Gene, Cell, & RNA Therapy Landscape

Q1 2022 Quarterly Data Report

Q1 2022

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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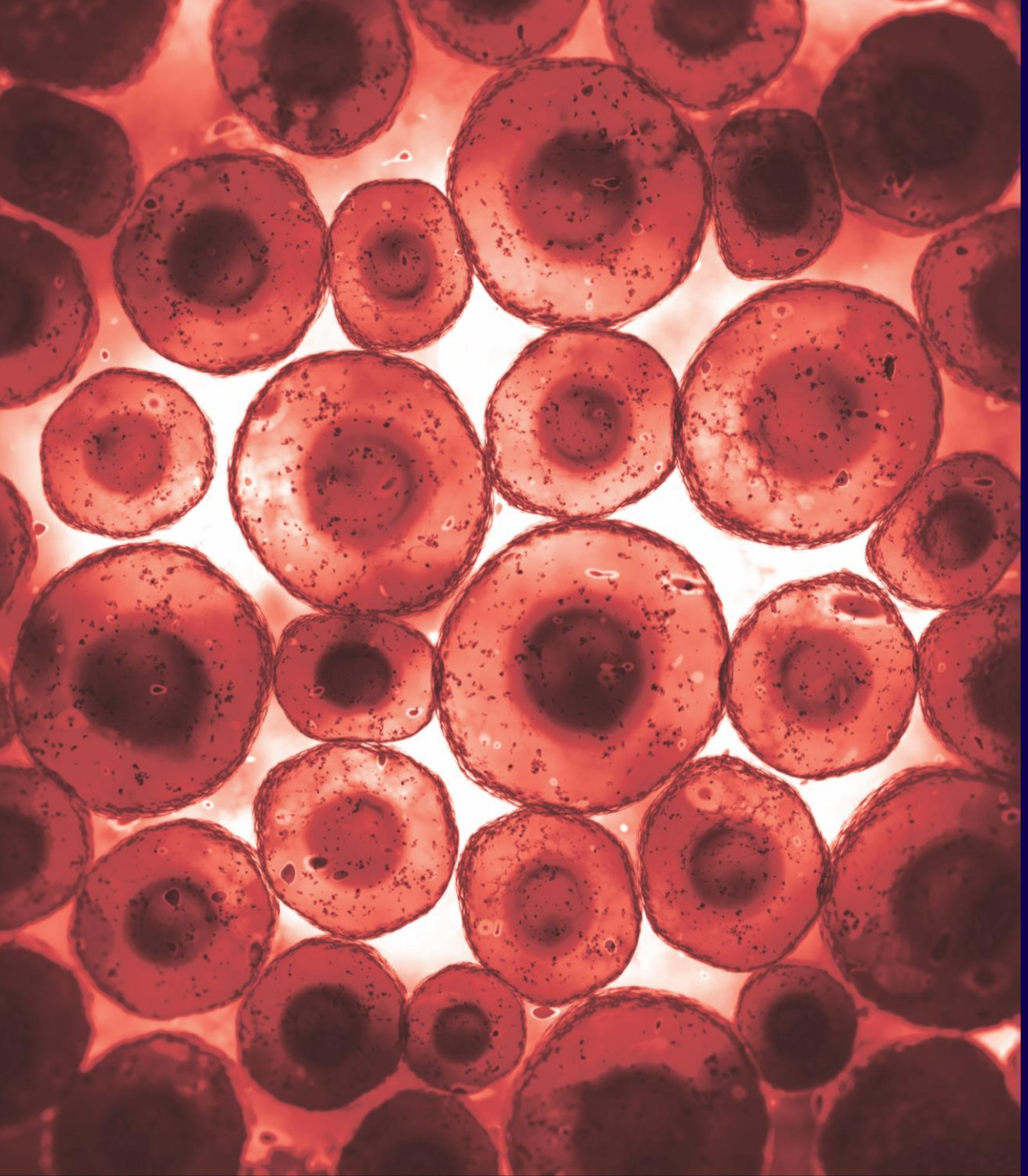

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Introduction

Welcome to the first quarterly report of the year from ASGCT and Informa Pharma Intelligence. We're excited to share the highlights of Q1 2022, including approval of a new CAR T-cell therapy to treat multiple myeloma in the U.S. and filing for approval of an AAV5 gene therapy to treat hemophilia B in the EU and the UK. Additionally, an RNA therapy was approved to treat coronavirus in Australia and South Korea.

This quarter, 25% of newly initiated gene therapy clinical trials were for non-oncology diseases, falling from 35% in Q4 2021. In non-genetically modified cell therapy development, oncology and rare diseases continue to be the top targeted areas. CAR-T cell therapies continue to dominate the pipeline of genetically modified cell therapies, representing 49% of technology. Similar to Q4 2021, 98% of CAR T-cell therapies are in development for cancer indications.

Q1 2022 saw the lowest quarter total of deals signed within the last year, representing a 26% decrease from Q1 2021. Alliance volume remained flat and financings trended down. Start-up financing dropped to $507.8 million, while the number of companies raising seed or Series A financing stayed at 15. Overall, however, the gene, cell, and RNA therapy landscape continues to expand. The gene therapy pipeline has increased 16% since Q1 2021. In the pipeline, there are 3,579 gene, cell, and RNA therapies in development from preclinical through pre-registration stages.

Key takeaways from Q1 2022

One new genetically modified cell therapy has been approved since Q4 2021, and one new gene therapy has filed for approval

- Carvykti, a CAR-T cell therapy developed by Legend Biotech and Johnson & Johnson, was approved for multiple myeloma in the U.S.
- EtranaDez (etranacogene dezaparvovec), an AAV5 gene therapy developed by uniQure, filed for approval in the EU and UK for hemophilia B

The gene, cell and RNA therapy landscape has continued to expand into 2022

- In the past year since Q1 2021, the gene therapy pipeline (preclinical to pre-registration) has increased by 16%

Oncology and rare diseases are the most targeted therapy areas for RNA, gene, and non-genetically modified cell therapy pipeline development

- For RNA therapy and non-genetically modified cell therapies the majority of the rare diseases targeted are in the non-oncology space, while for gene therapies the majority are oncological

Start-up financing remained steady in Q1 2022

- Volume and value of the 16 Series A and seed financings done by gene, cell, and RNA therapeutic companies, worth an aggregate $507.8M, was virtually flat from the previous quarter
- Overall dealmaking total across alliance, acquisitions, and financings saw a 15% decline
- In the largest start-up financing, Cellino Biotech, a Harvard University spin-out, raised $80M to support its large-scale production of autologous and allogeneic cell therapies

