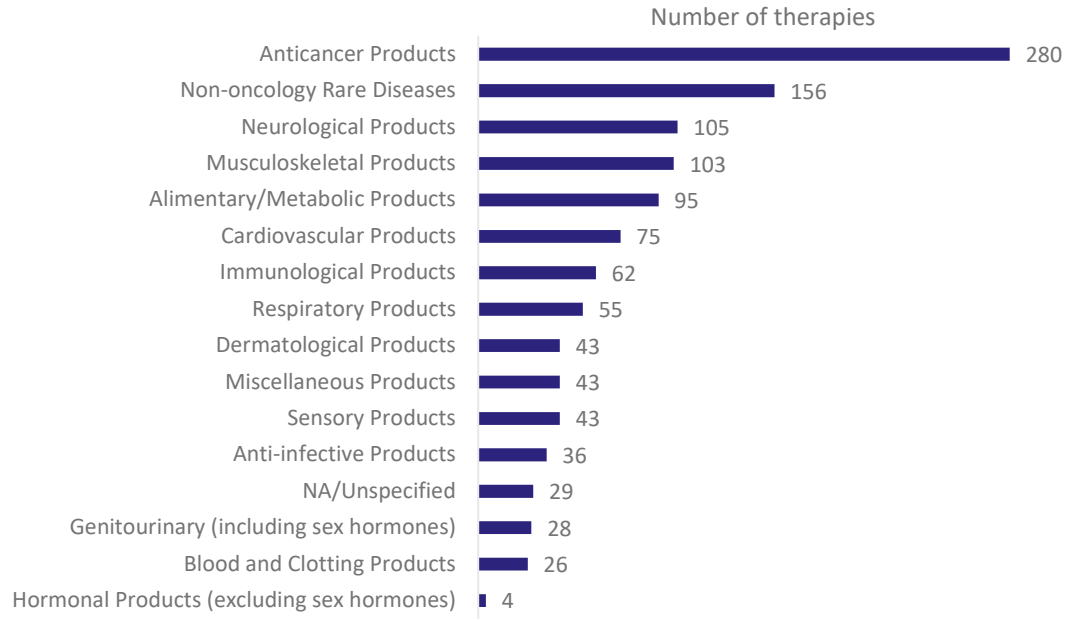
American Society of Gene + Cell Therapy

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

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

- As with gene therapies, non-genetically modified cell therapies continue to most commonly target oncology and rare diseases
- Of the non-genetically modified cell therapies in preclinical to pre-registration stages for rare diseases, 66% are in development for non-oncology rare diseases





Source: Pharmaprojects| Informa, October 2021

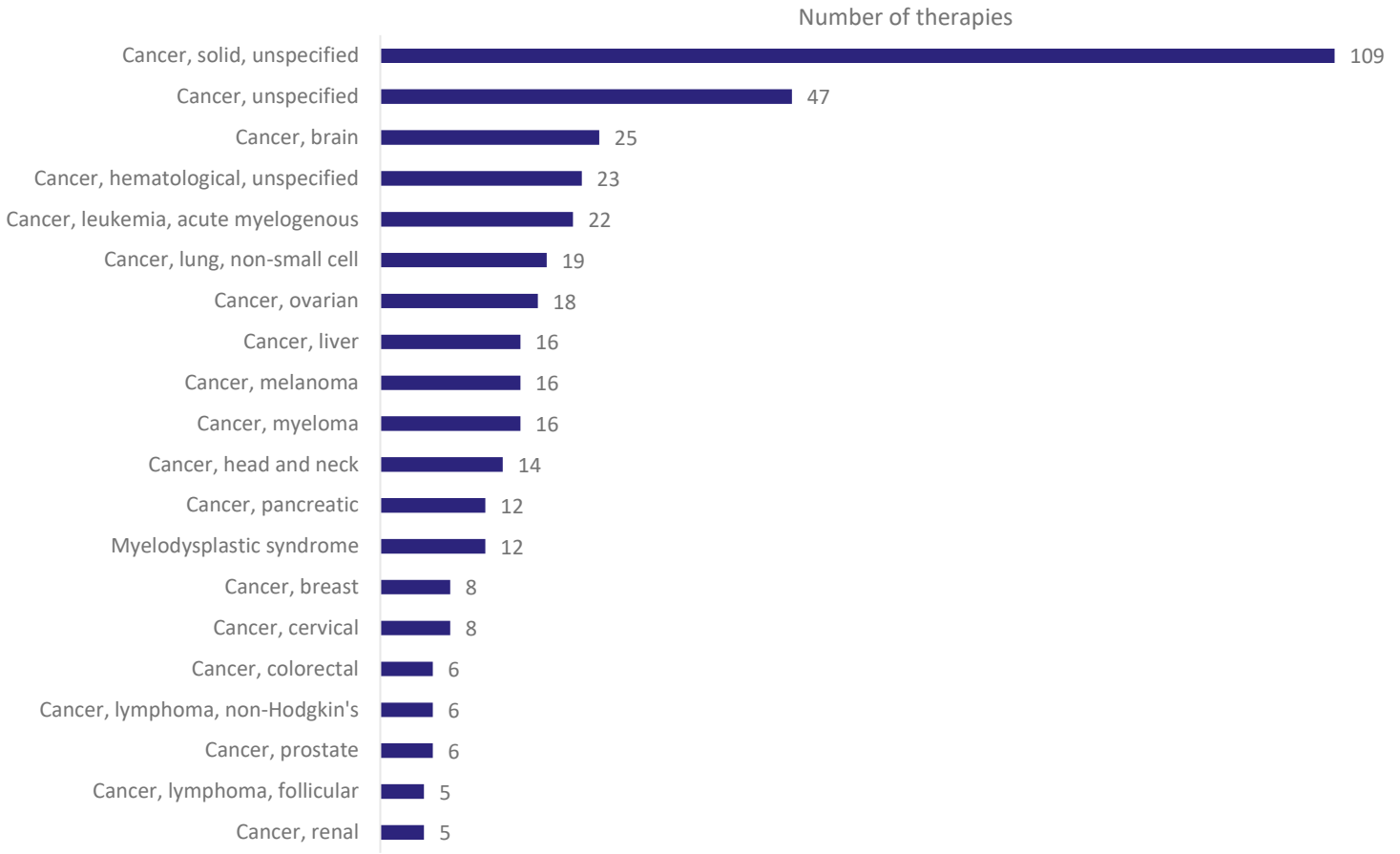
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

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

- Of the diseases for which indications are specified, the top three indications are brain cancer, acute myelogenous leukemia, and non-small cell lung cancer



