Gene, Cell, & RNA Therapy Landscape

Q4 2021 Quarterly Data Report

Q4 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.

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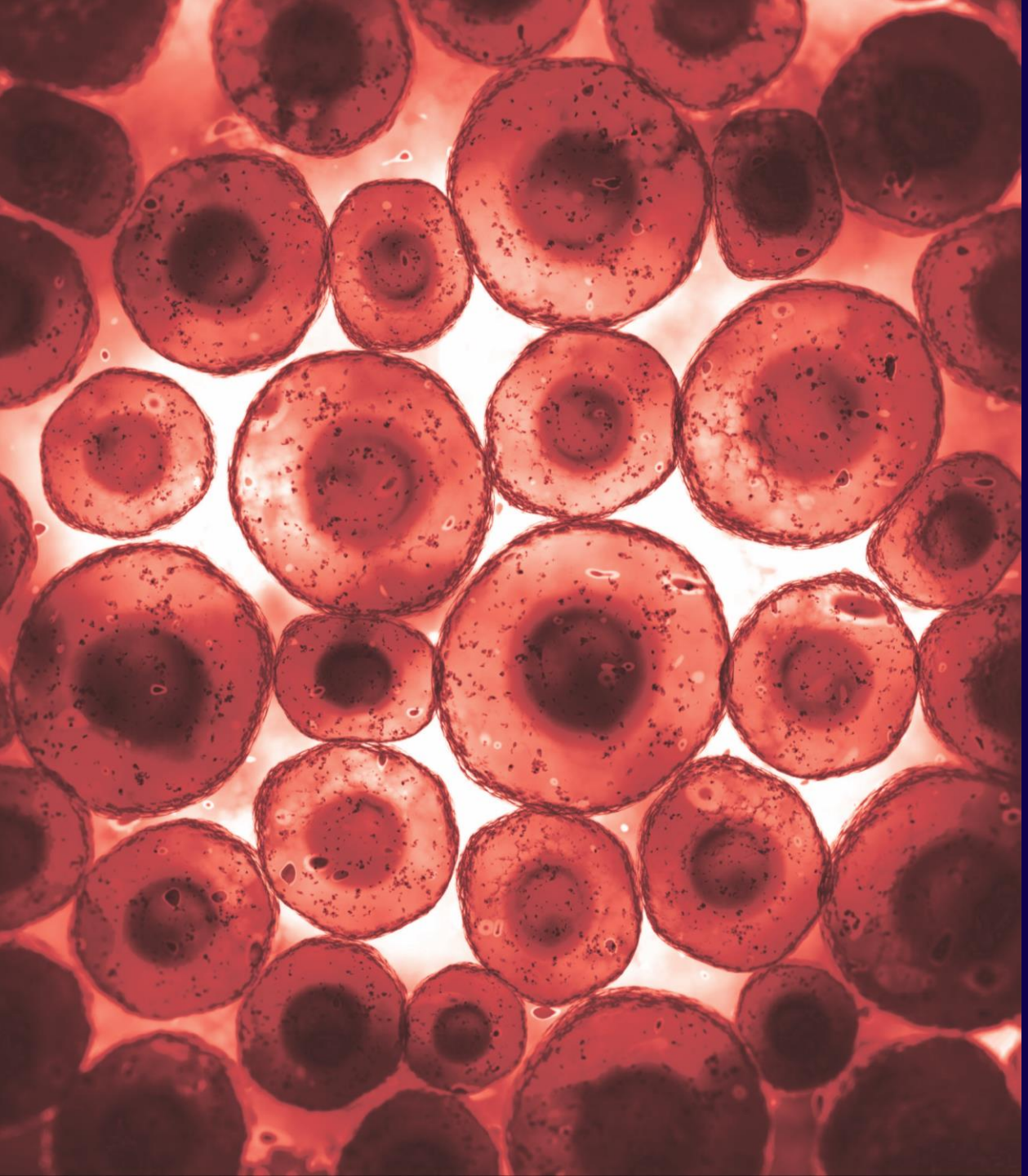

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American Society of Gene + Cell Therapy

Introduction

ASGCT would like to welcome you to the fourth quarter report of a series with our data partner, Informa Pharma Intelligence. Now completing its first year, this series continues to be the only field-wide report of this kind covering key data points in the therapeutics pipeline, clinical targets, developer progress, and more, over time. Globally, there are now 3,483 gene, cell, and RNA therapies in development from preclinical through pre-registration stages.

Highlights in Q4 2021 include approval of a new cell therapy and a new RNA therapy in the U.S., expansion of two RNA therapies for COVID-19 to new countries (Egypt, Malaysia, and Colombia) and expanded approval of a gene therapy for a new indication (acute lymphocytic leukemia).

This quarter, two of the pipeline's most commonly targeted indication groups are rare diseases—including gene therapy development for myeloma, non-Hodgkin's lymphoma, acute myelogenous leukemia, B-cell lymphoma, and ovarian cancer—and oncology. On the gene therapy side, Phase III development increased by 10%, which was the largest growth from the previous quarter.

Start-up financing for gene, cell, and RNA therapy companies continued to decline in dollar value and amount in Q4, dropping to $510.3 million. You can find more information on Q4 financing and start-up companies as well as noteworthy catalysts expected in Q1 2022 in the report.

Key takeaways from Q4 2021

One new cell therapy has been approved since Q3

- Rethymic, a tissue-based regenerative therapy developed by Enzyvant Sciences was approved for DiGeorge syndrome in the U.S.

Rare diseases are among the most commonly targeted indication groups across the gene, cell, and RNA therapeutic pipelines

- The other most commonly targeted indication group for cell and gene therapies is oncology, while for RNA therapies it is infectious diseases
- Of the rare diseases being targeted by gene therapies in the pipeline, the majority are oncological, while for non-genetically modified cell therapies and RNA therapies the majority are non-oncological
- The top five rare diseases for which gene therapies are being developed in the pipeline are: Myeloma, non-Hodgkin's lymphoma, acute myelogenous leukemia, B-cell lymphoma, and ovarian cancer

Start-up financing continues its downward trend

- After peaking in Q2, start-up financing has continued declining: With a total $510.3 million raised in 15 seed and Series A financings during Q4 2021, representing a 44% decrease in value from the previous quarter
- Chroma Medicine, the top fundraiser of Q4, brought in $125 million in a combined seed and Series A round to continue developing its epigenetic editing platform

Key highlights in Q4 2021

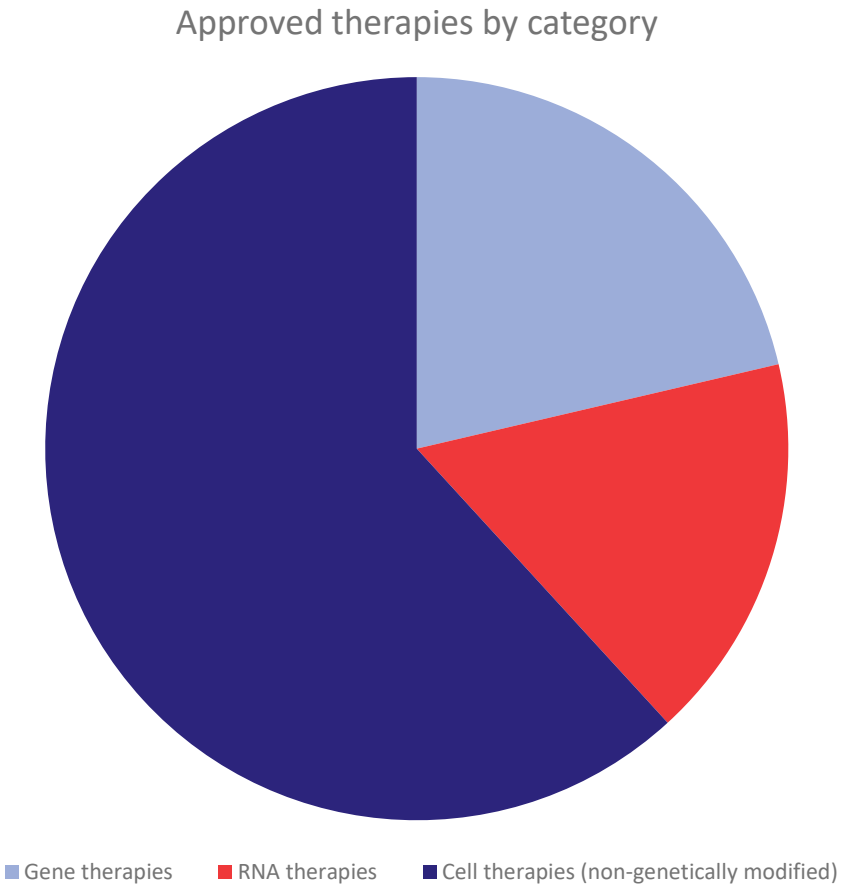
Q4 2021

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
- 55 non-genetically modified cell therapies approved
  - Since Q3 there has been one new cell therapy approval: Rethymic (Enzyvant Sciences) in the U.S.



Source: Pharmaprojects | Informa, January 2022

Approved gene therapies as of Q4 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; acute lymphocytic leukemia	US, EU, UK	Kite Pharma (Gilead)
Libmeldy	atidarsagene autotemcel	2020	Metachromatic Leukodystrophy	EU, UK	Orchard Therapeutics
Breyanzi	lisocabtagene maraleucel	2021	Diffuse large B-cell lymphoma; follicular lymphoma	US, Japan	Celgene (Bristol Myers Squibb)

Source: Pharmaprojects | Informa, January 2022

Text highlighted in yellow represent new approvals during Q4 2021

Approved gene therapies as of Q4 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, UK	bluebird bio
Delytact	teserpaturev	2021	Malignant Glioma	Japan	Daiichi Sankyo
Skysona	elivaldogene autotemcel	2021	Adrenoleukodystrophy	EU, UK	bluebird bio
Relma-cel	relmacabtagene autoleucel	2021	Diffuse large B-cell lymphoma	China	JW Therapeutics

Source: Pharmaprojects | Informa, January 2022

Text highlighted in yellow represent new approvals during Q4 2021

Approved RNA therapies as of Q4 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, South Africa, Thailand, Oman, Egypt, Malaysia	BioNTech

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

Source: Pharmaprojects | Informa, January 2022

Text highlighted in yellow represent new approvals during Q4 2021

Approved RNA therapies as of Q4 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, Colombia	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, US	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, January 2022