Key highlights in Q1 2022

Q1 2022

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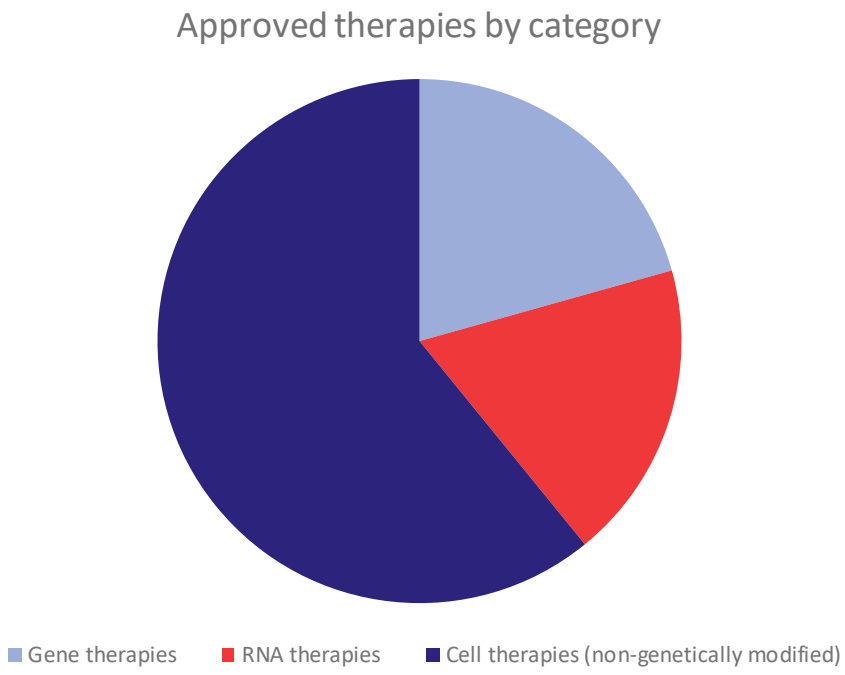
Approved gene, cell, and RNA therapies

Globally, for clinical use, there are:

- 19 gene therapies approved (including genetically modified cell therapies)
  - Since Q4 2021 there has been one new genetically modified cell therapy approval: Carvykti (Legend Biotech and Johnson & Johnson) in the U.S.
  - Due to the marketing authorization for elivaldogene autotemcel (Skysona) in the EU being officially withdrawn by the EMA, the status of this therapy has reverted from approved to pre-registration, as per the filing in the U.S. in 2021
- 17 RNA therapies approved
- 56 non-genetically modified cell therapies approved



Source: Pharmaprojects | Informa, April 2022

Approved gene therapies as of Q1 2022 (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	betibeglogene autotemcel	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, April 2022

Text highlighted in yellow represent new approvals during Q1 2022

Approved gene therapies as of Q1 2022 (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, Japan	bluebird bio
Delytact	teserpaturev	2021	Malignant Glioma	Japan	Daiichi Sankyo
Relma-cel	relmacabtagene autoleucel	2021	Diffuse large B-cell lymphoma	China	JW Therapeutics
Carvykti	ciltacabtagene autoleucel	2022	Multiple myeloma	US	Legend Biotech

Source: Pharmaprojects | Informa, April 2022

Text highlighted in yellow represent new approvals during Q1 2022

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Approved RNA therapies as of Q1 2022 (1/2)

Product name	Generic name	Year first approved	Disease(s)	Locations approved*	Originator company
Kynamro	mipomersen sodium	2013	Homozygous familial hypercholesterolemia	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
Ampligen	rintatolimod	2016	Chronic fatigue syndrome	Argentina	AIM ImmunoTech
Tegsedi	inotersen	2018	Amyloidosis, transthyretin-related hereditary	EU, UK, Canada, US, Brazil	Ionis Pharmaceuticals
Onpattro	patisiran	2018	Amyloidosis, transthyretin-related hereditary	US, EU, UK, Japan, Canada, Switzerland, Brazil, Taiwan, Israel, Turkey	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, April 2022

Text highlighted in yellow represent new approvals during Q1 2022

Approved RNA therapies as of Q1 2022 (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
Viltepso	viltolarsen	2020	Dystrophy, Duchenne muscular	US, Japan	NS Pharma
Leqvio	inclisiran	2020	Atherosclerosis; Heterozygous familial hypercholesterolemia; Hypercholesterolemia;	EU, UK, Australia, Canada, Israel, US	Alnylam
Amondys 45	casimersen	2021	Dystrophy, Duchenne muscular	US	Sarepta Therapeutics
Nulibry	fosdenopterin	2021	Molybdenum cofactor deficiency	US	Orphatec
Lagevrio	molnupiravir	2021	Infection, coronavirus, novel coronavirus	US, UK, Denmark, Ireland, India, Japan, Mexico, Morocco, Indonesia, Australia, South Korea	Ridgeback Biotherapeutics