Source: Pharmaprojects| Informa, October 2021

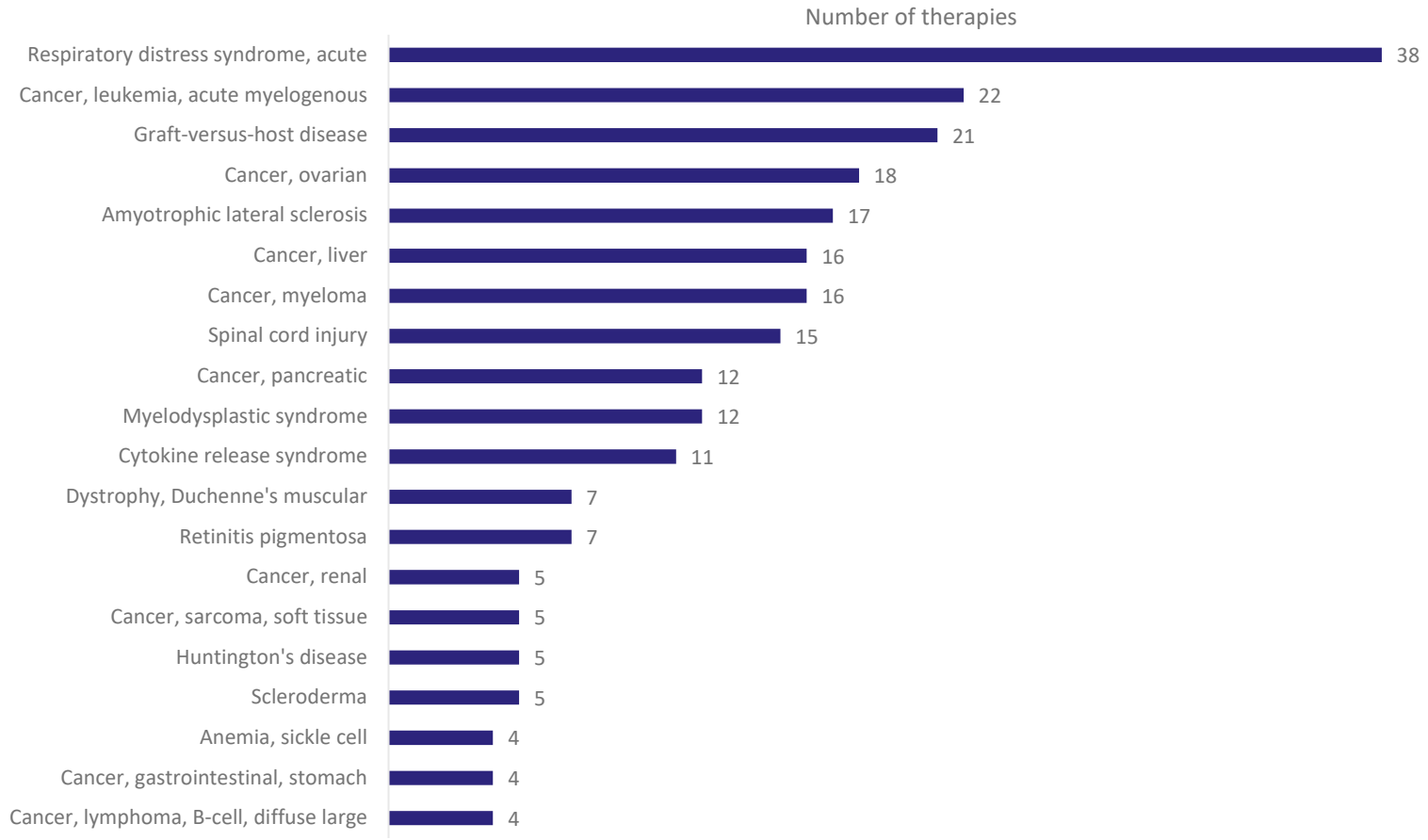
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

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

- The top three non-oncology indications are respiratory distress syndrome (ARDS), graft-versus-host disease (GVHD), and amyotrophic lateral sclerosis



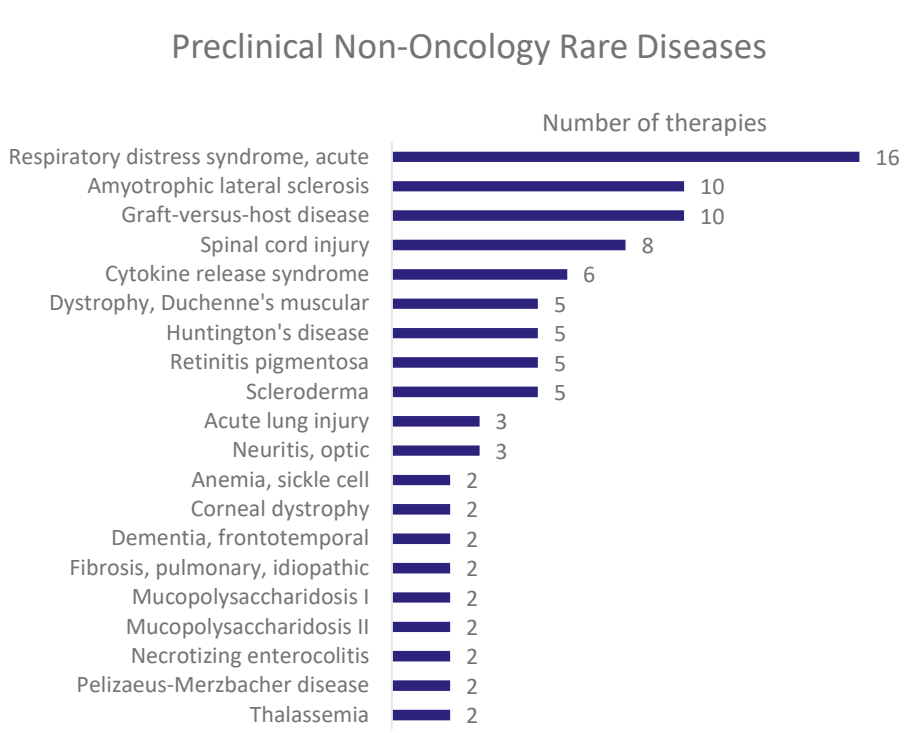
Source: Pharmaprojects| Informa, October 2021

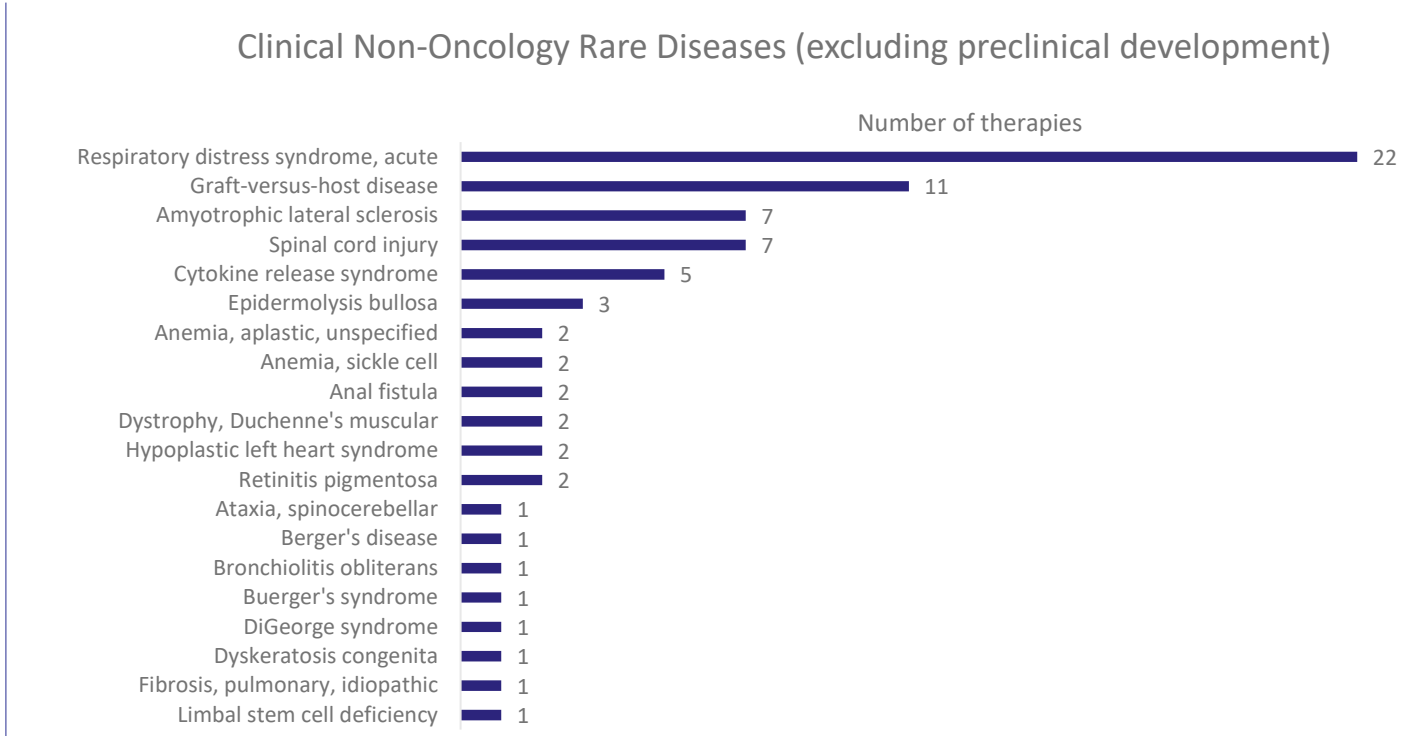
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

Non-oncology rare diseases: Preclinical vs. clinical

- Development is split more evenly between preclinical and clinical studies compared to gene therapies, with 103 therapies for non-oncology rare diseases in preclinical stages and 64 therapies for non-oncology rare diseases in phase I through pre-registration