Text highlighted in yellow represent new approvals during Q4 2021

Key highlights in Q4 2021

Noteworthy events that happened in Q4 2021

Drug	Event Type	Indication	Molecule	Event Date
CYNK-001	Fast Track Status	Acute Myelogenous Leukemia (AML)	Cellular	12/27/2021
LioCyx	Fast Track Status	Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)	Cellular	12/23/2021
Leqvio	Approval (U.S.)	Dyslipidemia / Hypercholesterolemia	siRNA/RNAi	12/22/2021
XT-150	Fast Track Status	Osteoarthritis and Osteoarthritis Pain	Non-Viral Gene Therapy	12/17/2021
Lenti-D	Priority Review	Adrenoleukodystrophy	Viral Gene Therapy	12/17/2021
NKX101	Orphan Drug Designation (U.S.)	Acute Myelogenous Leukemia (AML)	Cellular	12/16/2021
Oxlumo	sNDA/sBLA Filing	Hyperoxaluria	siRNA/RNAi	12/14/2021
FT516	Regenerative Medicine Advanced Therapy (RMAT) Designation	Hematologic Cancer	Cellular	12/13/2021
Lomecel-B	Orphan Drug Designation (U.S.)	Cardiovascular Disease	Cellular	12/02/2021
VAR002	Orphan Drug Designation (Europe)	Leber's Congenital Amaurosis (Ophthalmology)	Viral Gene Therapy	11/24/2021
Zynteglo	Priority Review	Thalassemia	Viral Gene Therapy	11/22/2021
CTX110	Regenerative Medicine Advanced Therapy (RMAT) Designation	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	Cellular	11/22/2021
Lomecel-B	Rare Pediatric Disease (RPD) Designation	Cardiovascular Disease	Cellular	11/18/2021
ET140203	Rare Pediatric Disease (RPD) Designation; Fast Track Status	Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)	Cellular	11/17/2021
RGX-202 (Regenxbio)	Orphan Drug Designation (U.S.)	Duchenne Muscular Dystrophy (DMD)	Viral Gene Therapy	11/08/2021
GC012F	Orphan Drug Designation (U.S.)	Multiple Myeloma (MM)	Cellular	11/04/2021
OST-HER2	Rare Pediatric Disease (RPD) Designation	Bone Cancer	Cellular	11/03/2021
AXO-AAV-GM2	Fast Track Status	GM2 Gangliosidoses (Tay-Sachs Disease, Sandhoff Disease, AB Variant)	Viral Gene Therapy	11/01/2021
GENV-HEM	Orphan Drug Designation (U.S.)	Hemophilia A; Hemophilia B	Viral Gene Therapy	10/27/2021
AXO-AAV-GM1	Fast Track Status	GM1 Gangliosidosis	Viral Gene Therapy	10/21/2021
Lenti-D	MAA Withdrawal	Adrenoleukodystrophy	Viral Gene Therapy	10/21/2021
AMB-301	Orphan Drug Designation (U.S.)	Buerger's Disease	Viral Gene Therapy	10/19/2021
NTLA-2001	Orphan Drug Designation (U.S.)	Transthyretin Amyloid Cardiomyopathy (ATTR-CM, Wild Type Or Hereditary)	Non-Viral Gene Therapy	10/19/2021
AOC 1001	Fast Track Status	Muscular Dystrophy	siRNA/RNAi	10/18/2021
GS-030	Fast Track Status	Retinitis Pigmentosa (RP) (Ophthalmology)	Viral Gene Therapy	10/12/2021
Rethymic	Approval (U.S.)	DiGeorge Syndrome	Cellular	10/08/2021

Pipeline overview

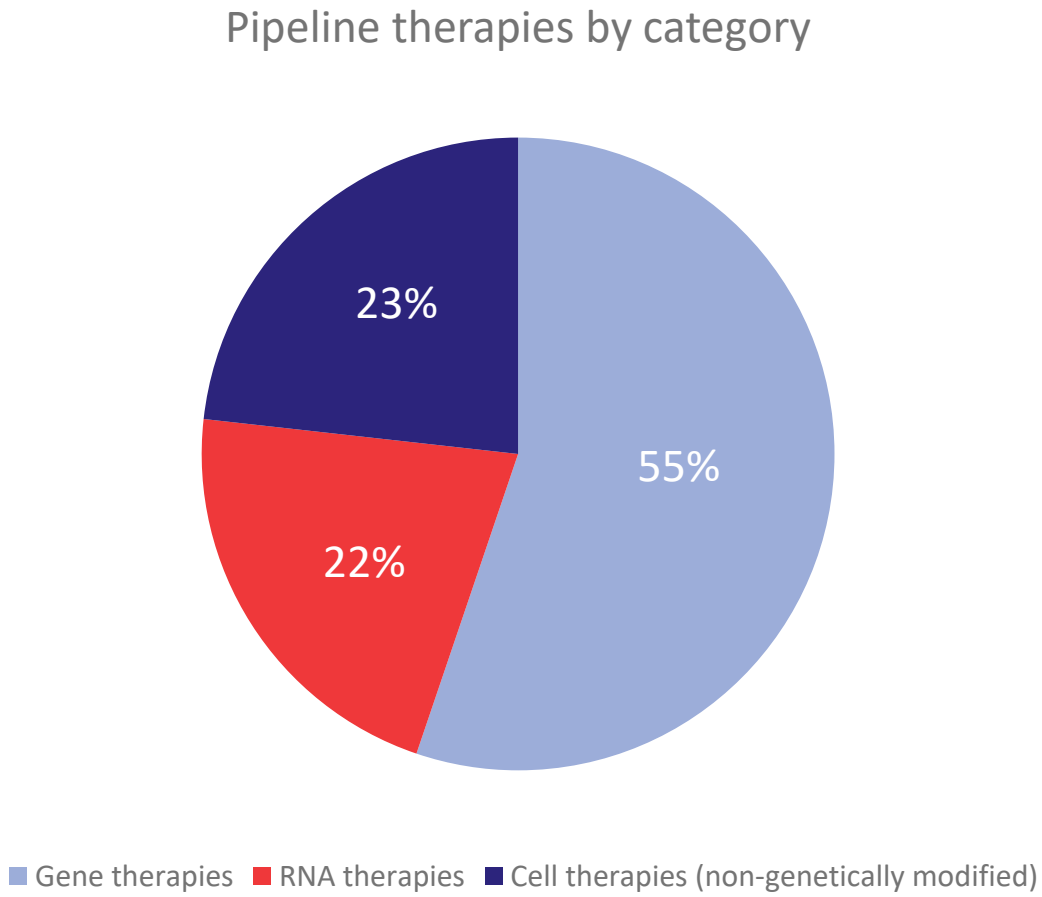
Q4 2021

American Society of Gene + Cell Therapy

Pipeline of gene, cell, and RNA therapies

3,483 therapies are in development, ranging from preclinical through pre-registration

- 1,941 gene therapies (including genetically-modified cell therapies such as CAR T-cell therapies) are in development, accounting for 55% of gene, cell, and RNA therapies
- 817 non-genetically modified cell therapies are in development, accounting for 23% of gene, cell, and RNA therapies



Source: Pharmaprojects| Informa, January 2022

American Society of Gene + Cell Therapy

Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q4 2021

American Society of Gene + Cell Therapy

Gene therapy pipeline: 2021 quarterly comparison

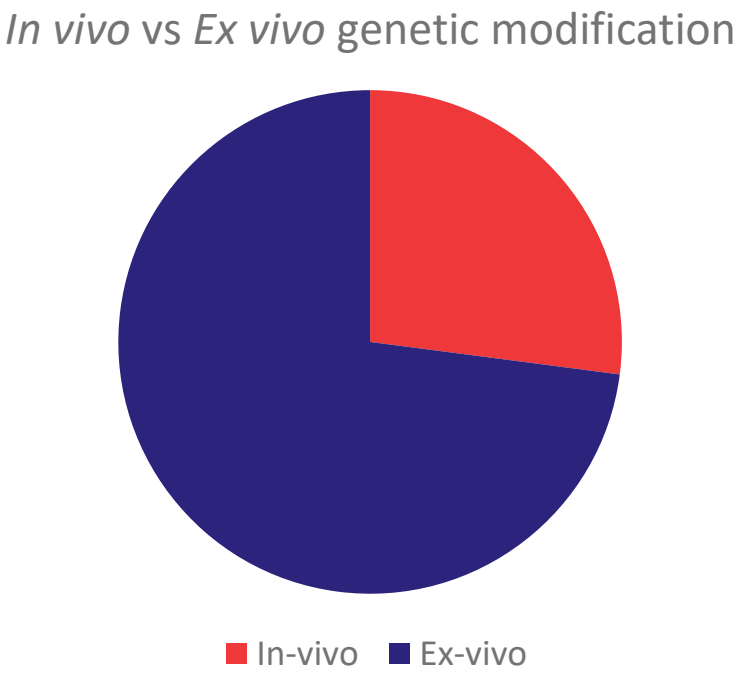
- The greatest percentage growth since Q3 is seen in Phase III development, which has increased by 10%
- Since Q2, gene therapies in preclinical development have continued to grow by 4% in each quarter
- With no new gene therapy approvals in Q4 2021, the number in pre-registration has remained the same since Q3
- 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	Oct. 2021	Jan. 2022
Preclinical	1,190	1,296	1,353	1,412
Phase I	225	269	264	248
Phase II	231	236	239	244
Phase III	27	27	29	32
Pre-registration	8	7	5	5
Total	**1,711**	**1,835**	**1,890**	**1,941**

Source: Pharmaprojects| Informa, January 2022

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

- *Ex vivo* genetic modification continues to be most commonly used for gene therapies in pipeline development
- In Q4 *in vivo* delivery techniques were used in 27% of gene therapies, only 2% higher than in Q3

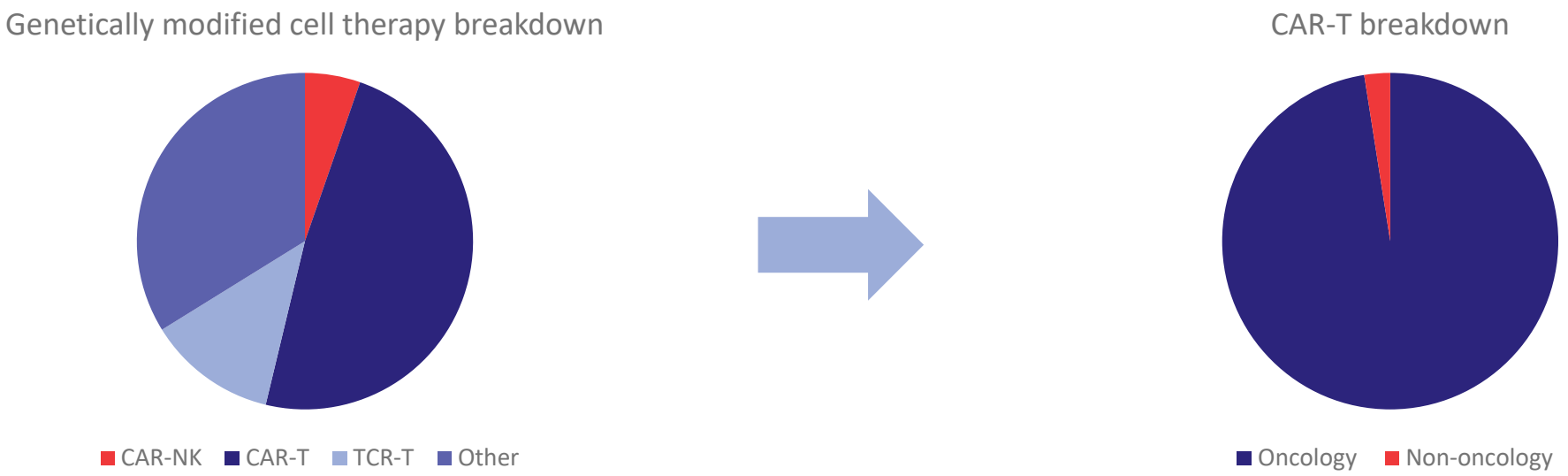


Source: Cell and Gene Therapy dashboard | Informa, January 2022

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 48%, 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 and autoimmune disease (unspecified)