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

Source: Pharmaprojects | Informa, April 2022

Text highlighted in yellow represent new approvals during Q1 2022

Key highlights in Q1 2022

Noteworthy events that happened in Q1 2022

Drug	Event Type	Indication	Molecule	Event Date
SPL84-23-1	Orphan Drug Designation (U.S. and Europe)	Cystic Fibrosis (CF)	Antisense	01/04/2022
ADVM-062	Orphan Drug Designation (U.S.)	Other Congenital Blindness Indications	Viral Gene Therapy	01/04/2022
Viralym-M	Regenerative Medicine Advanced Therapy (RMAT) Designation	Antiviral - Other Treatments	Cellular	01/05/2022
Eplontersen	Orphan Drug Designation (U.S.)	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)	Antisense	01/06/2022
DYN101	Fast Track Status	Centronuclear Myopathies (CNMs)	Antisense	01/06/2022
4D-125	Fast Track Status	Retinitis Pigmentosa (RP) (Ophthalmology)	Viral Gene Therapy	01/10/2022
C-CAR039	Regenerative Medicine Advanced Therapy (RMAT) Designation; Fast Track Status	Non-Hodgkin's Lymphoma (NHL)	Cellular	01/12/2022
NR082	Orphan Drug Designation (Europe)	Leber's Hereditary Optic Neuropathy (LHON) (Ophthalmology)	Viral Gene Therapy	01/17/2022
CYNK-101	Fast Track Status	Gastric Cancer	Cellular	01/18/2022
MT-601	Orphan Drug Designation (U.S.)	Pancreatic Cancer	Cellular	01/18/2022
Abecma	Approval (Japan)	Multiple Myeloma (MM)	Cellular	01/20/2022
ATA-100	Orphan Drug Designation (U.S.)	Muscular Dystrophy	Viral Gene Therapy	01/31/2022
CT-103A	Orphan Drug Designation (U.S.)	Multiple Myeloma (MM)	Cellular	01/31/2022
ET140203	Orphan Drug Designation (U.S.)	Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)	Cellular	02/08/2022
Omidubicel	Rolling NDA/BLA Initiated	Bone Marrow Transplant and Stem Cell Transplant	Cellular	02/09/2022
CYNK-101	Orphan Drug Designation (U.S.)	Gastric Cancer	Cellular	02/14/2022
SBT101	Fast Track Status	Adrenoleukodystrophy	Viral Gene Therapy	02/16/2022
ATA-100	Orphan Drug Designation (Europe)	Muscular Dystrophy	Viral Gene Therapy	02/24/2022
Carvykti	Approval (U.S.)	Multiple Myeloma (MM)	Cellular	02/28/2022
MuSK-CAART	Fast Track Status	Myasthenia Gravis (MG)	Cellular	03/01/2022
NTLA-5001	Orphan Drug Designation (U.S.)	Acute Myelogenous Leukemia (AML)	Cellular	03/09/2022
ALLO-316	Fast Track Status	Renal Cell Cancer (RCC)	Cellular	03/10/2022
SBT101	Orphan Drug Designation (U.S.)	Adrenoleukodystrophy	Viral Gene Therapy	03/14/2022
CAR-T Therapy Program (WUGEN)	Orphan Drug Designation (U.S.)	Hematologic Cancer	Cellular	03/15/2022
TCB002	Orphan Drug Designation (U.S.)	Acute Myelogenous Leukemia (AML)	Cellular	03/17/2022
EtranaDez	MAA Submission (Europe)	Hemophilia B	Viral Gene Therapy	03/28/2022
ASC-618	Fast Track Status	Hemophilia A	Viral Gene Therapy	03/29/2022

Pipeline overview

Q1 2022

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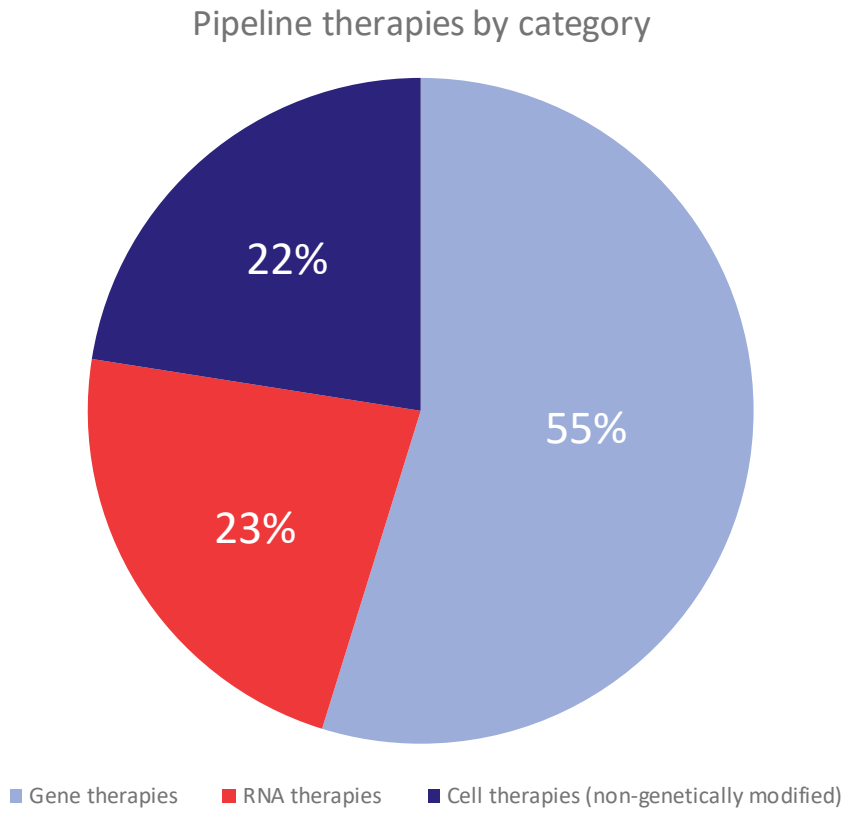
Pipeline of gene, cell, and RNA therapies

3,579 therapies are in development, ranging from preclinical through pre-registration

- 1,986 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
- 816 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies



Source: Pharmaprojects| Informa, April 2022

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Gene therapy pipeline

Gene therapy and genetically modified cell therapies

Q1 2022

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Gene therapy pipeline: Quarterly comparison

- The increase in preclinical development since Q4 2021 is the smallest quarterly increase since Q1 to Q2 2021, at 3%
- In Q1 2022 Amicus and Taysha saw reductions in their gene therapy R&D pipelines to focus on specific programs
- One new gene therapy has filed for approval in Q1 2022. 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
  - eladocagene exuparvovec (PTC Therapeutics)
    - In the EU and UK
  - elivaldogene autotemcel (bluebird bio)
    - In the US (due to the marketing authorization in the EU being officially withdrawn by the EMA, the status of this therapy has reverted to pre-registration, as per the US filing in 2021)
  - etranacogene dezaparvovec (uniQure)
    - In the EU and UK

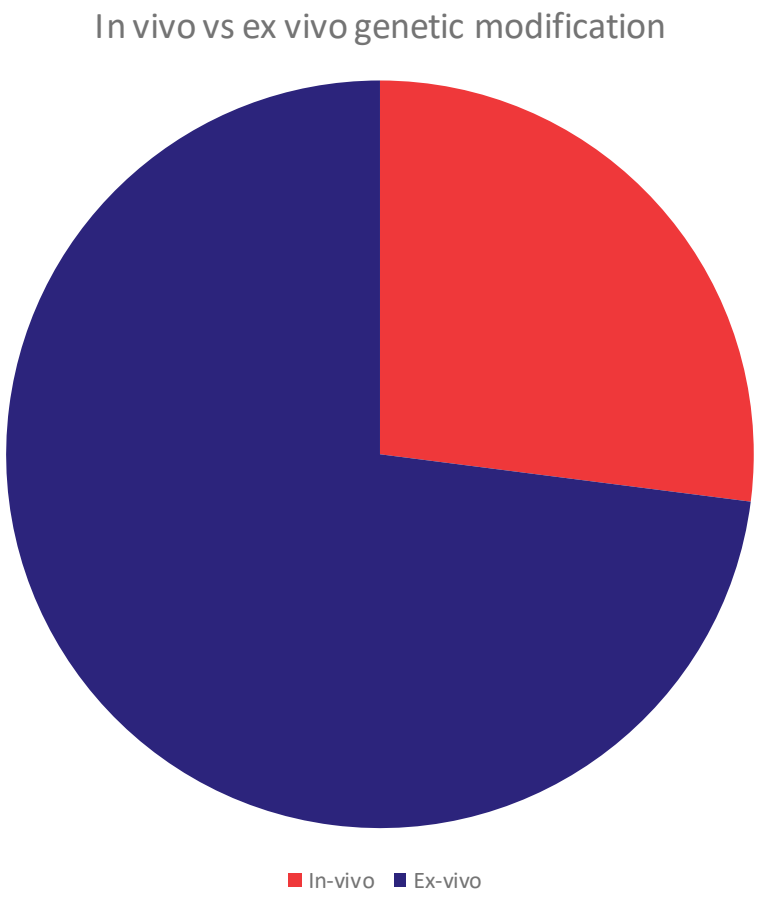
Global Status	Q1 2021	Q2 2021	Q3 2021	Q4 2022	Q1 2022
Preclinical	1,190	1,296	1,353	1,412	1,451
Phase I	225	269	264	248	248
Phase II	231	236	239	244	250
Phase III	27	27	29	32	31
Pre-registration	8	7	5	5	6
Total	**1,711**	**1,835**	**1,890**	**1,941**	**1,986**