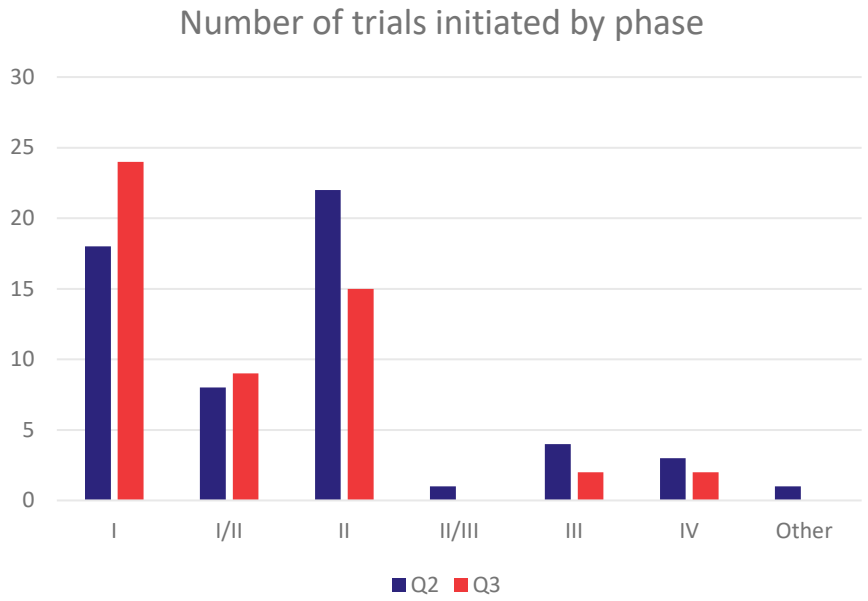
Source: Pharmaprojects| Informa, October 2021

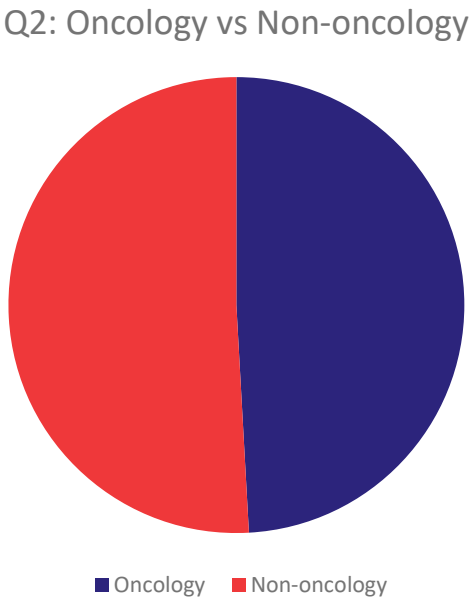
*figures based on indications in pipeline development only for each therapy

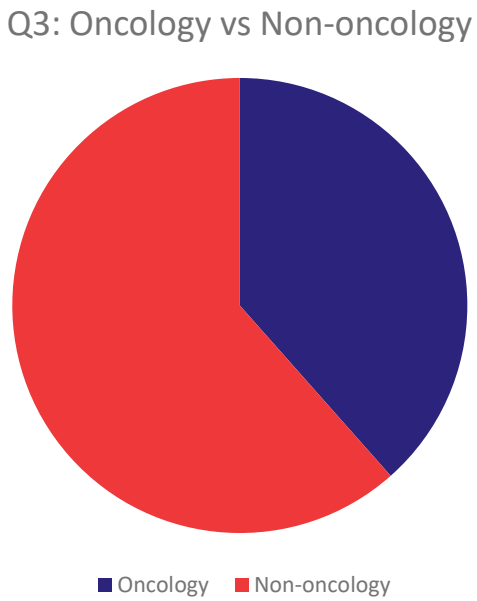
American Society of Gene + Cell Therapy

Non-genetically modified cell therapy trial activity in 2021

- 52 trials were initiated for non-genetically modified cell therapies in Q3, 62% of which were for non-oncology indications







Source: Trialtrove| Informa, October 2021

American Society of Gene + Cell Therapy

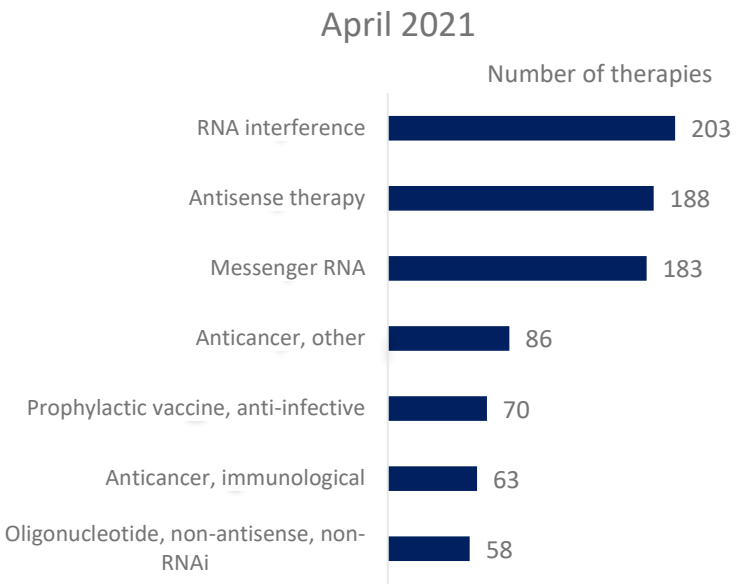
RNA therapy pipeline

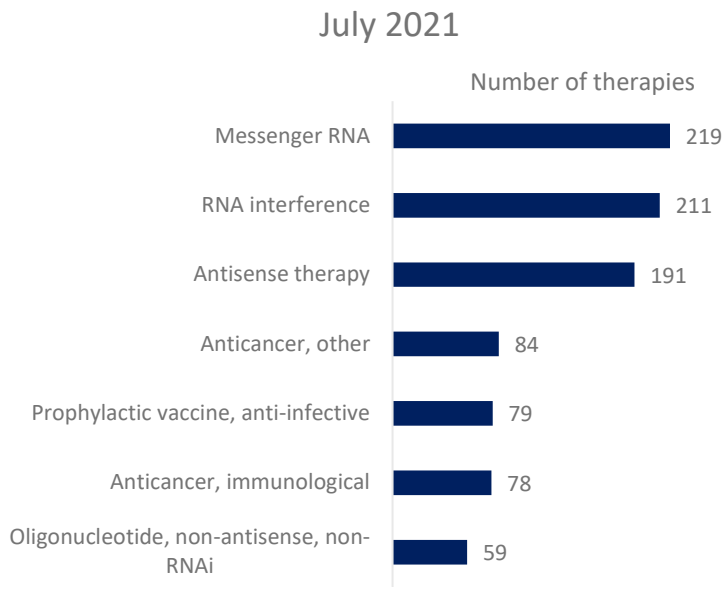
Q3 2021

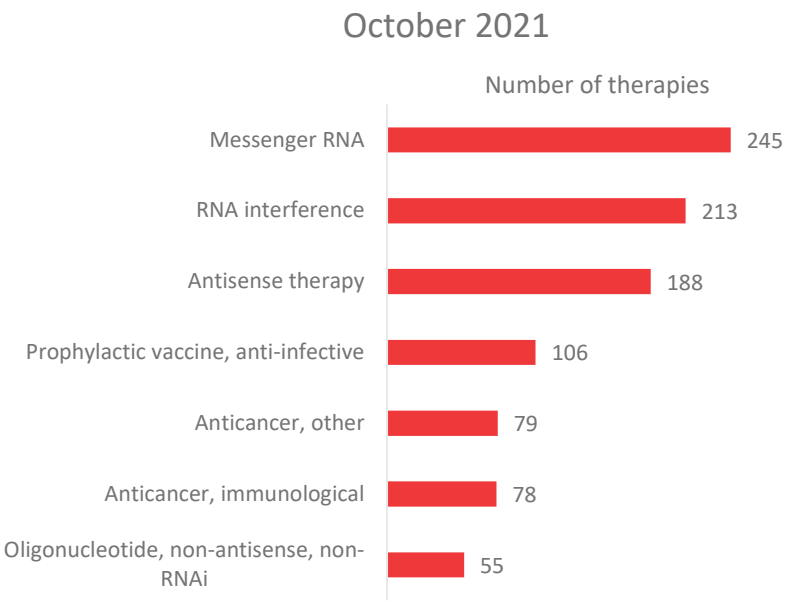
American Society of Gene + Cell Therapy

RNA therapy pipeline: Most common modalities

- Between Q2 and Q3 2021, messenger RNA therapeutics remain the top modality, while anti-infective prophylactic vaccines overtook “Anticancer, other” therapeutics as the fourth most common modality