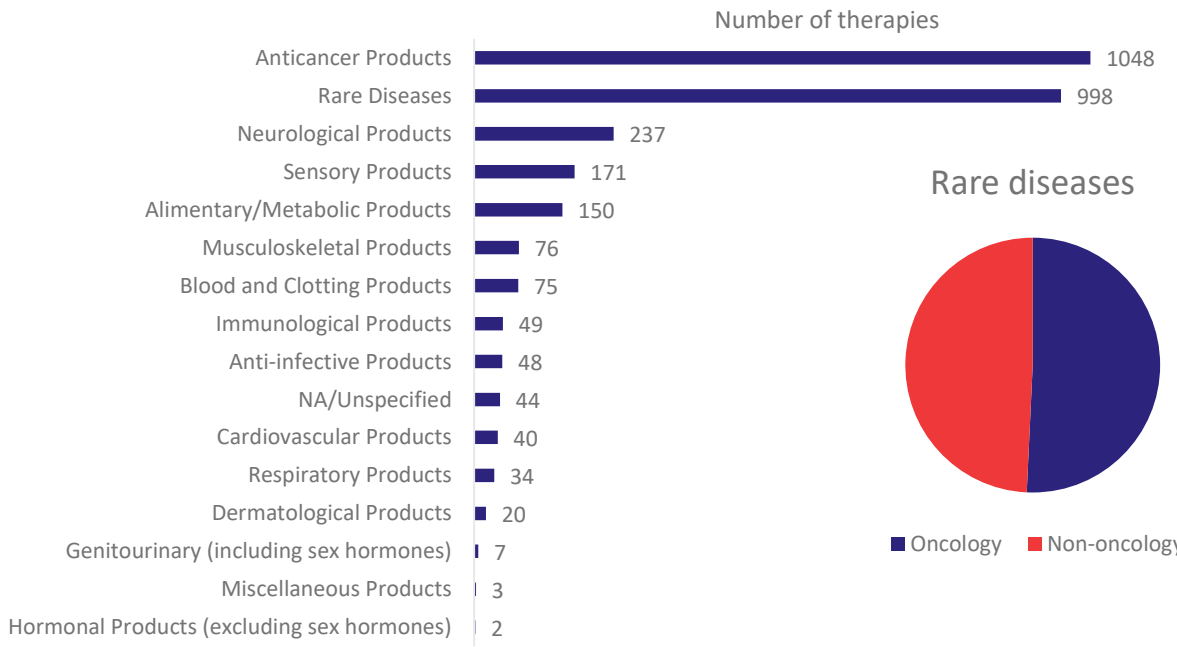


Source: Cell and Gene Therapy dashboard | Informa, January 2022

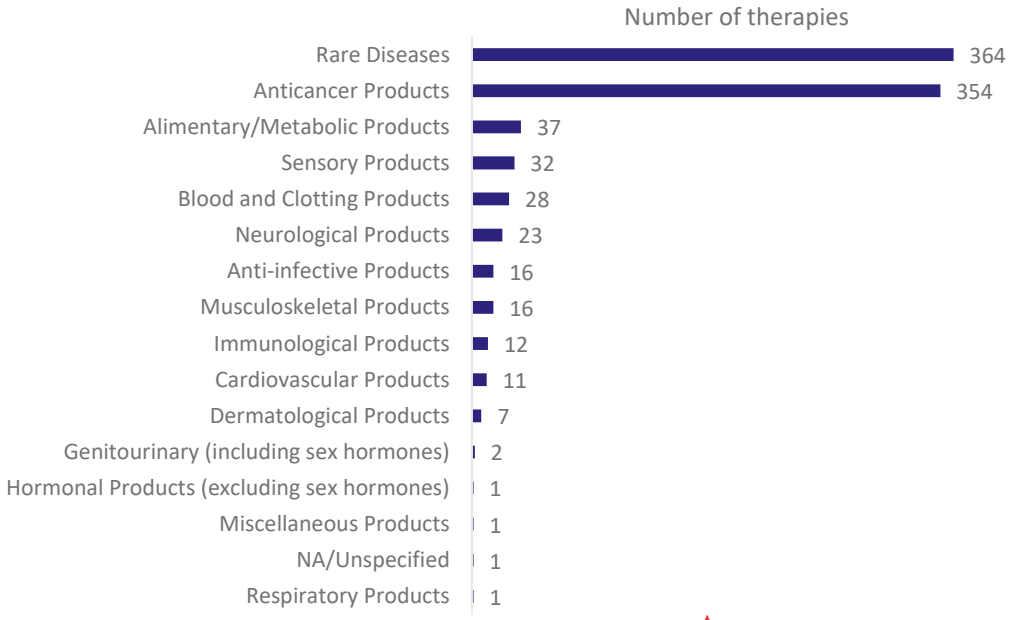
Gene therapy pipeline: Most commonly targeted therapeutic areas

- Anticancer therapies and therapies for rare diseases continue to be the top areas of development in both the pipeline (preclinical to pre-registration) and in the clinic (phase I to pre-registration) specifically
- Development for rare diseases is evenly split between rare oncology and non-oncology indications, however unlike Q3, oncology rare indications take the slight majority of 51%

Number of therapies from preclinical through pre-registration



Therapies in the clinic (excludes preclinical development)



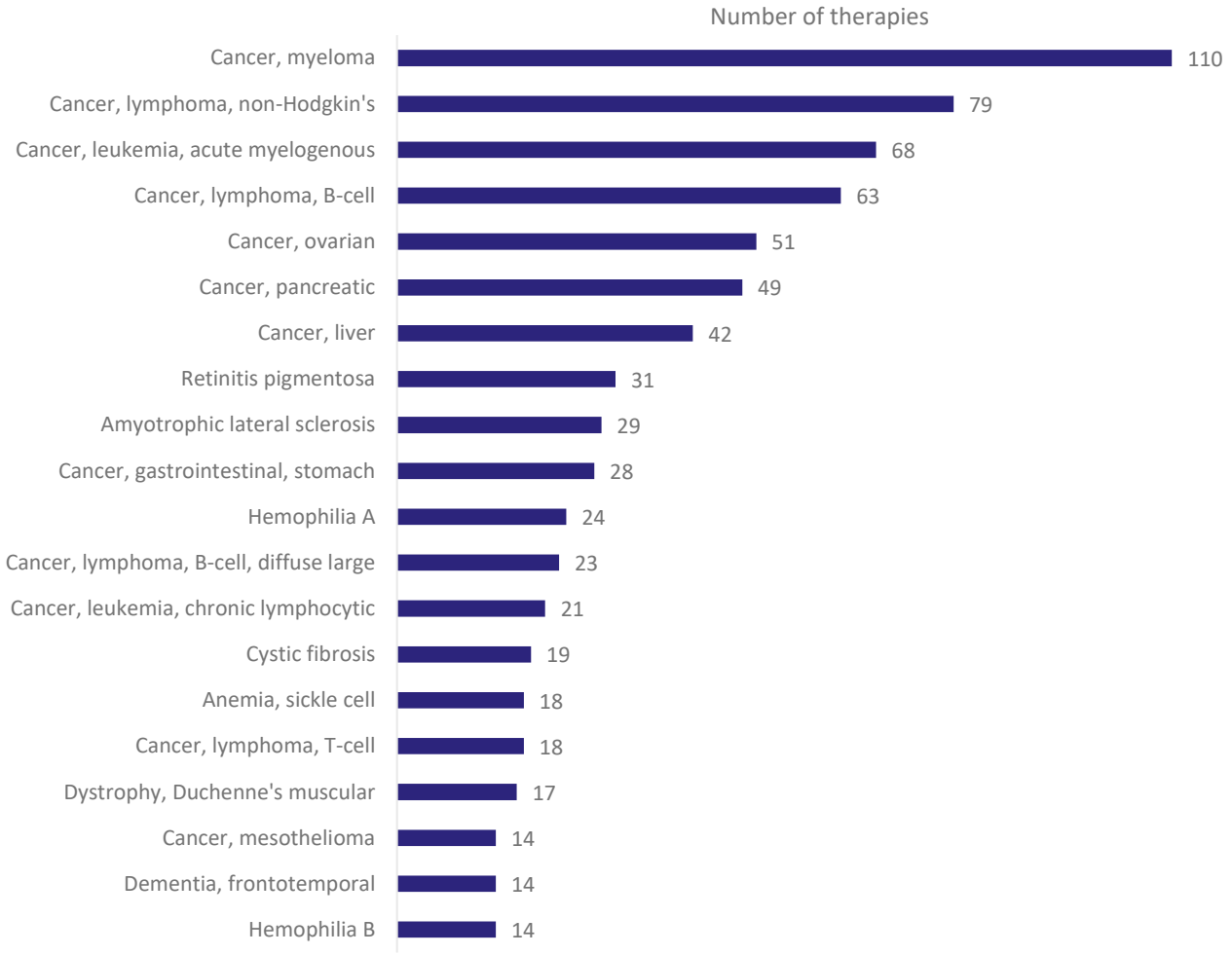
Source: Pharmaprojects| Informa, January 2022

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

American Society of Gene + Cell Therapy

Gene therapy pipeline: Most common rare diseases targeted

- Of the 998 gene therapies in preclinical to pre-registration stages of development for rare diseases, the majority of the top 20 indications are oncological
- The top 5 rare diseases for which gene therapies are being developed are:
  1. Myeloma
  2. Non-Hodgkin's lymphoma
  3. Acute myelogenous leukemia
  4. B-cell lymphoma
  5. Ovarian cancer