Source: Pharmaprojects| Informa, April 2022

Source: Amicus April 2022 Corporate Presentation; Taysha Fourth Quarter and Full Year 2021 Financial Results and Corporate Update; Pharmaprojects| Informa, April 2022

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

- As found in 2021, *ex vivo* genetic modification is most commonly used for gene therapies in pipeline development
- In Q1 2022 *in vivo* delivery techniques were used in 27% of gene therapies, the same proportion as in Q4 2021



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

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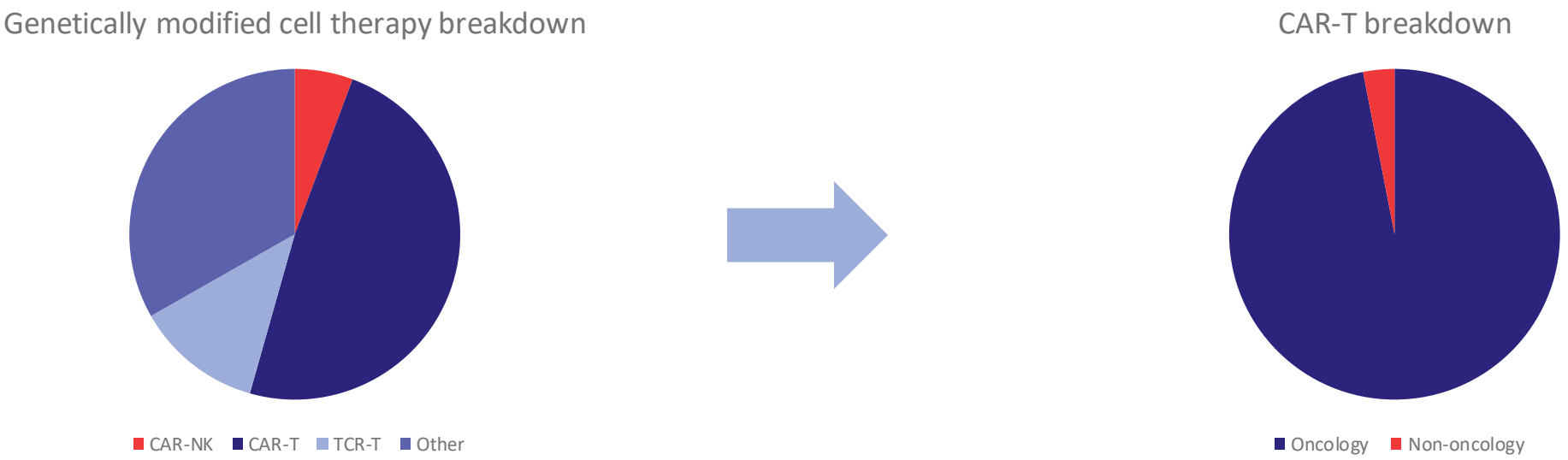
Gene therapy breakdown: CAR-Ts continue to dominate pipeline in 2022

- CAR T-cell therapies remain the most common technology used in the pipeline of genetically modified cell therapies (preclinical through to pre-registration), representing 49%, followed by the “other” category, which includes a list of less commonly used technologies such as TAC-T, CAR-M, and TCR-NK
- As found in Q4 2021, 98% of CAR-T cell therapies are in development for cancer indications. The remaining non-oncology indications include scleroderma, HIV/AIDs and autoimmune disease (unspecified)