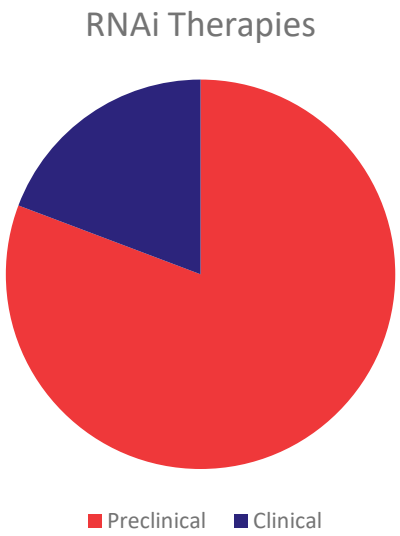


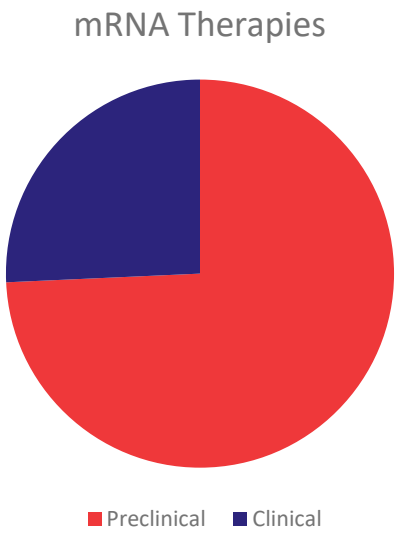
Source: Pharmaprojects| Informa, October 2021

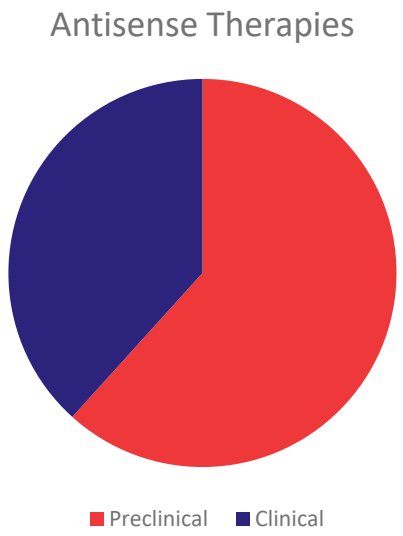
American Society of Gene + Cell Therapy

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

- Preclinical development dominates RNAi, mRNA, and antisense therapeutics, representing 81%, 74%, and 62% of development respectively





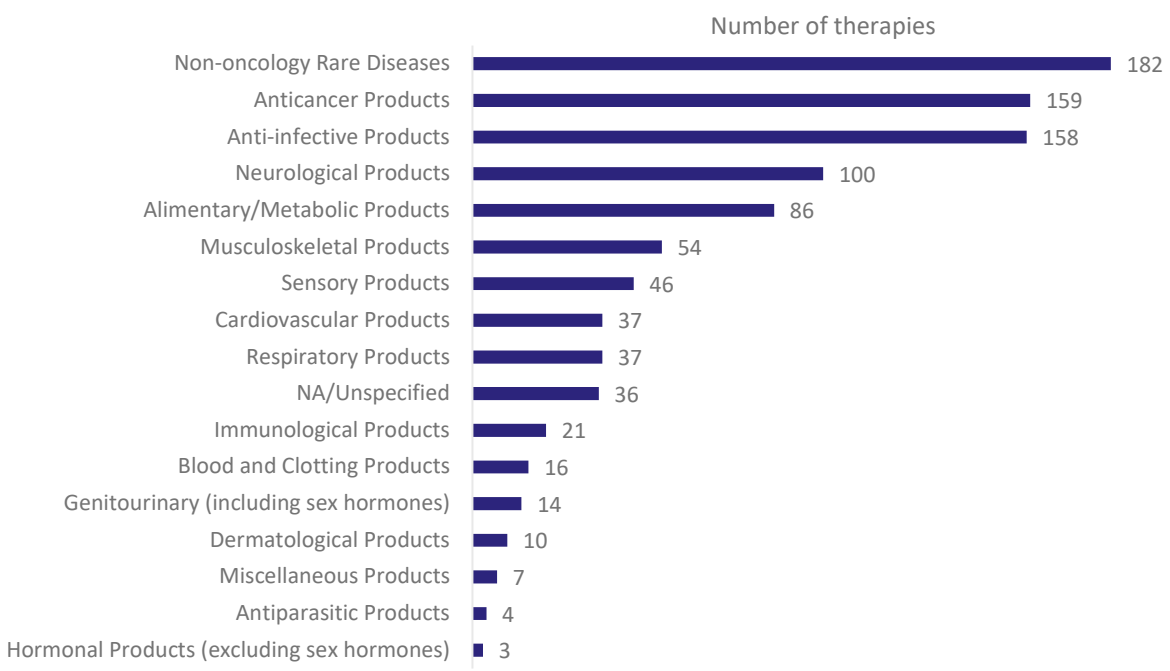


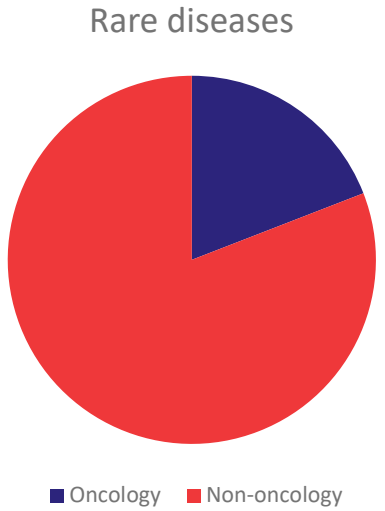
Source: Pharmaprojects| Informa, October 2021

RNA therapies: most common diseases targeted

Of the 705 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Rare diseases and oncology continue to be the top two therapeutic areas being targeted, with rare diseases (including oncology rare diseases) remaining on top
- Of all the RNA therapies in preclinical to pre-registration development for rare diseases, 83% are in development for non-oncology rare diseases





Source: Pharmaprojects| Informa, October 2021

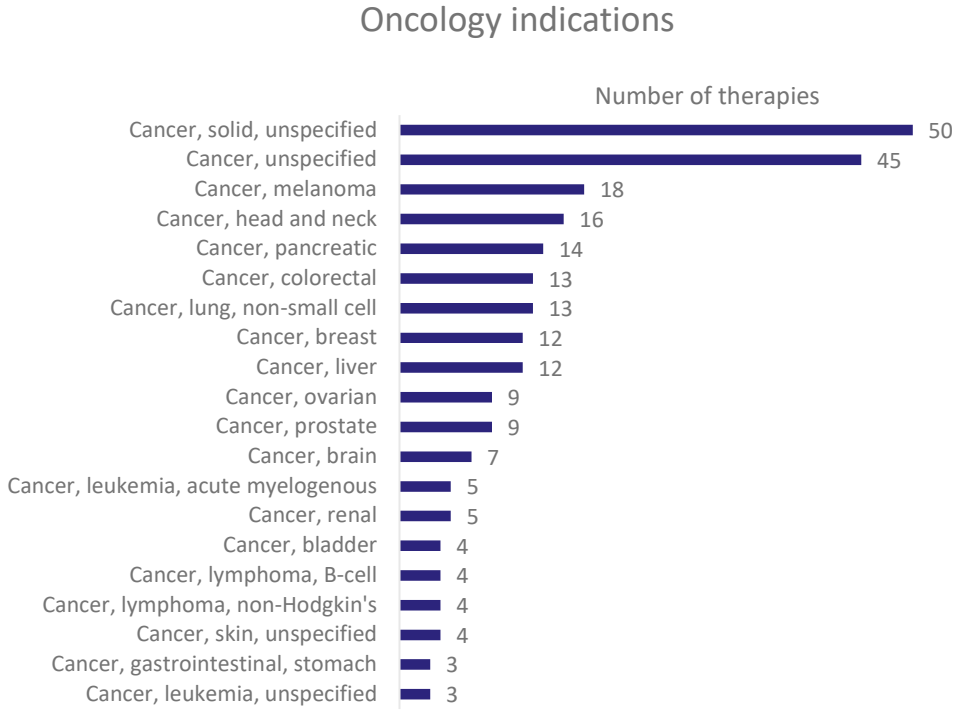
*figures based on indications in pipeline development only for each therapy