Source: Pharmaprojects| Informa, January 2022

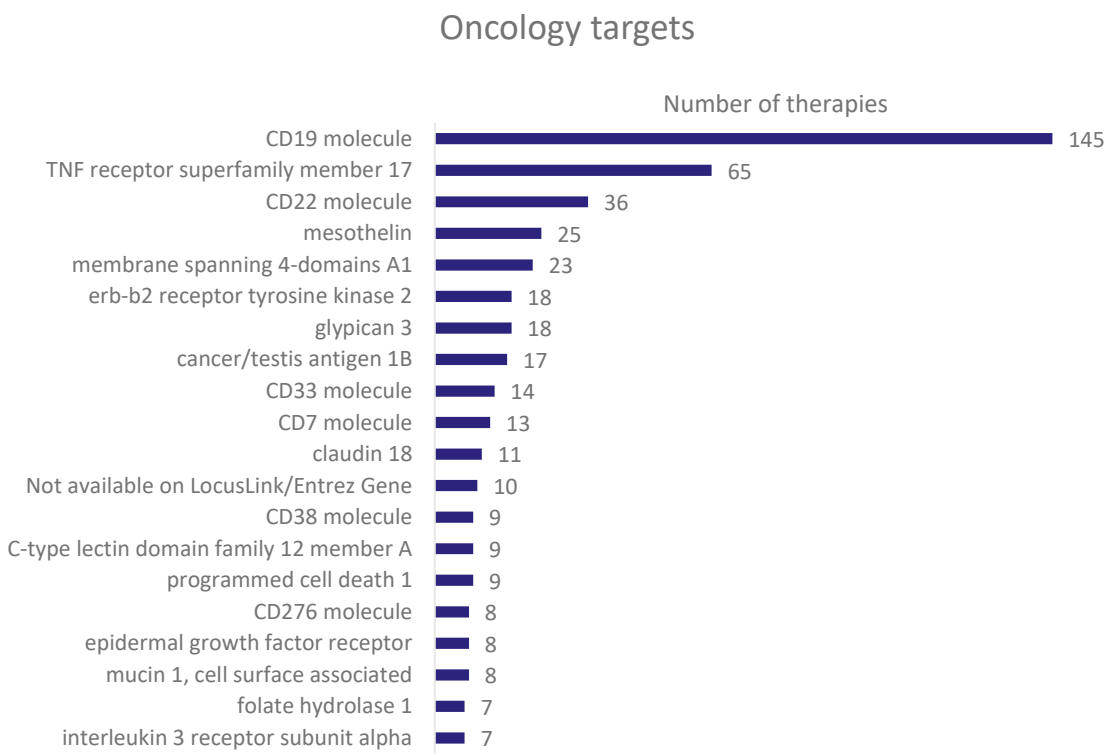
*figures based on indications in pipeline development only for each therapy

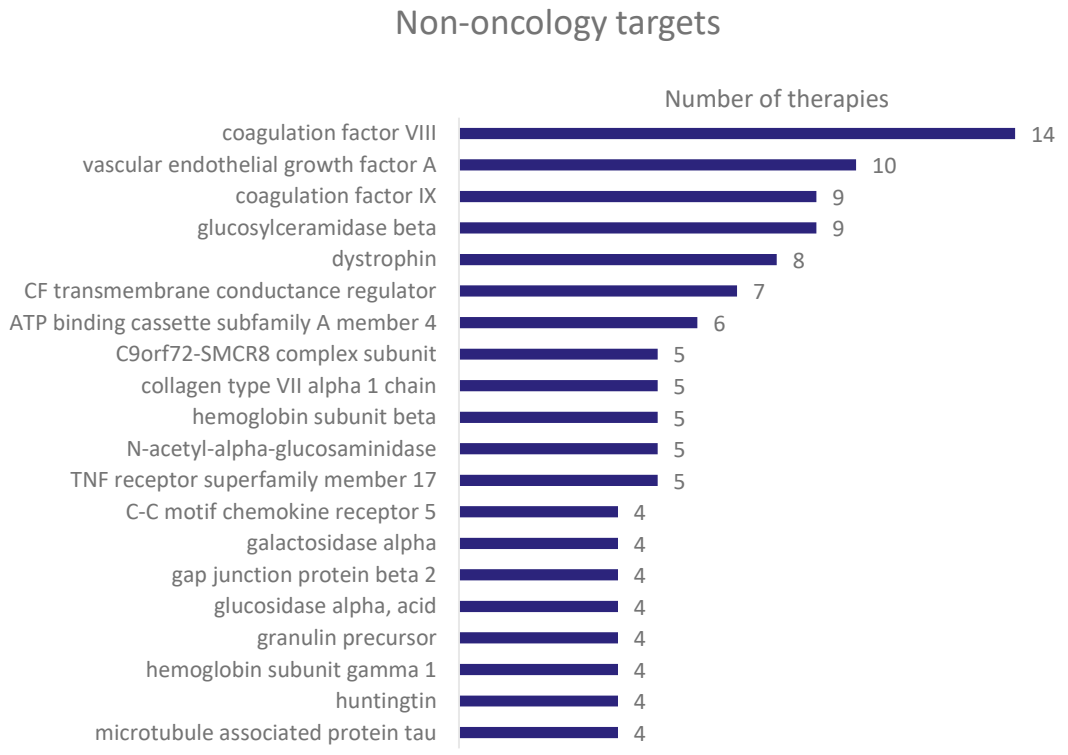
American Society of Gene + Cell Therapy

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, remain the most common targets for oncology indications
- Coagulation factor VIII also remains the most common target for non-oncology indications



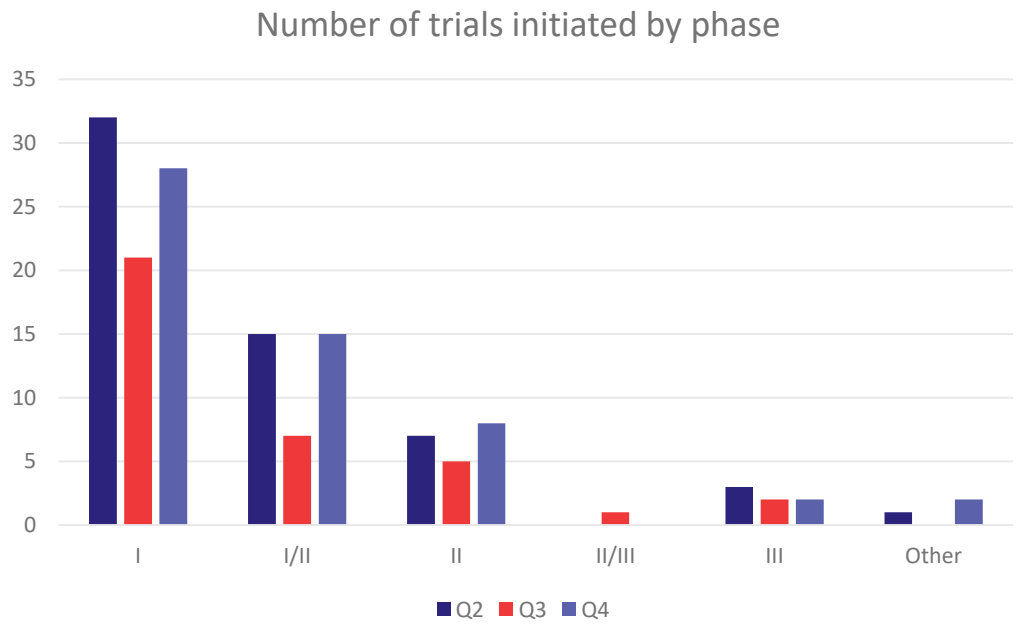


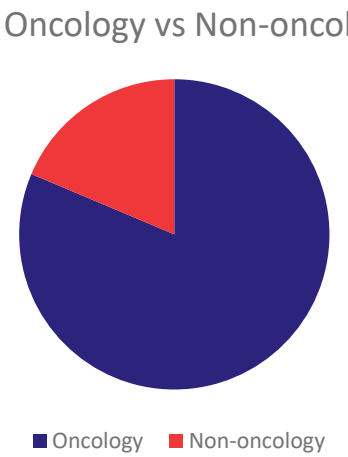
Source: Pharmaprojects| Informa, January 2022

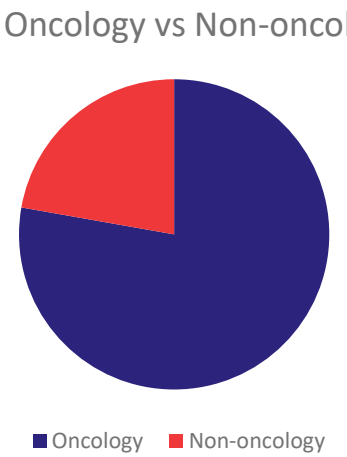
American Society of Gene + Cell Therapy

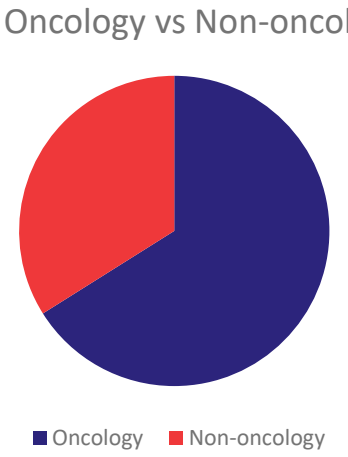
Gene therapy clinical trial activity in 2021

- 55 trials were initiated in Q4 for gene therapies, compared to 36 in Q3
- The proportion of newly started trials in Q4 that target non-oncology diseases increased to 35%, continuing the trend of growing non-oncology gene therapy trials since Q2









Source: Trialtrove| Informa, January 2022

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Non-genetically modified cell therapy pipeline

Q4 2021

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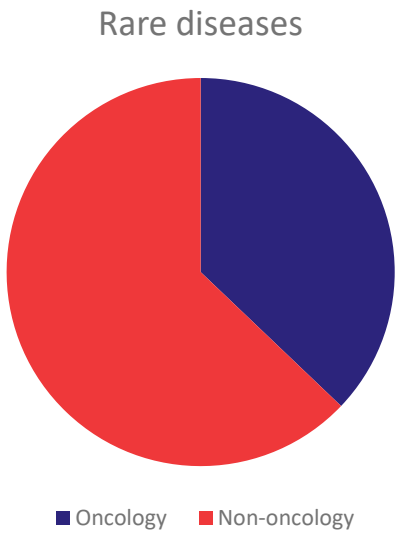
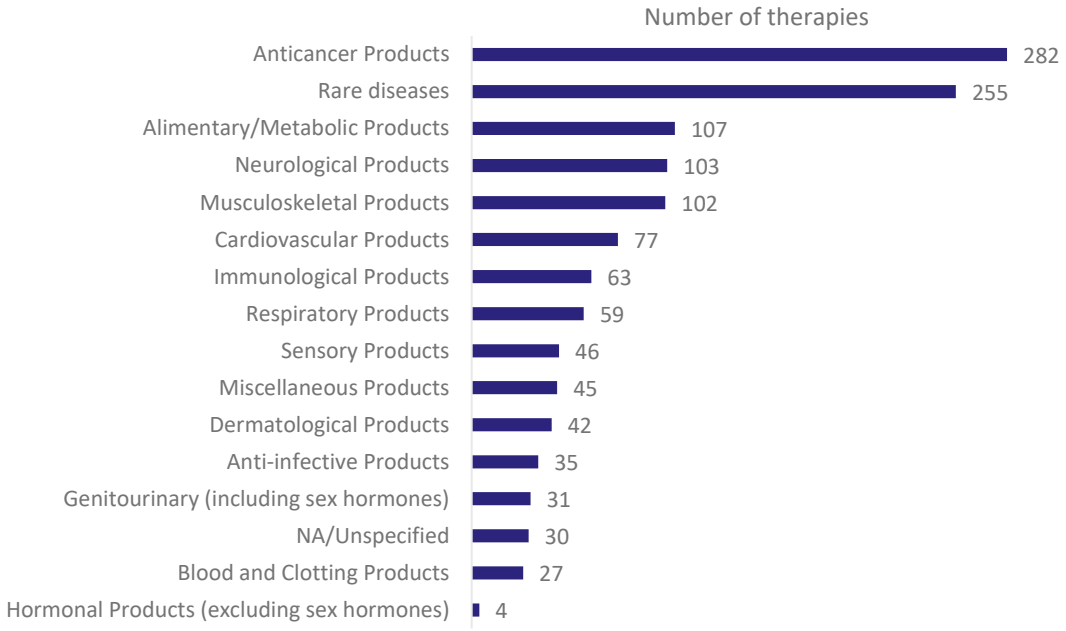
Non-genetically modified cell therapy pipeline: Most common therapeutic areas targeted