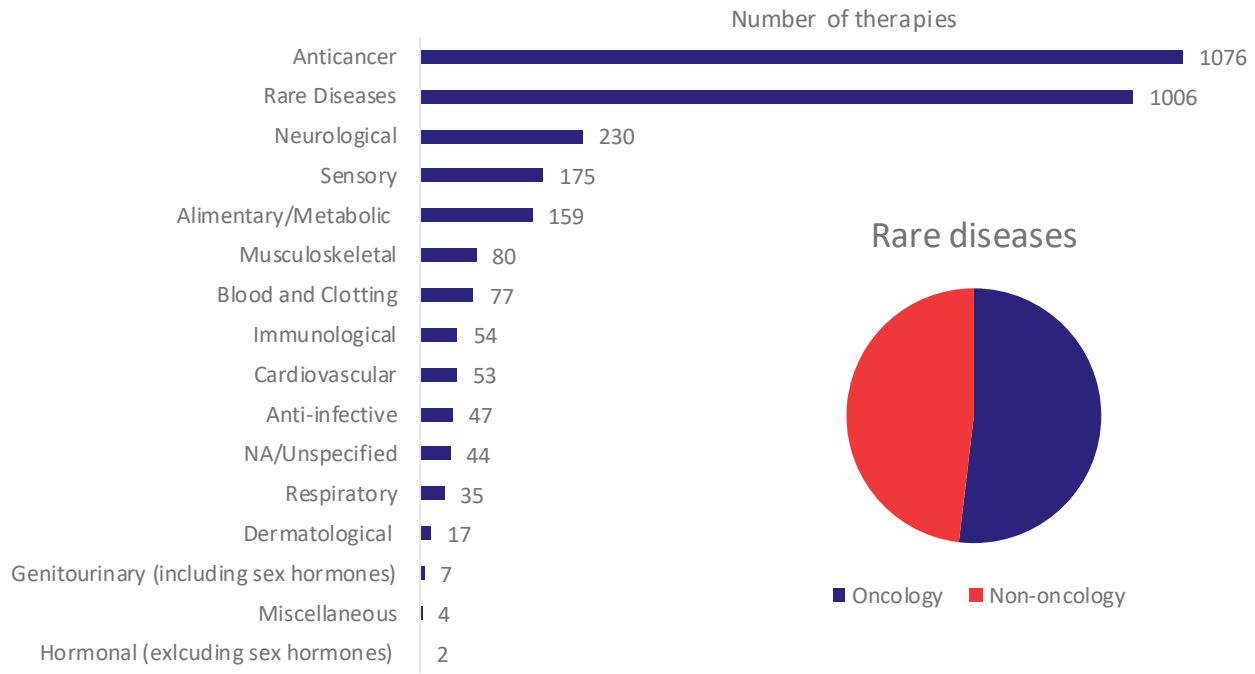


Source: Cell and Gene Therapy dashboard | Informa, April 2022

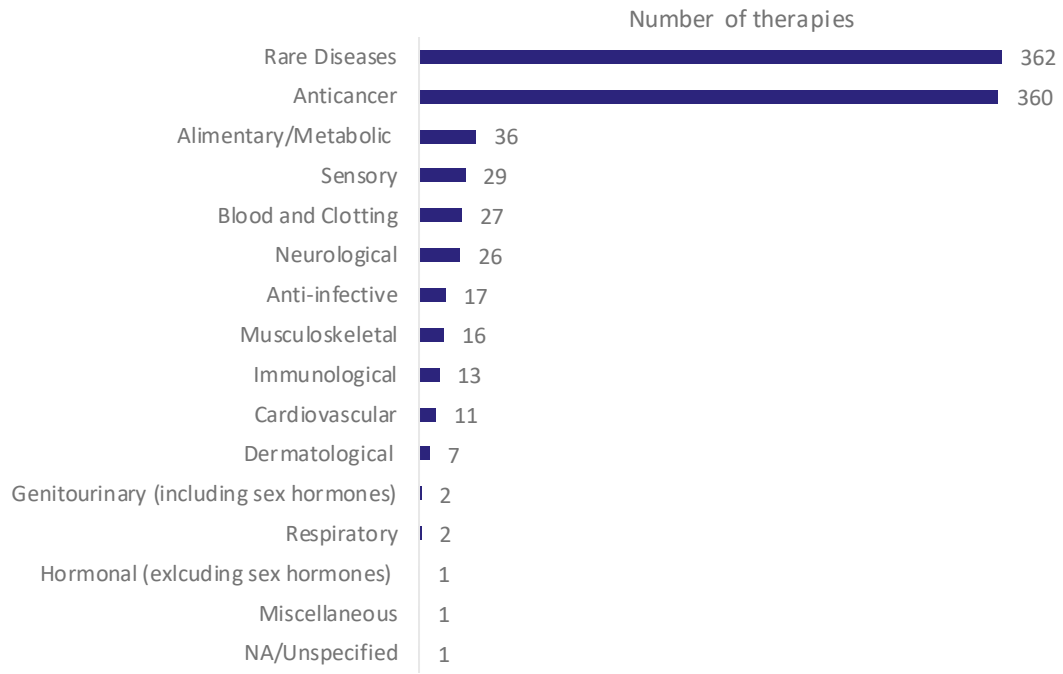
Gene therapy pipeline: Most commonly targeted therapeutic areas

- Oncology and rare diseases continue to be the top areas of gene therapy development in both the overall pipeline (preclinical to pre-registration) and in the clinic (phase I to pre-registration)
- Development for rare diseases most commonly occurs in the oncology space, representing a majority of 52% compared to non-oncology rare disease gene therapy pipeline development

Number of therapies from preclinical through pre-registration



Therapies in the clinic (excludes preclinical development)



Source: Pharmaprojects| Informa, April 2022

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

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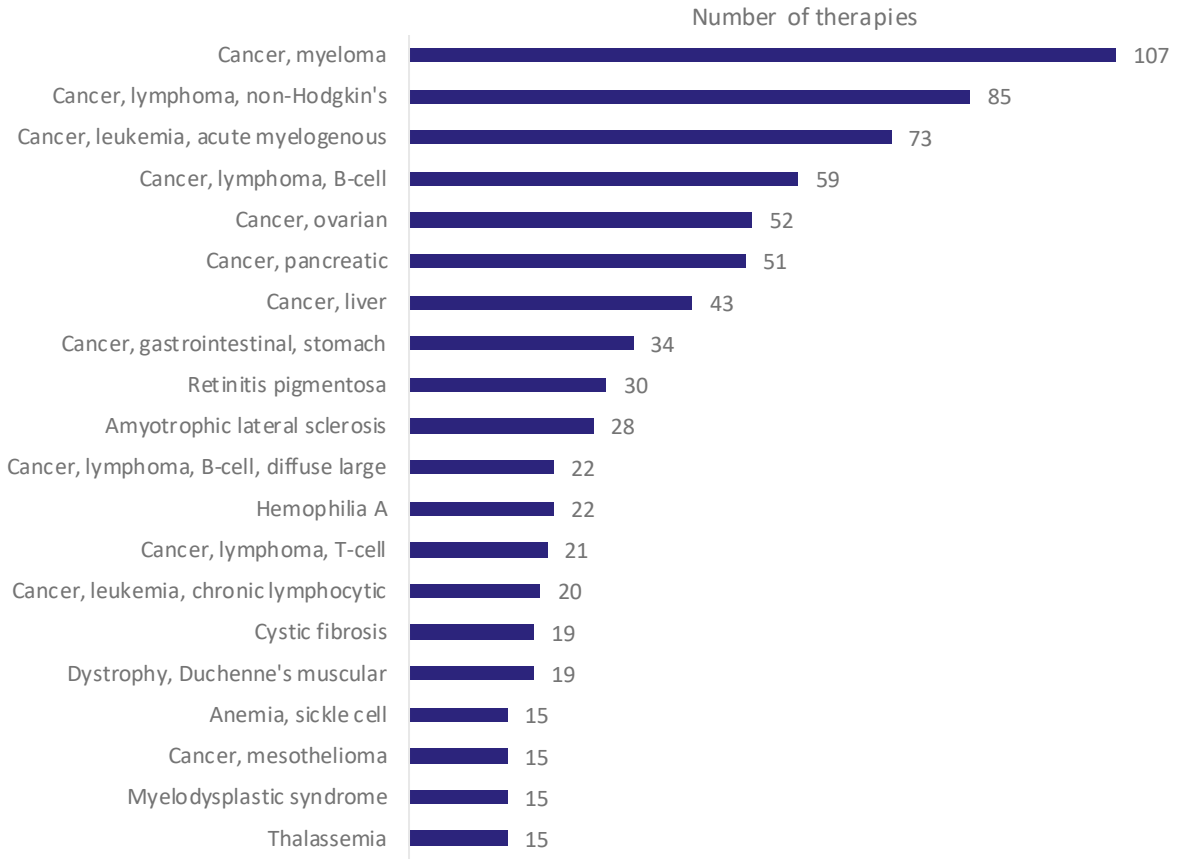
Gene therapy pipeline: Most common rare diseases targeted