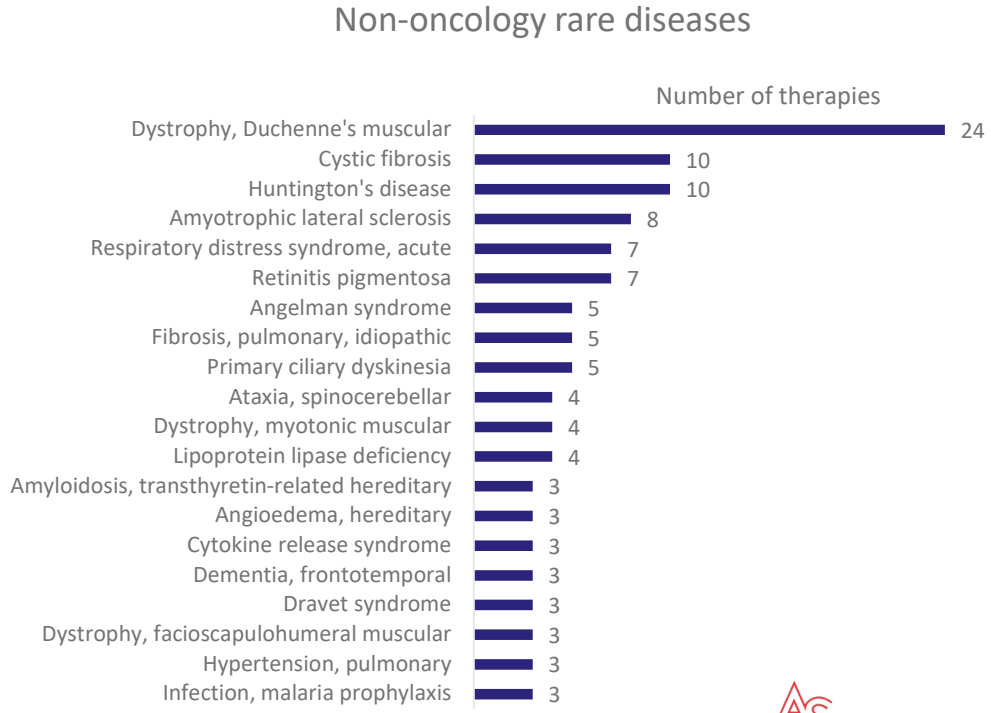
American Society of Gene + Cell Therapy

RNA therapies: most common diseases targeted

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

- Top specified oncology indications are melanoma, head and neck, pancreatic, colorectal, non-small cell lung cancer
- For non-oncology rare diseases, Duchenne's muscular dystrophy, cystic fibrosis, Huntington's disease, amyotrophic lateral sclerosis (ALS), and acute respiratory distress syndrome (ARDS) are the top five targeted diseases





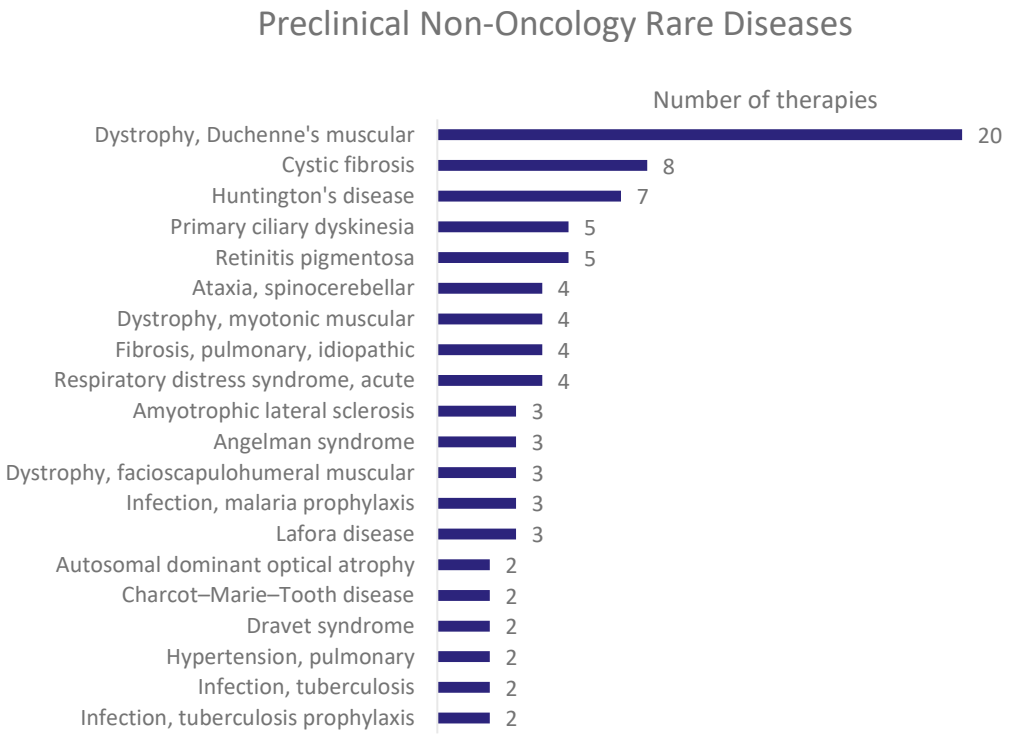
Source: Pharmaprojects| Informa, October 2021

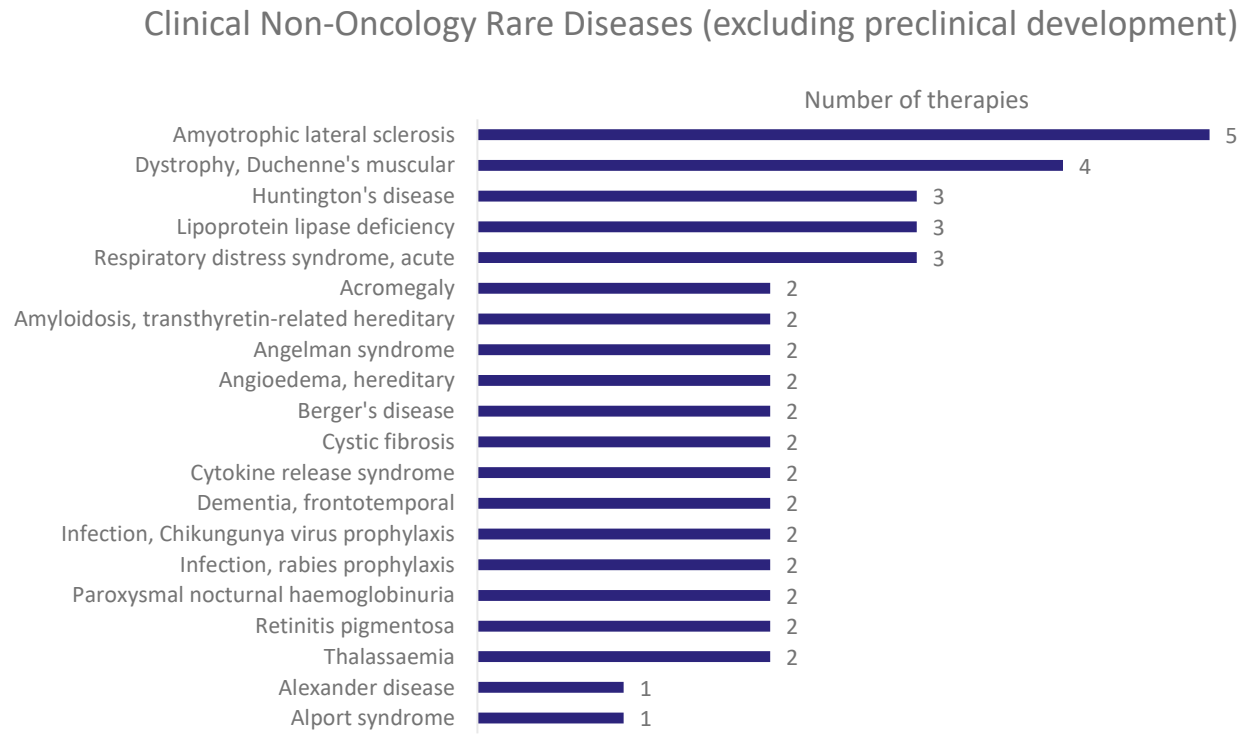
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