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

- 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, 74% are in development for non-oncology rare diseases, an increase of 8% compared to Q3





Source: Pharmaprojects| Informa, January 2022

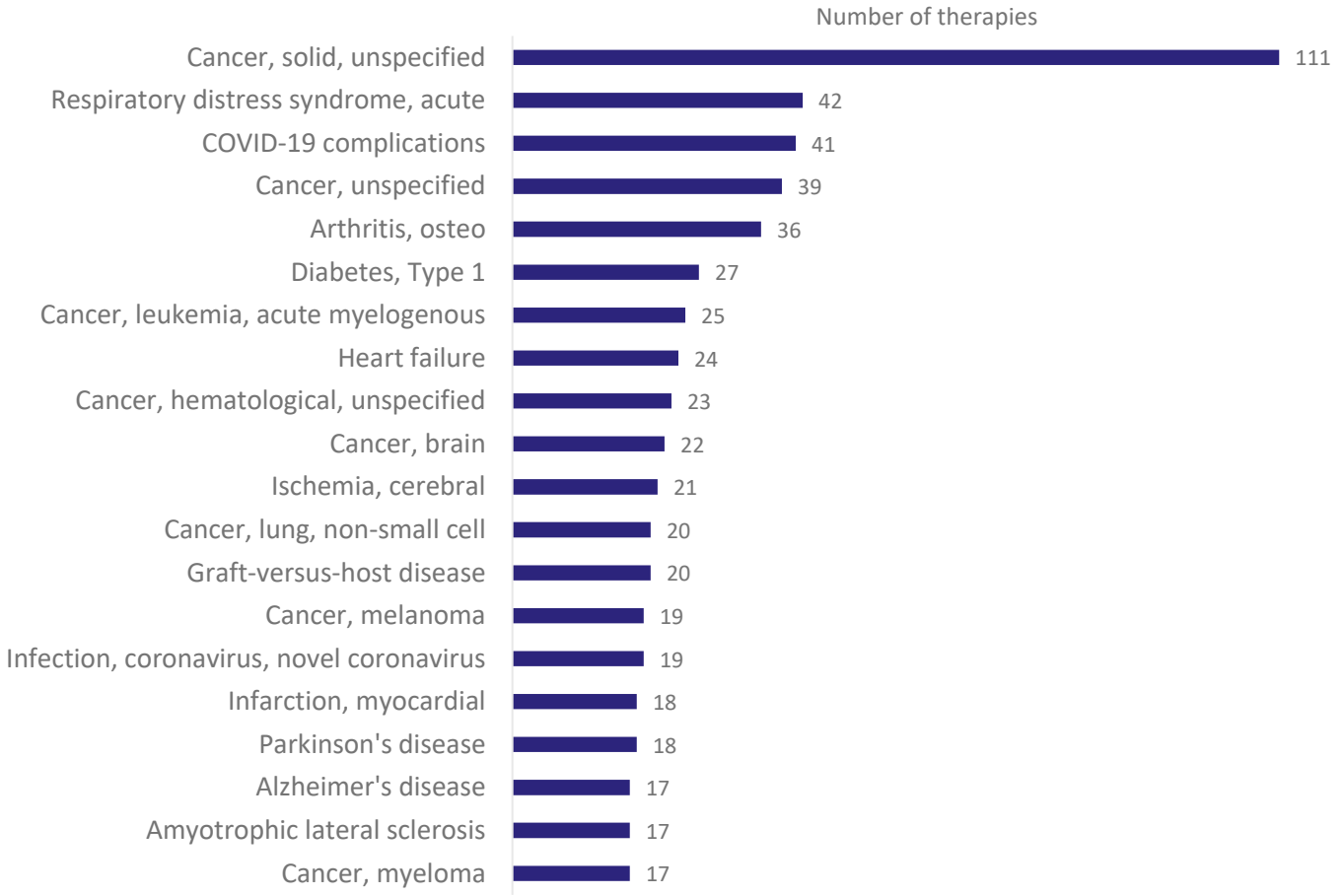
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

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

Of the diseases for which indications are specified, the top three indications are:

1. Respiratory distress syndrome
2. COVID-19 complications
3. Osteo arthritis



Source: Pharmaprojects| Informa, January 2022

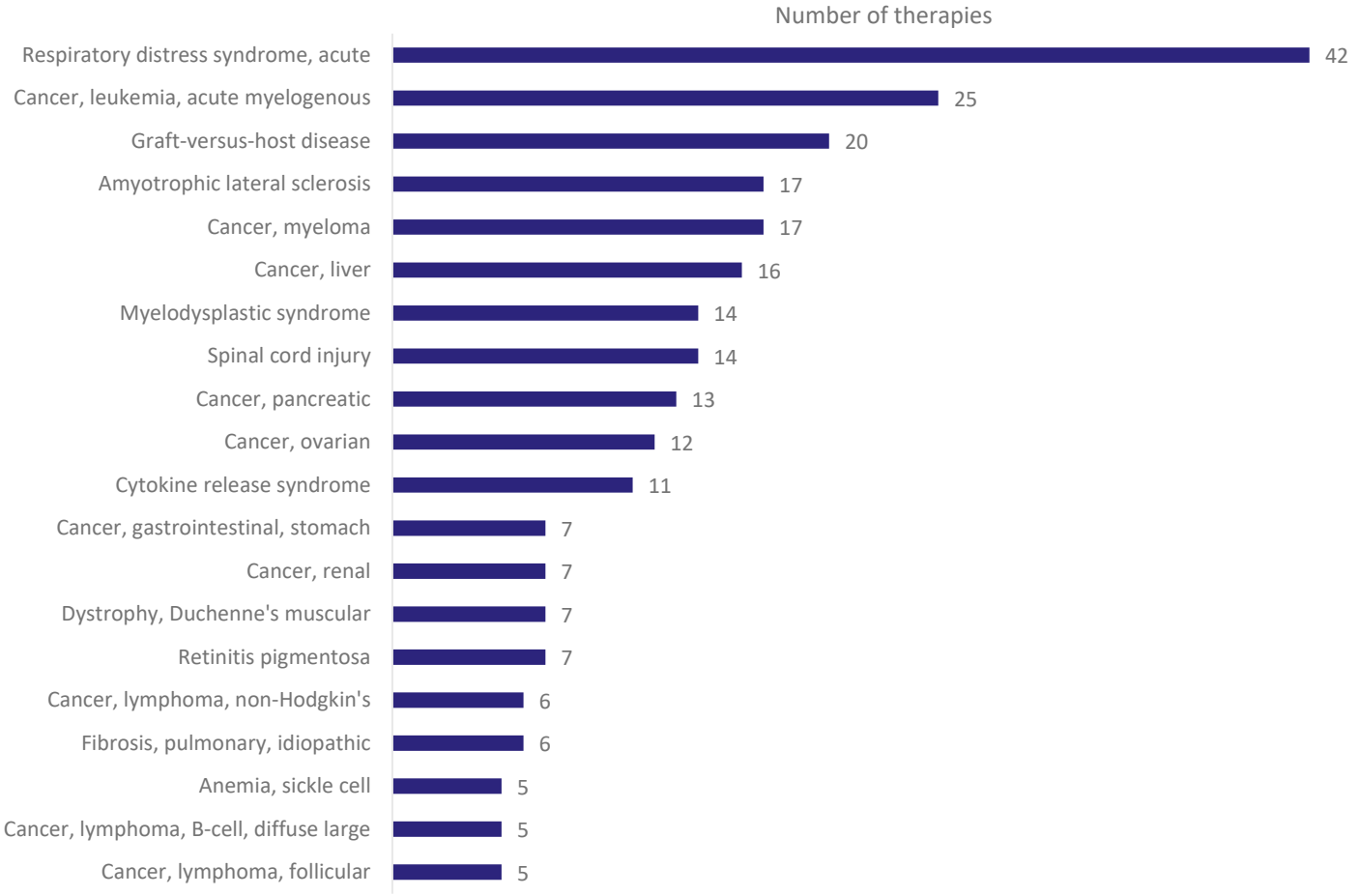
*figures based on indications in pipeline development only for each therapy

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 oncology indications are acute myelogenous leukemia, myeloma, and liver cancer
- The top three non-oncology indications are acute respiratory distress syndrome, graft-versus-host disease, and amyotrophic lateral sclerosis



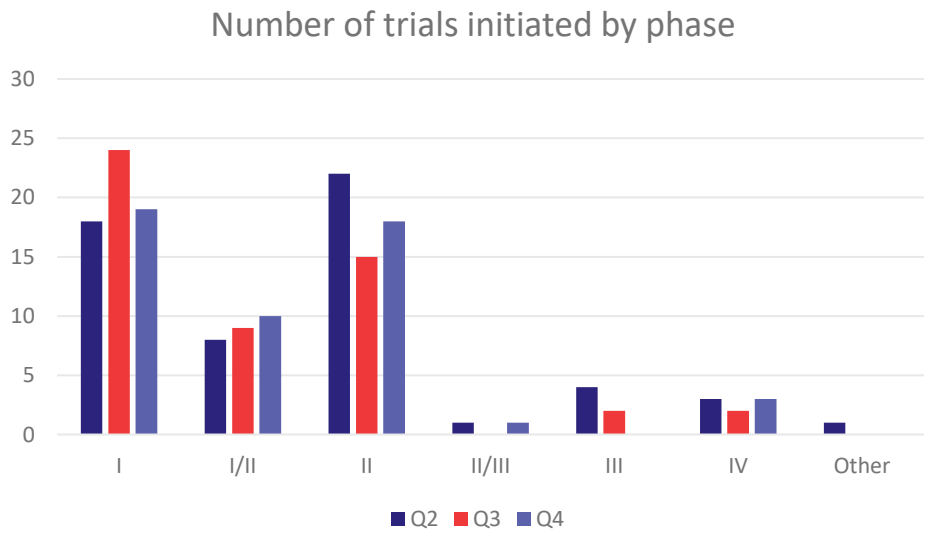
Source: Pharmaprojects| Informa, January 2022

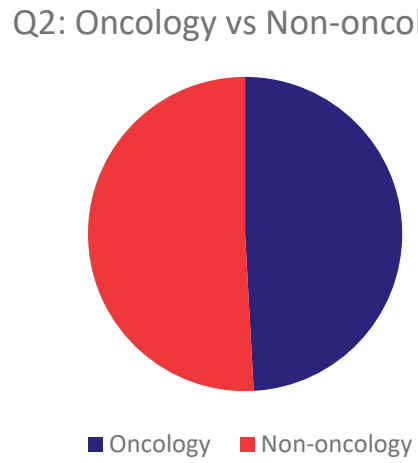
*figures based on indications in pipeline development only for each therapy