- For the 1006 pipeline (preclinical to pre-registration) gene therapies which are being developed for rare diseases, eight out of the top 10 rare diseases are oncological
- In the same order as in Q4 2021, the top five rare diseases for which gene therapies are being developed are:
  1. Myeloma
  2. Non-Hodgkin's lymphoma
  3. Acute myelogenous leukemia
  4. B-cell lymphoma
  5. Ovarian cancer



Source: Pharmaprojects| Informa, April 2022

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

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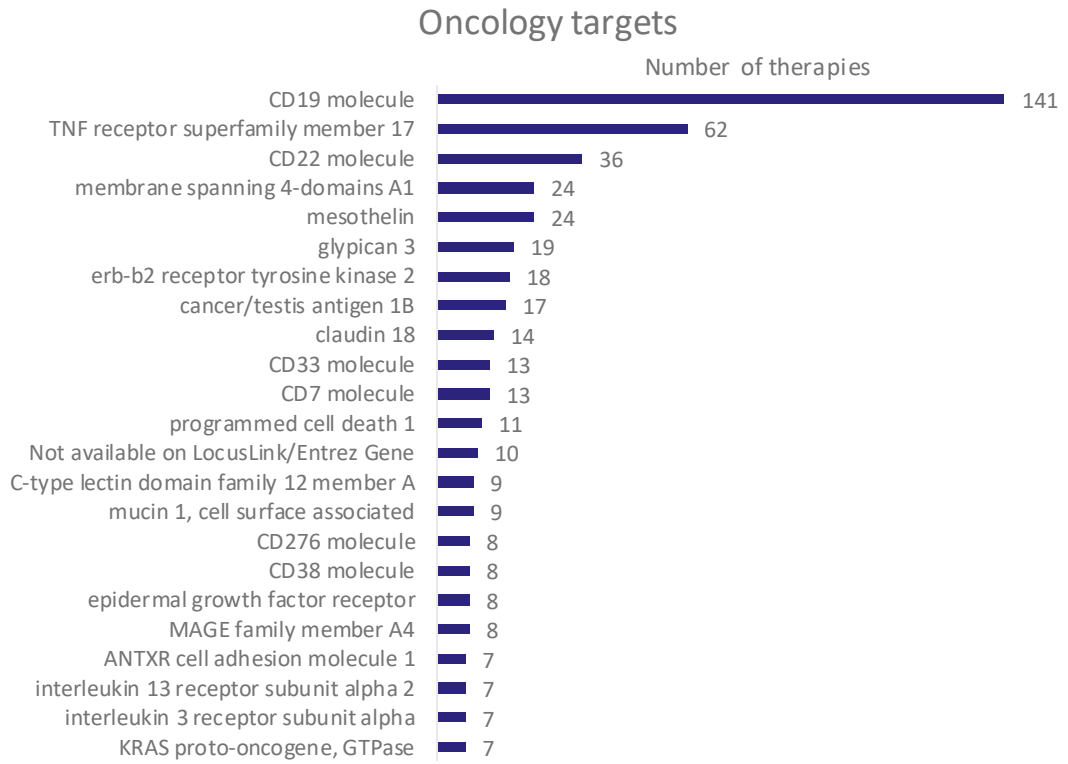
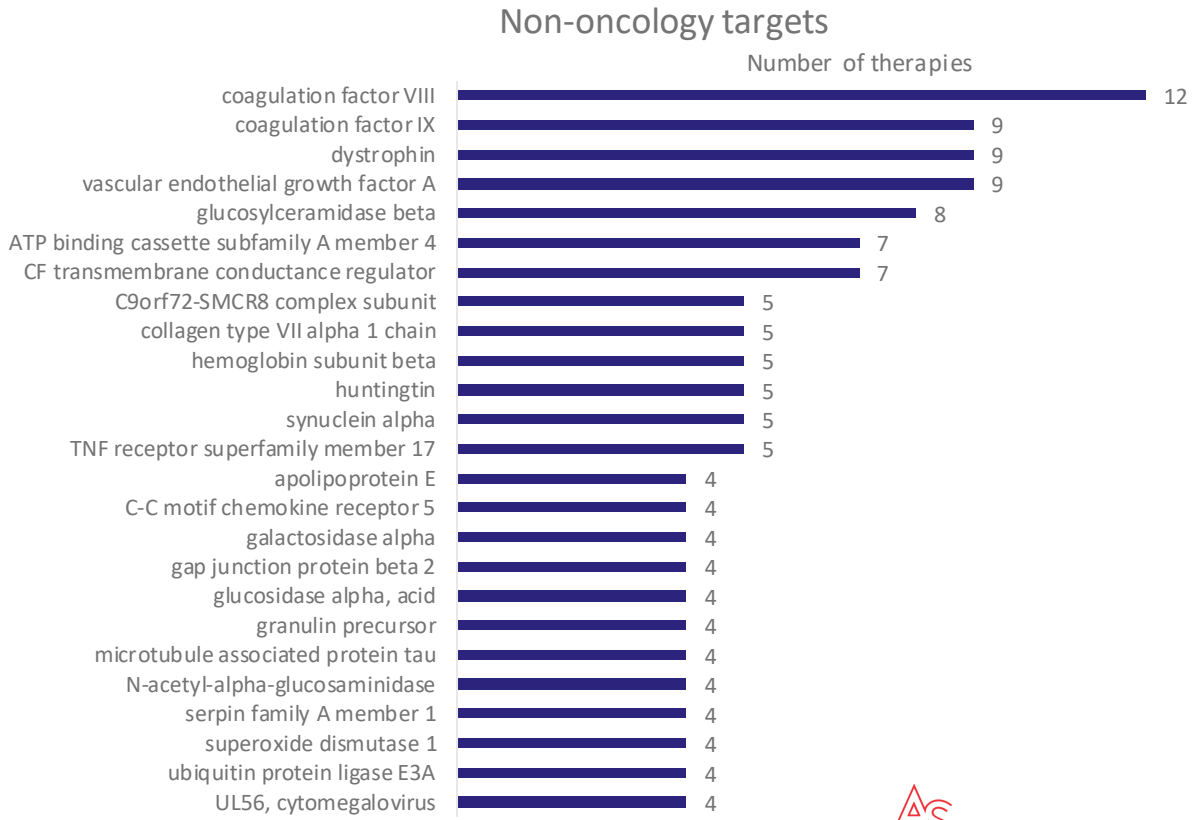
Gene therapy pipeline: Most common targets