Non-oncology rare diseases: Preclinical vs. clinical

- 126 therapies are for non-oncology rare diseases at preclinical stages
- 60 therapies are for non-oncology rare diseases in phase I to pre-registration





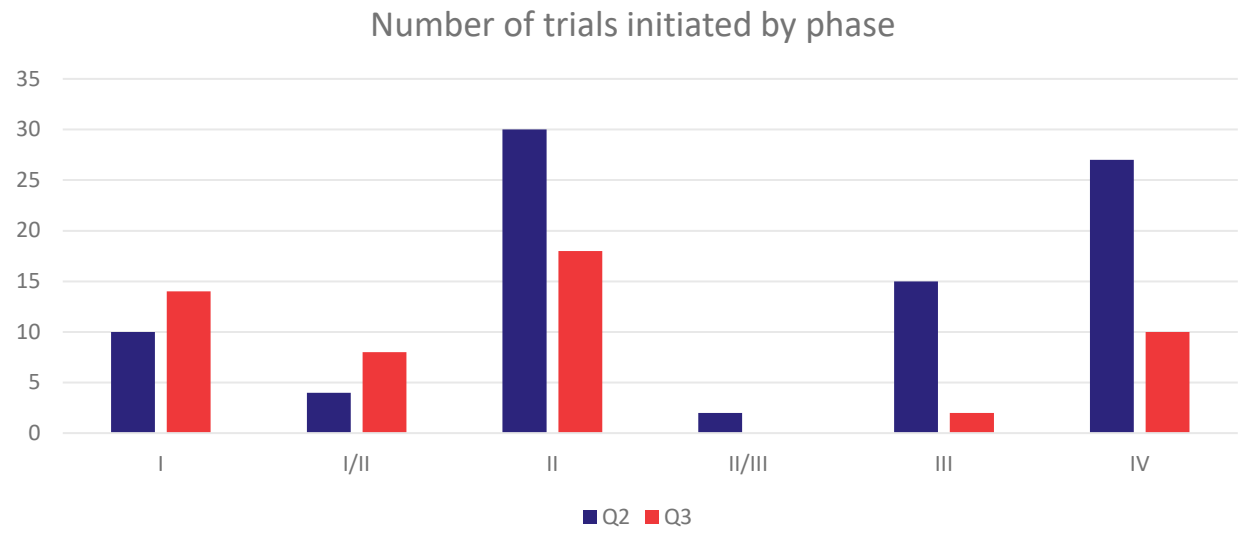
Source: Pharmaprojects| Informa, October 2021

*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

RNA therapy pipeline: Clinical trial activity

- 52 RNA trials were initiated in Q3 of 2021, compared to 88 in Q2
- As in Q2, the number of trials initiated in Q3 were most commonly for non-oncology diseases, representing a vast majority of 96%



Source: Trialtrove| Informa, October 2021

American Society of Gene + Cell Therapy

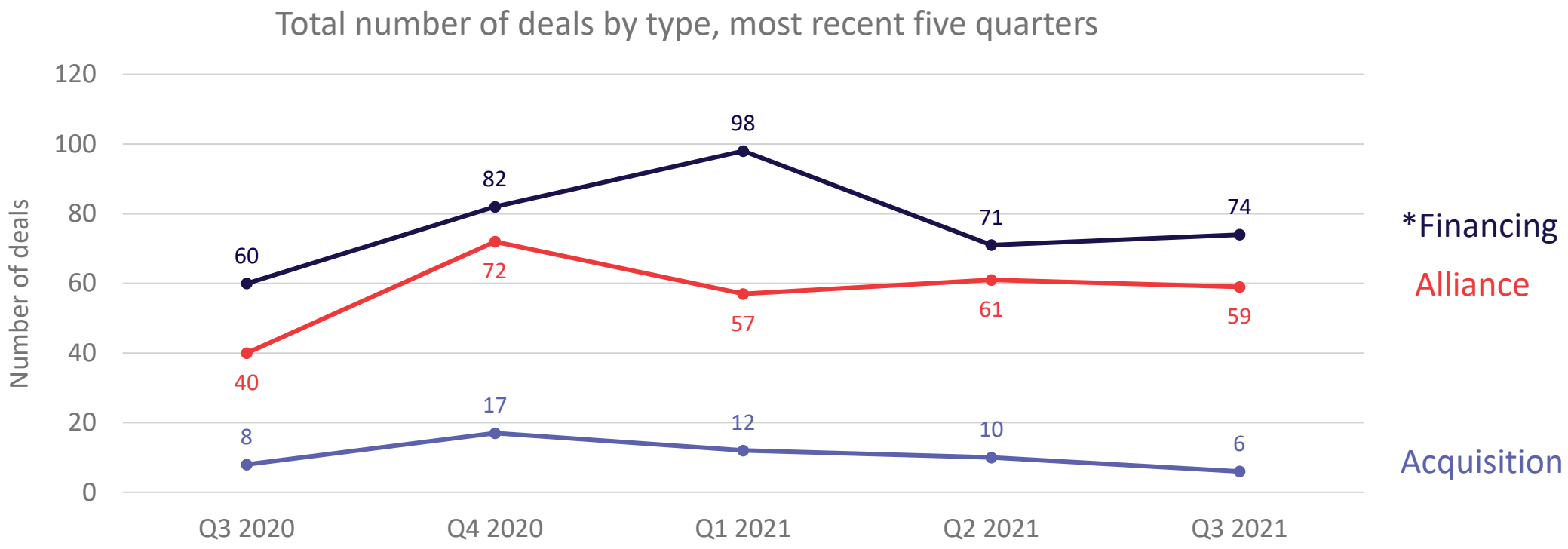
Overview of dealmaking for gene, cell, and RNA therapy companies

Q3 2021

American Society of Gene + Cell Therapy

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

- A total of 139 alliance, acquisition, and financing deals were announced in Q3 2021, which was almost flat with the previous quarter's volume; there was a slight increase in the financing activity compared with Q2, but also four fewer acquisitions than Q2
- Q3's activity shows a 29% increase over the 108 deals signed during the same quarter last year



Source: Biomedtracker| Informa, October 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

Q3 2021 acquisitions in gene, cell, & RNA therapy

- There were four fewer acquisitions in Q3 2021 than in Q2, for a total of six
- Leading this group was Sanofi's $3.2 billion acquisition of Translate Bio, its former partner; and a developer of mRNA vaccines and therapeutics in multiple disease areas including cystic fibrosis, immuno-oncology, and inflammation

Deal Date	Deal Title	Potential Deal Value (USD)
07/02/2021	Sartorius Acquires Majority Stake in CellGenix	118,520,000
07/21/2021	Lexeo Therapeutics Expands Cardiac Gene Therapy Pipeline with Acquisition of Stelios Therapeutics	Undisclosed
07/22/2021	ImmPACT Bio Completes Merger with Kalthera to Progress Next-Generation CAR T Therapies for the Treatment of Cancer	Undisclosed
08/03/2021	Sanofi to Acquire Translate Bio for $3.2B	3,200,000,000
09/29/2021	Amicus Spins Out Gene Therapy Assets into Caritas Therapeutics, Which Reverse Merges with ARYA Sciences Acquisition (SPAC) to Gain Nasdaq Listing	Undisclosed
09/21/2021	Novartis Acquires Arctos Medical, Expanding its Optogenetics Portfolio	Undisclosed