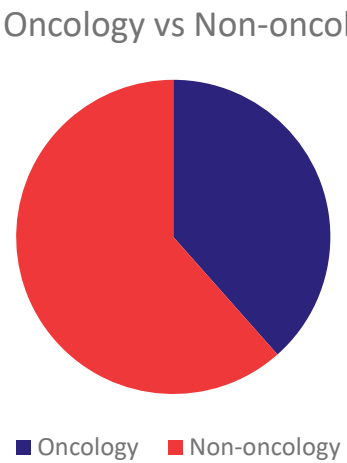
American Society of Gene + Cell Therapy

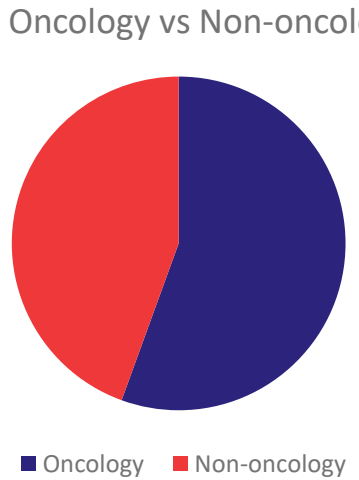
Non-genetically modified cell therapy trial activity in 2021

- 51 trials were initiated for non-genetically modified cell therapies in Q4, and unlike the previous two quarters, the majority (59%) of these newly initiated trials were for oncology indications









Source: Trialtrove| Informa, January 2022

American Society of Gene + Cell Therapy

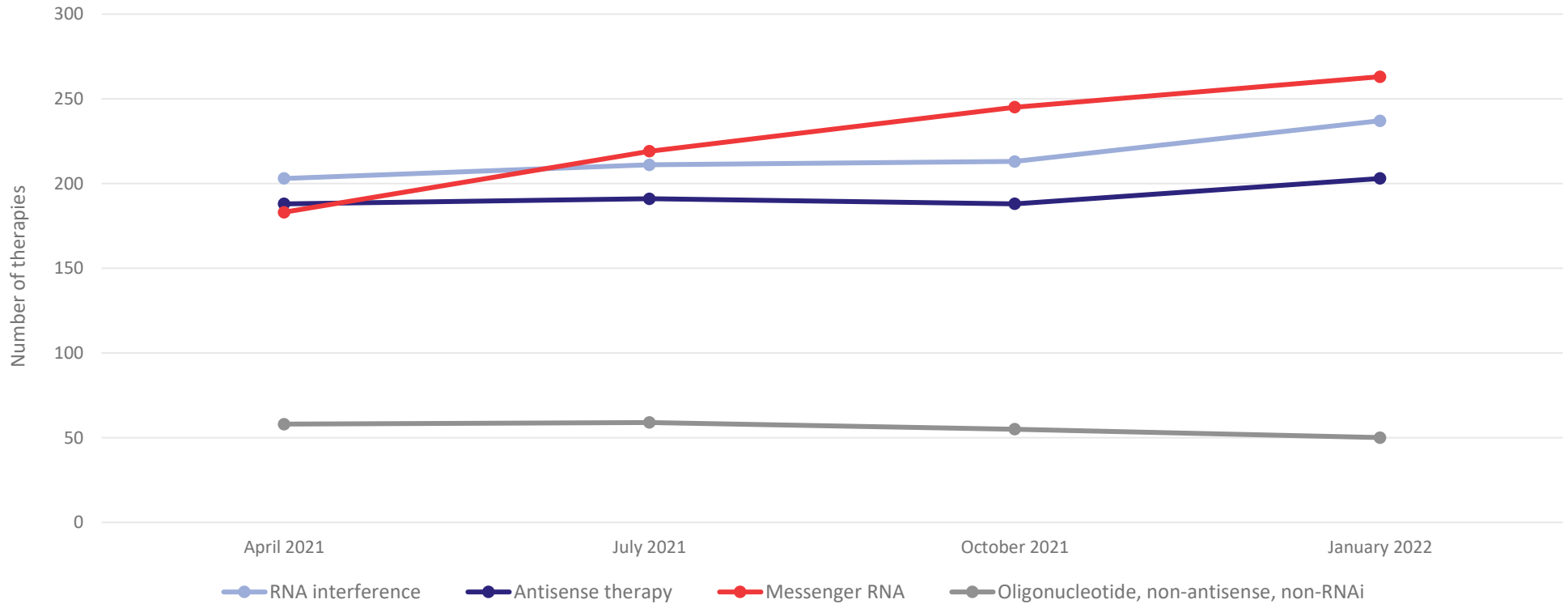
RNA therapy pipeline

Q4 2021

American Society of Gene + Cell Therapy

RNA therapy pipeline: Most common modalities

- Over the course of 2021 the number of messenger RNA therapies in the RNA therapy pipeline has shown the greatest increase, from 203 to 237, while the number of oligonucleotides (non-antisense, non-RNAi) has decreased from 58 to 50



Source: Pharmaprojects| Informa, January 2022

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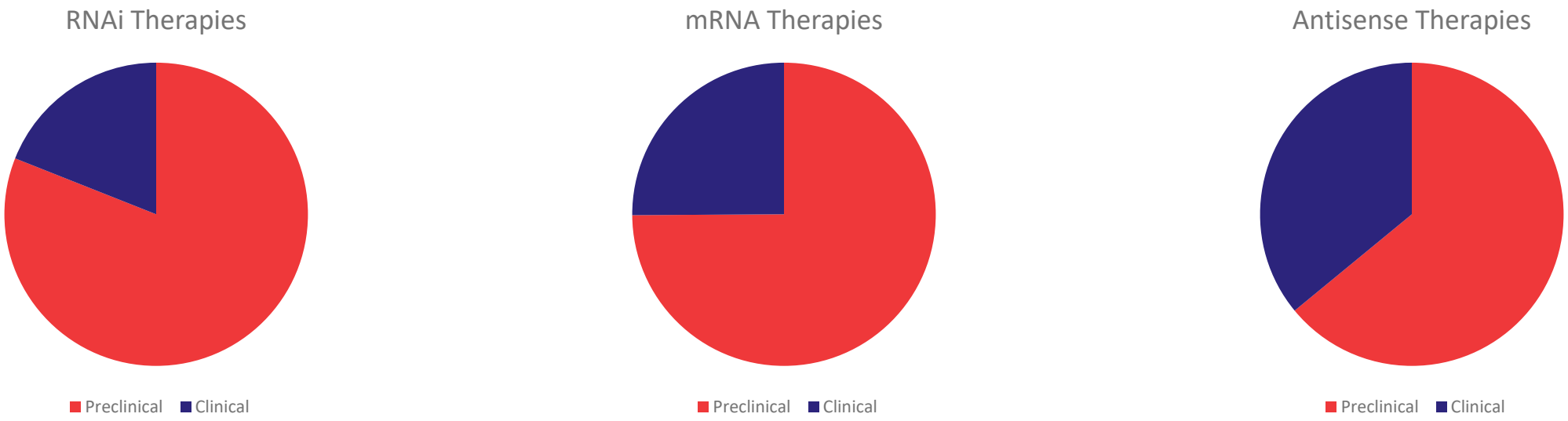
RNAi, mRNA, and antisense oligonucleotides: Preclinical vs. clinical

- Preclinical development dominates RNAi, mRNA, and antisense therapeutics, representing 81%, 75%, and 64% of development respectively

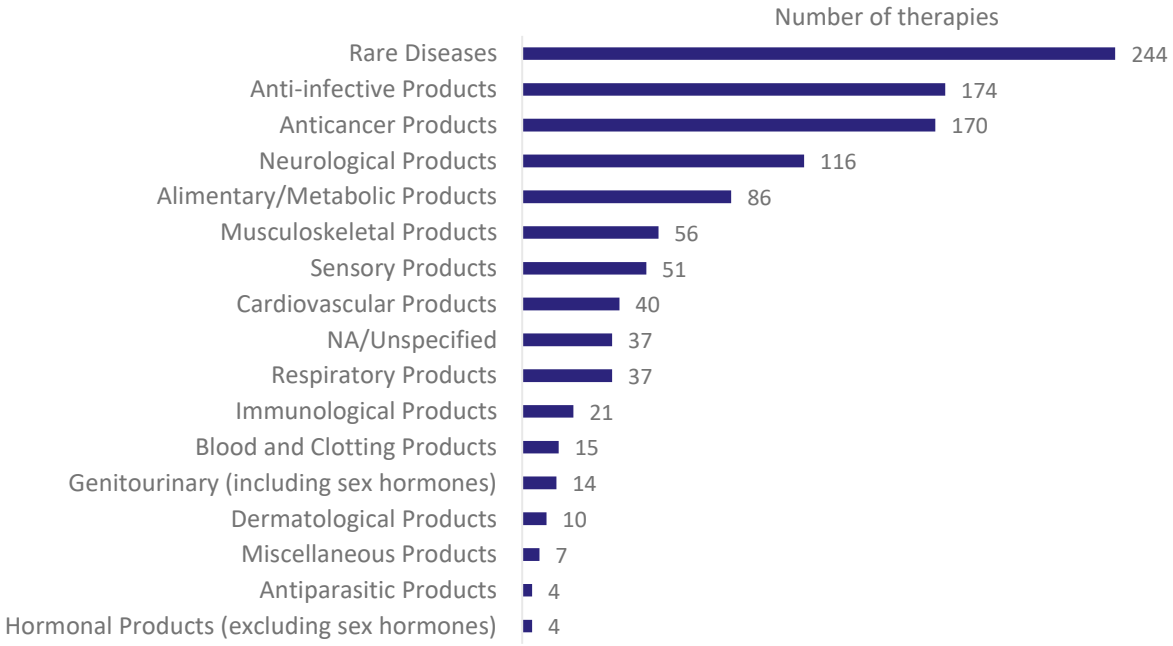


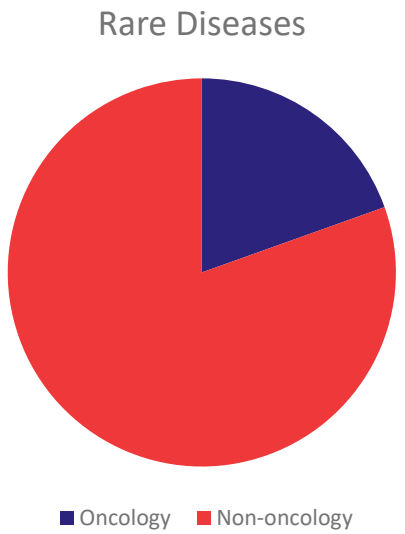
Source: Pharmaprojects| Informa, January 2022

RNA therapies: most common diseases targeted

Of the 758 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Rare diseases remain the top therapeutic area being targeted by RNA therapies, with anti-infective therapies over-taking oncology therapies since Q3 as the second most common therapy type
- Of all the RNA therapies in preclinical to pre-registration development for rare diseases, 80% are in development for non-oncology rare diseases, down from 83% in Q3