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

- CD19, B-cell maturation antigen (BCMA), also known as TNF receptor superfamily member 17, and CD22 molecule all remain the top 3 most common targets for oncology indications since Q4 2021
- Coagulation factor VIII remains the most common target for non-oncology indications and coagulation factor IX has risen to second most common since Q4 2021





Source: Pharmaprojects| Informa, April 2022

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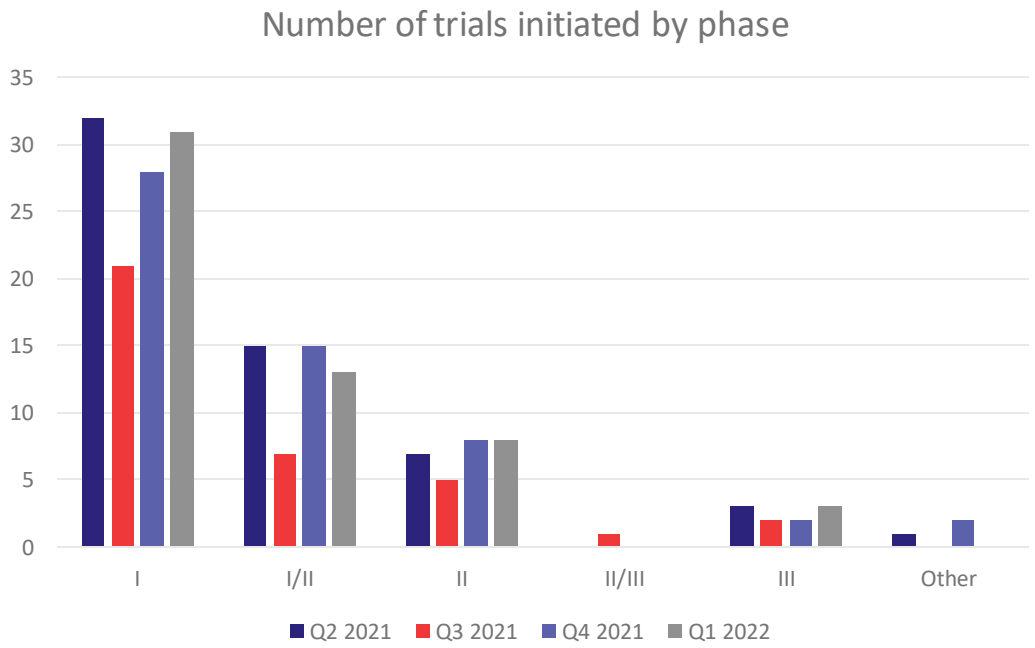
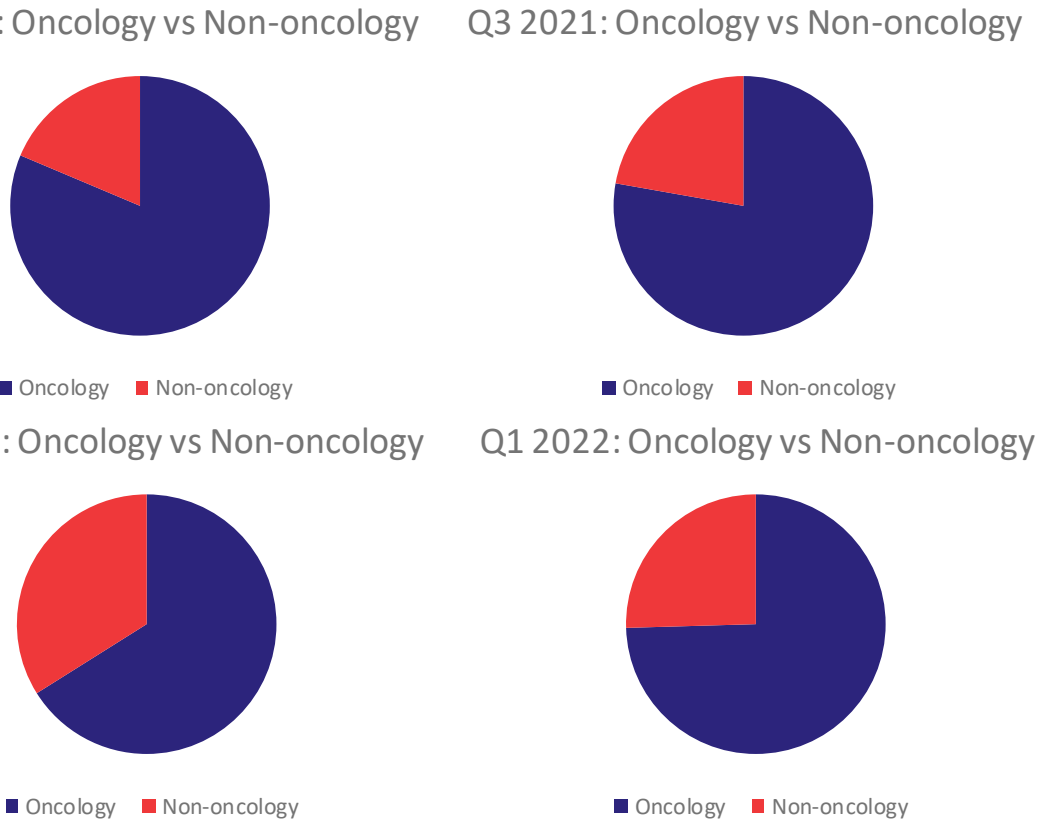
Gene therapy clinical trial activity

- As in Q4 2021, 55 trials were initiated in Q1 2022 for gene therapies
- The trend of an increasing proportion of gene therapy trials for non-oncology indications has not continued into 2022 so far, with 25% of the newly initiated trials in Q1 2022 being for non-oncology diseases compared to 35% in Q4 2021





Source: Trialtrove| Informa, April 2022

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Non-genetically modified cell therapy pipeline