Source: Biomedtracker| Informa, October 2021

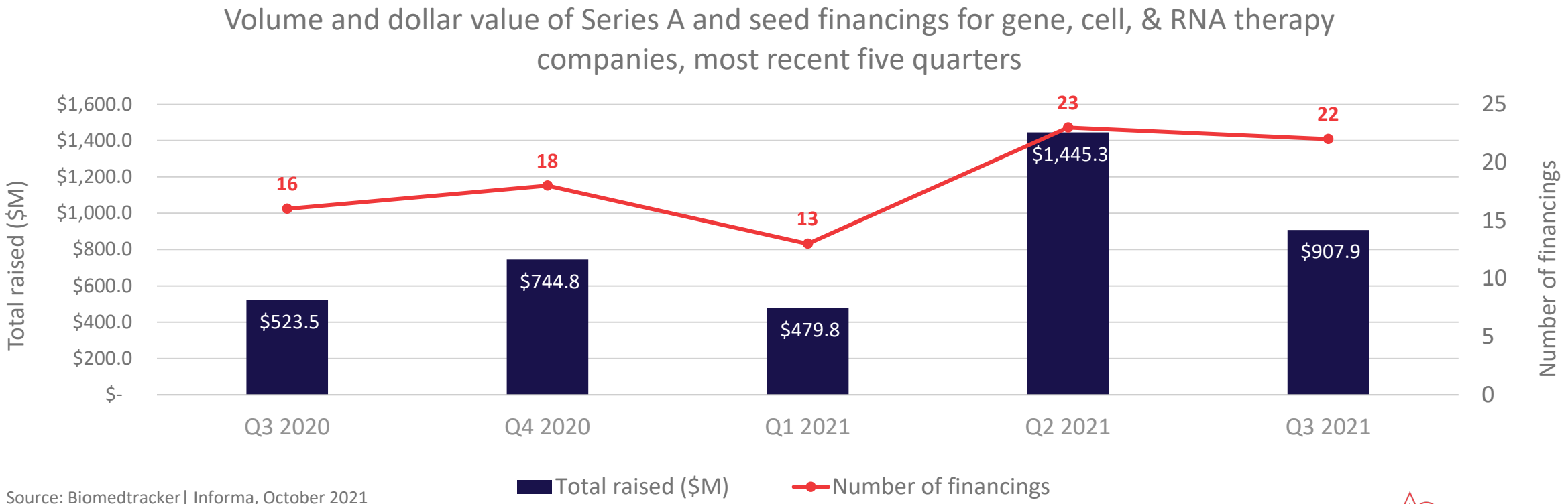
Start-up funding for gene, cell, & RNA therapy companies

Q3 2021

American Society of Gene + Cell Therapy

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

- 22 companies raised seed or Series A financing in Q3 2021, reaching an aggregate $907.9 million, a 37% decrease in dollar volume from Q2, which had almost the same number of companies raising funds but included three biotechs raising >$200 million each
- 82% (18/22) of biotechs are based in the US (mainly Massachusetts and California), the others in China and Canada
- GentiBio led with a $157 million Series A round to support work on engineered Treg including a lead program in Type 1 diabetes



Source: Biomedtracker| Informa, October 2021

American Society of Gene + Cell Therapy

Q3 2021 start-up financing for gene, cell, & RNA therapy companies (1/3)

Deal Date	Deal Title	Modality type	Company Location	Academic Source	Potential Deal Value (USD, $M)
07/12/2021	Incisive Genetics Closes $2.5M Seed Investment	Gene editing	Canada, Vancouver	University of British Columbia	3
07/13/2021	Suono Bio, Inc. Raises $8.5M in Oversubscribed Series A Funding Round Led by Axil Capital and Mizuho Securities Principal Investment	Gene therapy	United States, Massachusetts, Cambridge	Massachusetts Institute of Technology; Brigham and Women's Hospital	9
07/13/2021	Prime Medicine raises $115M in Launch Round	Gene editing (prime editing)	United States, Massachusetts, Cambridge	Broad Institute of MIT and Harvard	115
07/15/2021	Stemson Therapeutics Secures $15M Series A Funding to Cure Hair Loss	Non-genetically modified cell therapy	United States, California, San Diego	Sanford Burnham Prebys Medical Discovery Institute	15
07/15/2021	Grit Biotechnology Completes Series A+ Financing to Accelerate Development of its Tumor Infiltrating Lymphocyte (TIL) Therapy Pipeline	TILs	China, Shanghai	Duke University; University of Southern California	Undisclosed
07/22/2021	Kernal Bio Closes 10.5M Seed Round Funding	mRNA	United States, Massachusetts, Cambridge	Massachusetts Institute of Technology; Harvard	11
08/03/2021	SeQure Dx Secures $17.5M Series A Funding	Gene editing diagnostics	United States, Massachusetts, Waltham	Massachusetts General Hospital	18
08/05/2021	Encellin Closes $5.9M Seed Financing	Cell factory implant	United States, California, San Francisco	University of California San Francisco	6
08/11/2021	GentiBio Raises $157M in Series A Financing to Advance Engineered Regulatory T-cells to Treat Autoinflammation	Genetically modified Tregs	United States, Massachusetts, Boston	Seattle Children's Research Institute, Benaroya Research Institute at Virginia Mason, and MIGAL Galilee Research Institute	157

Source: Biomedtracker| Informa, October 2021

Q3 2021 start-up financing for gene, cell, & RNA therapy companies (2/3)

Deal Date	Deal Title	Modality type	Company Location	Academic Source	Potential Deal Value (USD, $M)
8/30/2021	NeuExcell Therapeutics Raises Over $10M in Series Pre-A Round	AAV gene therapy	United States, Pennsylvania, State College	Penn State University	10
08/31/2021	HebeCell Raises $53M in Series A Financing to Advance Off-The-Shelf PSC-CAR-NK Products Into Clinics	Non-genetically modified NK cell therapy	United States, Massachusetts, Natick	n/a (co-founded by Shi-Jiang (John) Lu [formerly of Advanced Cell Technology/Ocata Therapeutics] and Allen Feng [formerly of Semma Therapeutics])	53
09/08/2021	Replicate Bioscience Secures $40M in Series A Fundraising	Self-replicating RNA	United States, California, San Diego	Duke University, in collaboration with Nathaniel Wang (formerly of Synthetic Genomics) and Andy Geall (formerly of Novartis Vaccines and Diagnostics)	40
09/09/2021	iECURE Launches With $50M Series A Financing	Gene editing	United States, Pennsylvania, Philadelphia	University of Pennsylvania Gene Therapy Program	50
9/13/2021	Walking Fish Therapeutics Launches with $50M Series A Financing	Engineered B cells	United States, California, San Francisco	n/a (co-founded by Lewis T. "Rusty" Williams [formerly of Five Prime Therapeutics])	50
09/13/2021	Cytovia's Newly Formed China-Focused CytoLynx JV Raises $45M in Financing Round	Allogeneic cell therapy	China, Shanghai	n/a (joint venture betweeen Cytovia Therapeutics and TF Capital)	45
09/16/2021	Anjarium Biosciences Raises $61M Series A Financing to Develop Non-viral Gene Therapies	Non-viral (nanoparticle) gene therapy	Switzerland, Schlieren	Undisclosed	61
09/22/2021	Opus Genetics Launches with $19M Seed Funding to Advance Gene Therapy Treatments for Blinding Conditions	AAV gene therapy	United States, North Carolina, Raleigh	Perelman School of Medicine at the University of Pennsylvania, Penn's Center for Advanced Retinal Ocular Therapeutics, Harvard Medical School, and Massachusetts Eye and Ear	19
09/23/2021	Garuda Therapeutics Launches with $72M Series A Financing	Allogeneic cell therapy	United States, Massachusetts, Natick	Harvard Stem Cell Institute, Broad Institute of MIT and Harvard, Brigham and Women's Hospital	72

Source: Biomedtracker| Informa, October 2021

Q3 2021 start-up financing for gene, cell, & RNA therapy companies (3/3)