Source: Pharmaprojects| Informa, January 2022

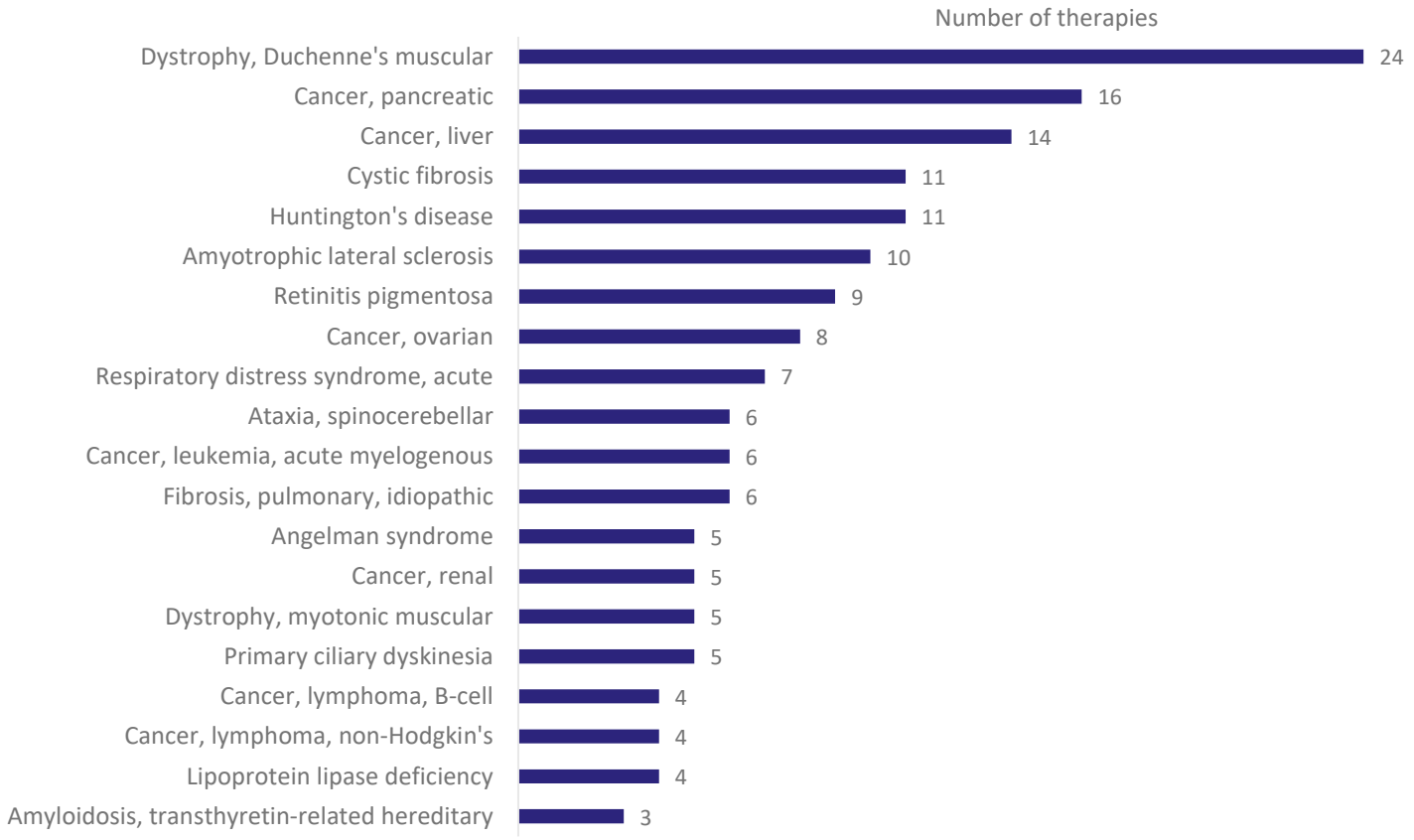
*figures based on indications in pipeline development only for each therapy

American Society of Gene + Cell Therapy

RNA therapies: most common rare diseases targeted

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

- Top specified rare oncology indications are pancreatic, liver, ovarian, acute myelogenous leukemia, and renal cancer
- For non-oncology rare diseases, Duchenne's muscular dystrophy, cystic fibrosis, Huntington's disease, amyotrophic lateral sclerosis (ALS), retinitis pigmentosa, and acute respiratory distress syndrome (ARDS) are the top five targeted diseases



Source: Pharmaprojects| Informa, January 2022

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

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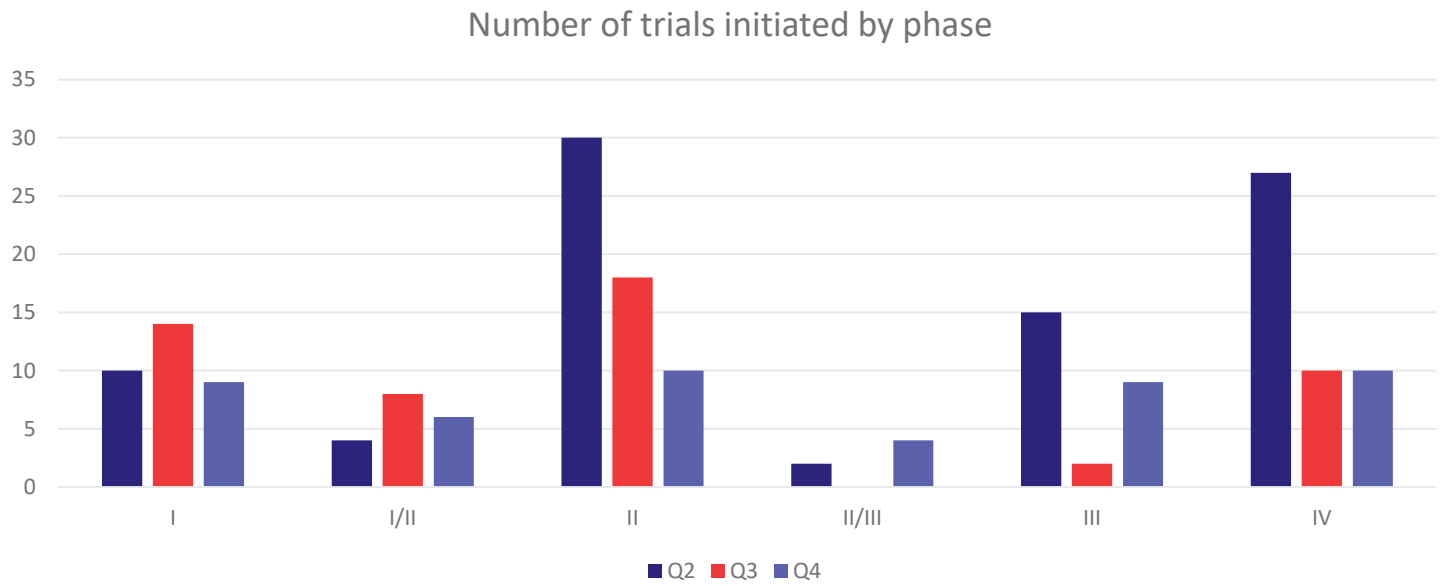
RNA therapy pipeline: Clinical trial activity

- 49 RNA trials were initiated in Q4 of 2021, compared to 52 in Q3
- As in Q3, the number of trials initiated in Q3 were most commonly for non-oncology diseases, representing a vast majority at 96%



Source: Trialtrove| Informa, January 2022

American Society of Gene + Cell Therapy

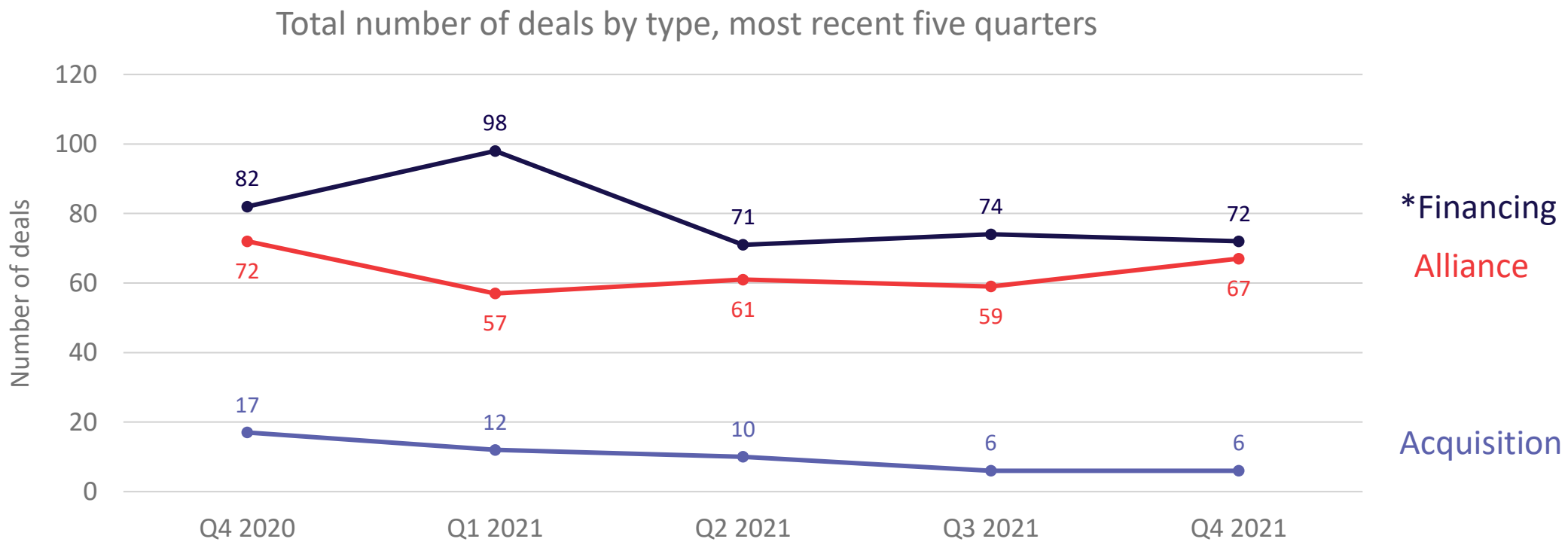
Overview of dealmaking for gene, cell, and RNA therapy companies

Q4 2021

American Society of Gene + Cell Therapy

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

- Q4 2021's total of 145 financings, alliances, and acquisitions was a slight increase over the 139 transactions done in Q3
- During 2021, there was generally a decline in volume quarter to quarter, except for the increase seen from Q3 to Q4
- The final quarter of 2021 saw a 15% decrease in dealmaking activity versus 2020's final quarter featuring 171 deals



Source: Biomedtracker| Informa, January 2022

*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

Q4 2021 acquisitions in gene, cell, & RNA therapy

- Acquisition activity in Q4 2021 remained constant with 6 takeovers announced, the same as Q3
- Overall, acquisition volume decreased throughout 2021, which opened with twice as many deals; Q4 2021's total was also almost one-third of the total acquisitions (17) announced in the same quarter of 2020
- Q4 2021 was highlighted by two billion-dollar acquisitions: Novo Nordisk's $3.3 billion buy of RNAi player Dicerna, and Novartis' $1.5 billion offer for Gyroscope, which is developing an AAV2 gene therapy for geographic atrophy

Deal Date	Deal Title	Potential Deal Value (USD)
10/15/2021	Treadwell Therapeutics Announces Acquisition of TCRyption Inc.	Undisclosed
10/27/2021	Takeda to Acquire GammaDelta Therapeutics	Undisclosed
11/18/2021	Novo Nordisk to Acquire Dicerna	3,300,000,000
11/22/2021	Twist Bioscience Enters into Definitive Agreement to Acquire Abveris for up to $190M	190,000,000
12/02/2021	EOM Pharmaceuticals Merges with Immunocellular Therapeutics to Focus on Advancing Immunomodulatory and Retinal Disease Therapies	Undisclosed
12/22/2021	Novartis to Acquire Gyroscope Therapeutics in a $1.5B Transaction	1,500,000,000

Source: Biomedtracker| Informa, January 2022

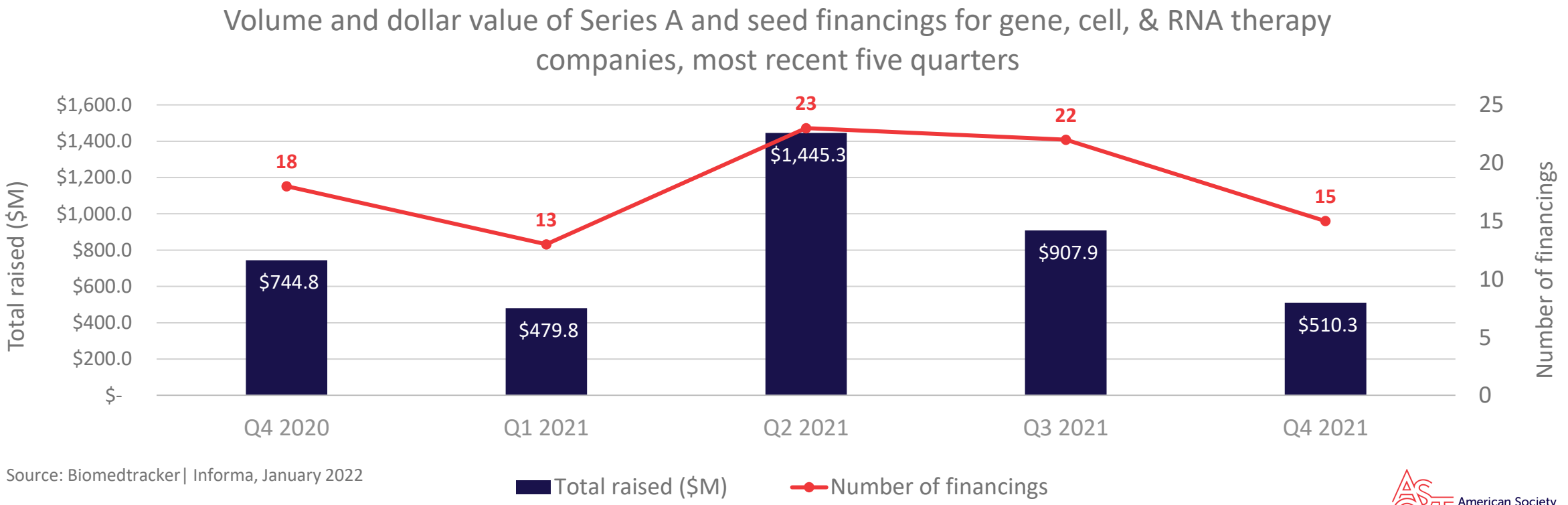
Start-up funding for gene, cell, & RNA therapy companies

Q4 2021

American Society of Gene + Cell Therapy

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

- 15 companies raised seed or Series A financing in Q4 2021 together worth $510.3 million, a decrease from the 22 financings valued at $907.9 million in Q3
- Q4 2021's volume and value was the second-lowest of 2021, still ahead of the opening quarter of year, but behind the numbers seen in 2020's final quarter
- Chroma Medicine completed the largest financing, raising $125 million to focus on precision therapeutics developed via its modular epigenetic editors



Source: Biomedtracker| Informa, January 2022

American Society of Gene + Cell Therapy

Q4 2021 start-up financing for gene, cell, & RNA therapy companies (1/2)

Deal Date	Deal Title	Modality Type	Company Location	Academic Source	Potential Deal Value (USD, $M)
10/06/2021	Amplo Biotechnology Closes Series Seed Financing to Advance Gene Therapies for The Treatment of Neuromuscular Junction Disorders	Gene therapy (AAV)	United States, Florida, Pompano Beach	University of Tokyo's Institute of Medical Science	Undisclosed
10/07/2021	AffyImmune Therapeutics Secures $30M Series A+ Financing	Genetically modified cell therapy (CAR-T)	United States, Massachusetts, Natick	Harvard Medical School, Weill Cornell Medical College	30
10/07/2021	Intergalactic Therapeutics Launched with $75M in Series A Funding	Gene therapy (non-viral)	United States, Massachusetts, Boston	Undisclosed	75
10/07/2021	Sapreme Raises €15M in a Series A to Boost Development of its Endosomal Escape Technology Platform and Proprietary Pipeline	Ab-targeted ASOs (endosomal escape platform)	Netherlands, Utrecht	Undisclosed	17
10/21/2021	Leucid Bio Raises Approximately $15.88M in Series A Financing to Develop Chimeric Antigen Receptor T cell Therapies	Genetically modified cell therapy (CAR-T)	United Kingdom, London	King's College London, NIHR Guy's and St Thomas' Biomedical Research Centre	16
11/03/2021	Clade Therapeutics Raises $87M Series A Financing	Cell therapy (allogeneic)	United States, Massachusetts, Cambridge	Harvard University	87
11/03/2021	Lynx Biosciences Closes Seed Equity Round	Cell therapy (in which suspension cells play critical role)	United States, California, San Diego	Undisclosed	Undisclosed
11/04/2021	Cellenkos Secures $15M Series A Financing to Accelerate the Development of Transformative Cell-Based Therapies	Cell therapy (Treg)	United States, Texas, Houston	University of Texas MD Anderson Cancer Center	15
11/09/2021	Novo Holdings Co-Leads $6.9M Seed Financing in Asgard Therapeutics	Gene therapy	Sweden, Lund	Lund University's Cell Reprogramming and Immunity Lab	7

Source: Biomedtracker| Informa, January 2022

Q4 2021 start-up financing for gene, cell, & RNA therapy companies (2/2)

Deal Date	Deal Title	Modality Type	Company Location	Academic Source	Potential Deal Value (USD, $M)
11/10/2021	Mekonos Raises $25M in Series A Financing	Genetically modified cell therapy (DNA, RNA, CRISPR)	United States, California, San Francisco	Stanford University	25
11/17/2021	Chroma Medicine Launches with $125M in Financing	Epigenetic editing	United States, Massachusetts, Cambridge	Scientific founders from UC San Francisco, MassGen Hospital, Harvard Medical School, Broad Institute, San Raffaele Telethon Institute for Gene Therapy, and Vita-Salute San Raffaele University	125
11/18/2021	Cellevolve Bio Closes $6M Seed Round	Cell therapy	United States, California, San Francisco	Undisclosed	6
12/02/2021	AviadoBio Raises $77.97M via Series A Financing to Advance Neurodegenerative Gene Therapy Platform	Gene therapy	United Kingdom, London	King's College London's Institute of Psychiatry, Psychology & Neuroscience	78
12/14/2021	Cargene Closes a $19.2M Pre-A Round	ASOs	Singapore	Agency for Science, Technology and Research	19
12/29/2021	Curi Bio Closes $10M Series A in Oversubscribed Round	Cell therapy	United States, Washington, Seattle	University of Washington Department of Bioengineering	10

Source: Biomedtracker| Informa, January 2022

Notable Q4 2021 start-up gene, cell, & RNA therapy companies

	Company details	Academic source	Financing type/amount raised	Lead investor(s)	Therapy areas of interest
CHROMA MEDICINE	Epigenetic editing through two primary mechanisms: precise targeting of gene to be silenced or activated, and control of chromatin conformation	Scientific founders from UC San Francisco, MassGen Hospital and Harvard Medical School, Broad Institute, San Raffaele Telethon Institute for Gene Therapy and Vita-Salute San Raffaele University	Seed round and Series A/$125M	Atlas Venture and Newpath Partners (seed) and Cormorant Asset Management (Series A)	Undisclosed
Clade Therapeutics	Immune cloaking of induced pluripotent stem cells to develop off-the-shelf cell therapies	Harvard University	Series A/$87M	Syncona	Oncology
AVIADOBIO	Viral vector gene therapies (gene supplementation and gene knock-down) based on neuroanatomy-led approach to drug delivery	King's College London's Institute of Psychiatry, Psychology & Neuroscience	Series A/$78M	New Enterprise Associates and Monograph Capital	Neurodegenerative diseases (including frontotemporal dementia and amyotrophic lateral sclerosis)

Source: Biomedtracker| Informa, January 2022

Upcoming catalysts

Q4 2021

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward looking events) expected in Q1 2022

Therapy	Generic Name	Disease	Catalyst	Catalyst Date
EDIT-201		Solid Tumors	IND Filing	6 Dec 2021 – 31 Jan 2022
Ciltacabtagene Autoleucel	Ciltacabtagene Autoleucel	Multiple Myeloma (MM)	PDUFA for BLA - First Review	28 Feb 2022 – 28 Feb 2022
Lantidra	Allogeneic Islets of Langerhans	Diabetes Mellitus, Type I	PDUFA for BLA - First Review	22 Nov 2021 – 31 Mar 2022
Lumevoq	rAAV2/2-ND4	Leber's Hereditary Optic Neuropathy (LHON) (Ophthalmology)	CHMP Opinion	1 Jan 2022 – 30 Jun 2022
Roctavian	Valoctocogene Roxaparvovec	Hemophilia A	CHMP Opinion	9 Jan 2022 – 30 Jun 2022
Ciltacabtagene Autoleucel	Ciltacabtagene Autoleucel	Multiple Myeloma (MM)	CHMP Opinion	1 Jan 2022 – 31 Jul 2022
Kymriah	tisagenlecleucel-t	Indolent Non-Hodgkin's Lymphoma (Including Follicular Lymphoma) - NHL	Supplemental CHMP Opinion	1 Mar 2022 – 31 Aug 2022
Breyanzi	Lisocabtagene Maraleucel	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	CHMP Opinion	1 Nov 2021 – 31 Oct 2022
CTX001	Autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells	Thalassemia	BLA Filing	10 Jan 2022 – 31 Dec 2022
CTX001	Autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells	Sickle Cell Anemia	BLA Filing	10 Jan 2022 – 31 Dec 2022

Source: Biomedtracker| Informa, January 2022

Appendix

Methodology, sources, & glossary of key terms

Q4 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

Report Contributors

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

Shardha Millington
Consultant
Informa Pharma Intelligence

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

Amanda Micklus, MSc
Managing Consultant
Informa Pharma Custom Intelligence

Devin Rose
Communications Manager
American Society of Gene + Cell Therapy

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

American Society of Gene + Cell Therapy

American Society of Gene + Cell Therapy

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

Pharma Intelligence
Informa

Contact: pharma@informa.com