Deal Date	Deal Title	Modality type	Company Location	Academic Source	Potential Deal Value (USD, $M)
9/23/2021	GenEdit Announces $26m Series A Financing	Non-viral (nanoparticle) gene therapy	United Stage, California, San Francisco	University of California Berkeley	26
09/28/2021	Kytopen Raises $30M in Series A Funding	Genetically modified cell therapy manufacturing	United States, Massachusetts, Cambridge	Massachusetts Institute of Technology	30
09/28/2021	Acrigen Biosciences Raises Seed Financing to Advance Precision Gene Editing Technology and Therapeutic Pipeline	Gene editing	United States, California, Berkeley	University of California Berkeley	Undisclosed
09/30/2021	CBMG Holdings Completes $120M in Series A Funding	CAR T-cell therapy	United States, New York, New York	n/a (was taken private in management buy-out in 2019)	120

Source: Biomedtracker| Informa, October 2021

Notable Q3 2021 start-up gene, cell, & RNA therapy companies

	Company details	Academic source	Financing type/amount raised	Lead investor(s)	Therapy areas of interest
gentibio	Engineers Tregs to target tissues damaged by abnormal immune responses	Seattle Children's Research Institute, Benaroya Research Institute at Virginia Mason, and MIGAL Galilee Research Institute	Series A/$157M	Matrix Capital Management	Autoimmune, alloimmune, autoinflammatory, and allergic diseases; lead program for Type 1 diabetes
NeuExcell THERAPEUTICS	Performs astrocyte-to-neuron conversion *in vivo* through AAV gene therapy that introduces neural transcription factors	Penn State University	Series Pre-A/>$10M	Co-Win Ventures	Neurodegeneration
OPUS GENETICS	Develops AAV gene therapies for inherited forms of blindness	Perelman School of Medicine at the University of Pennsylvania, Penn's Center for Advanced Retinal Ocular Therapeutics, Harvard Medical School, and Massachusetts Eye and Ear	Seed/$19M	Retinal Degeneration Fund	Ophthalmology (Leber congenital amaurosis)

Source: Biomedtracker| Informa, October 2021

Upcoming catalysts

Q3 2021

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward looking events) that are expected in Q4 2021

Therapy	Generic Name	Disease	Catalyst	Catalyst Date
RVT-802 (Rethymic)	Allogeneic processed thymus tissue–agdc	DiGeorge Syndrome	PDUFA for BLA - Second Review	8 Oct 2021 – 8 Oct 2021
CVnCoV Vaccine	COVID-19 vaccine (CureVac)	COVID-19 Prevention	Rolling MAA Completed (EU)	30 Sep 2021 – 31 Oct 2021
Ciltacabtagene Autoleucel	Ciltacabtagene Autoleucel	Multiple Myeloma (MM)	PDUFA for BLA - First Review	29 Nov 2021 – 29 Nov 2021
Breyanzi	Lisocabtagene Maraleucel	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	CHMP Opinion	30 Sep 2021 – 30 Nov 2021
PTC-AADC	Eladocagene exuparvovec	Neurology - AADC deficiency	CHMP Opinion	1 Oct 2021 – 31 Dec 2021
Leqvio	Inclisiran	Dyslipidemia / Hypercholesterolemia	PDUFA for NDA – Second Review	31 Dec 2021 – 31 Dec 2021
Yescarta	Axicabtagene ciloleucel	Marginal Zone Lymphoma - NHL	PDUFA for sBLA - First Review	30 Sep 2021 – 31 Dec 2021
Roctavian	Valoctocogene roxaparvovec	Hemophilia A	CHMP Opinion	31 Dec 2021 – 28 Feb 2022

Source: Biomedtracker| Informa, October 2021

Appendix

Methodology, sources, & glossary of key terms

Q3 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 use of genetic material to treat or prevent disease. For the purpose of this report, the following terms shall mean the following:

Gene therapy	Therapies containing an active ingredient synthesized following vector-mediated introduction of a genetic sequence into target cells *in-* or *ex-vivo*. Used to replace defective or missing genes (as in cystic fibrosis) as well as to introduce broadly acting genetic sequences for the treatment of multifactorial diseases (e.g. cancer). Direct administration of oligonucleotides without using vectors is covered separately in the antisense therapy class; RNA interference class; or oligonucleotide, non-antisense, non-RNAi class. Platform technologies for gene delivery are covered separately in the gene delivery vector class.
Cellular therapy, chimeric antigen receptor **Falls under gene therapy in this report*	Cellular therapy consisting of T cells that have been modified to express a chimeric antigen receptor (CAR) – this is a cell surface receptor that gives the T cells the ability to target a specific protein and fight the targeted cells.
Cellular therapy, T cell receptor **Falls under gene therapy in this report*	Cellular therapies whereby natural T-cells collected for the patient, are engineered to express artificial receptors (usually through viral transfections) that would target specific intracellular antigens (as peptides bound to proteins encoded by the major histocompatibility complex, MHC).
Lytic virus **Falls under gene therapy in this report*	Therapies which have a replication-competent virus, that lyse pathogenic cells directly. These are normally genetically modified to render them harmless to normal tissues. Examples include oncolytic viruses which specifically attack cancer cells.

Glossary of Key Terms

Therapy type definitions, cont.

Cell therapy includes the following therapeutic classes:

Cellular therapy, stem cell	Regenerative therapy which promotes the repair response of injured tissue using stem cells (cells from which all other specialized cells would originate).
Cellular therapy, tumor infiltrating lymphocyte	Adoptive cellular transfer of tumor resident T cells from tumor material, their expansion *ex vivo,* and transfer back into the same patient after a lymphodepleting preparative regimen.
Cellular therapy, other	Cellular therapies that do not fall under the categories of cellular therapy, stem cell; cellular therapy, CAR; cellular therapy, TIL; cellular therapy, TCR; or the specific cellular therapy are unspecified.

Glossary of Key Terms

Therapy type definitions, cont.

RNA therapy includes the following therapeutic classes:

Messenger RNA	Therapies that carry the desired mRNA code to overcome genetic mutations. The mRNA sequence will replace the defective mRNA in a patient and starts producing the desired protein.
Oligonucleotide, non-antisense, non-RNAi	Synthetic therapeutic oligonucleotides which operate by a mechanism other than antisense or RNA interference (RNAi). This includes ribozymes, aptamers, decoys, CpGs, and mismatched and immunostimulant oligonucleotides. Sequences delivered using vectors (gene therapy) are covered separately in “gene therapy.“ Antisense and RNAi oligonucleotides are covered separately in “antisense therapy" and "RNA interference,“ respectively.
RNA interference	Includes products which act therapeutically via an RNA interference (RNAi) mechanism, including small interfering RNAs (siRNAs). These may be synthetic oligonucleotides, or RNAi sequences may be expressed from a vector as a form of gene therapy (see “gene therapy" therapeutic class). *In vivo*, these sequences block the expression of a specific protein by forming an RNA-induced silencing complex, which then specifically binds to and degrades a complementary mRNA encoding the target protein. The use of RNAi purely as a drug discovery tool (e.g., in transgenic animal model production or in target validation) is not covered in this section.
Antisense therapy	Antisense compounds under development as potential therapeutics. These may be synthetic oligonucleotides, or antisense RNA may be expressed from a vector as a form of gene therapy. They may prevent the expression of a specific protein *in vivo* by binding to and inhibiting the action of mRNA, since they have a specific oligonucleotide sequence which is complementary to the DNA or RNA sequence which codes for the protein.

Glossary of Key Terms

Development status definitions

Pipeline	Drugs that are in active development
Preclinical	Not yet tested in humans
Phase I	Early trials, usually in volunteers, safety, PK, PD
Phase II	First efficacy trials in small numbers of patients
Phase III	Large scale trials for registrational data
Pre-registration	Filing for approval made to regulatory authorities
Approved	Approval from relevant regulatory authorities for human use

Unspecified indications

Cancer, unspecified	Indications for which the specific tumor type is not specified
Cancer, hematological, unspecified	Indications for which the specific hematological cancer is not specified
Cancer, solid, unspecified	Indications for which the specific solid tumor is not specified

Deal type categories

Alliances	Co-marketing, co-promotion, disease management, joint venture, manufacturing or supply, marketing-licensing, product or technology swap, product purchase, R+D and marketing-licensing, reverse licensing, trial collaborations
Financing	Convertible debt, FOPO, IPO, nonconvertible debt, financing/other, private investment in public equity, private placement, royalty sale, special-purpose financing vehicle, spin-off
Acquisitions	Buy-out, divestiture, spin-out, full acquisition, partial acquisition, reverse acquisition

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