Q1 2022

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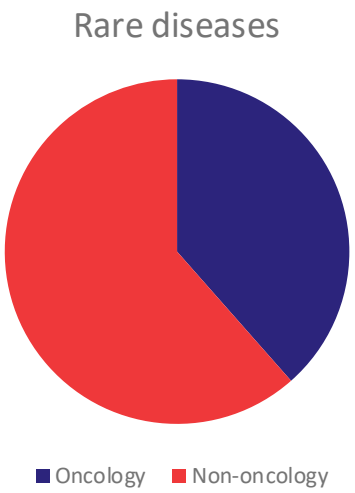
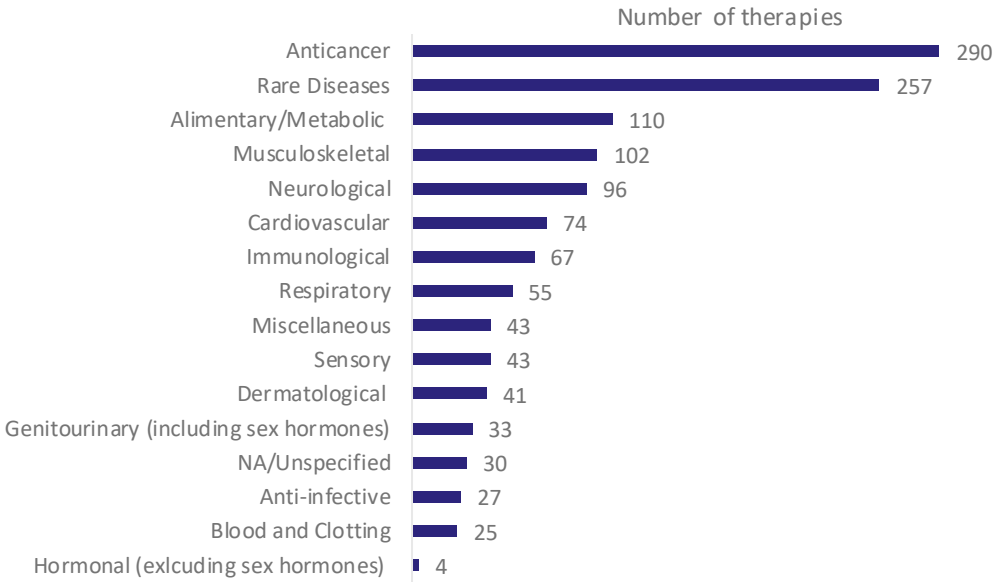
Non-genetically modified cell therapy pipeline: Most common therapeutic areas targeted

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

- Oncology and rare diseases continue to be the top areas of non-genetically modified cell therapy development
- Of the non-genetically modified cell therapies in preclinical to pre-registration stages for rare diseases, 63% are in development for non-oncology rare diseases, a decrease of 11% compared to Q4 2021





Source: Pharmaprojects| Informa, April 2022

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

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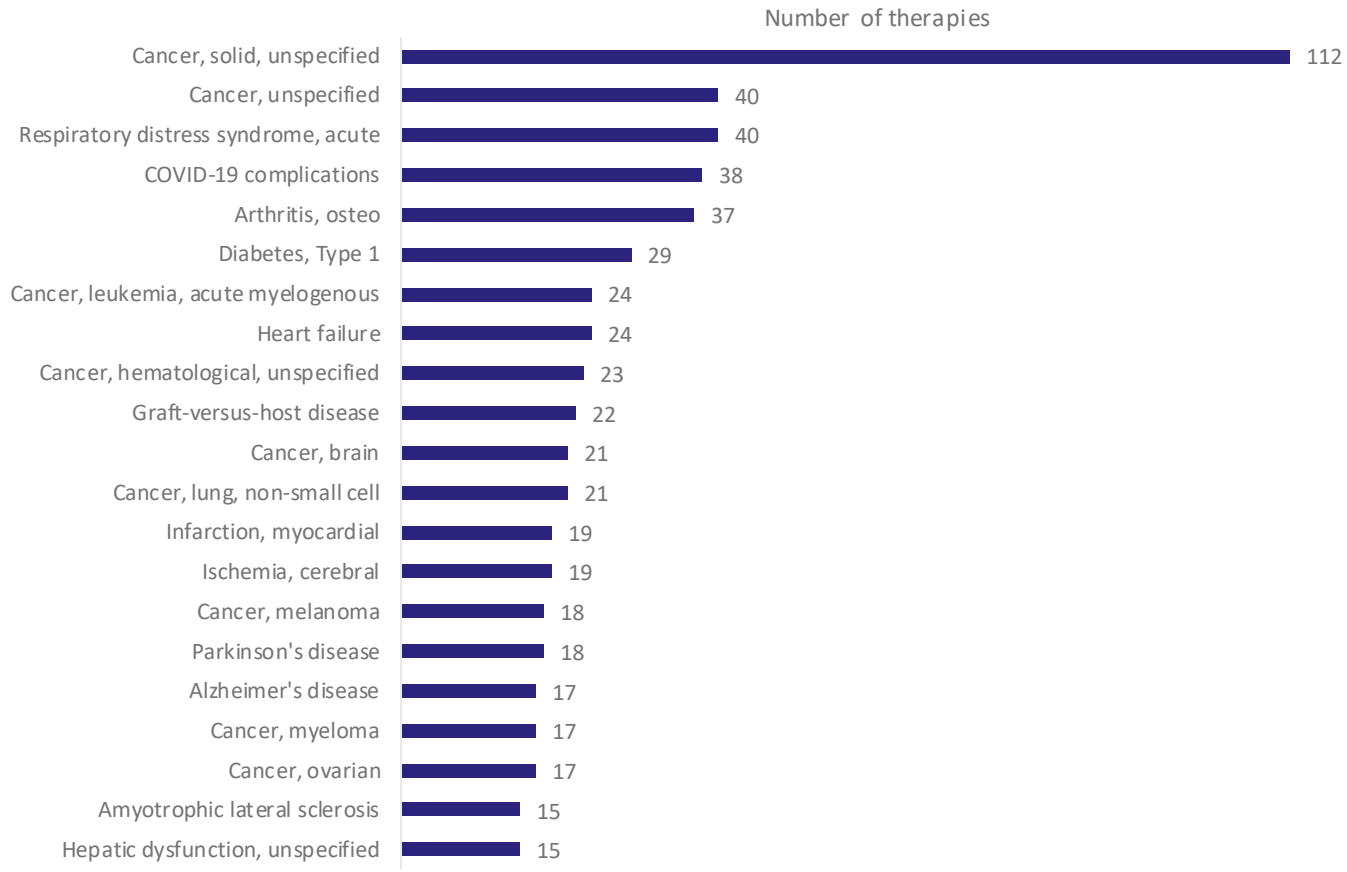
Non-genetically modified cell therapy pipeline: Most common diseases targeted

Of the diseases for which indications are specified, the top three indications remain the same as in Q4 2021:

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



Source: Pharmaprojects| Informa, April 2022

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

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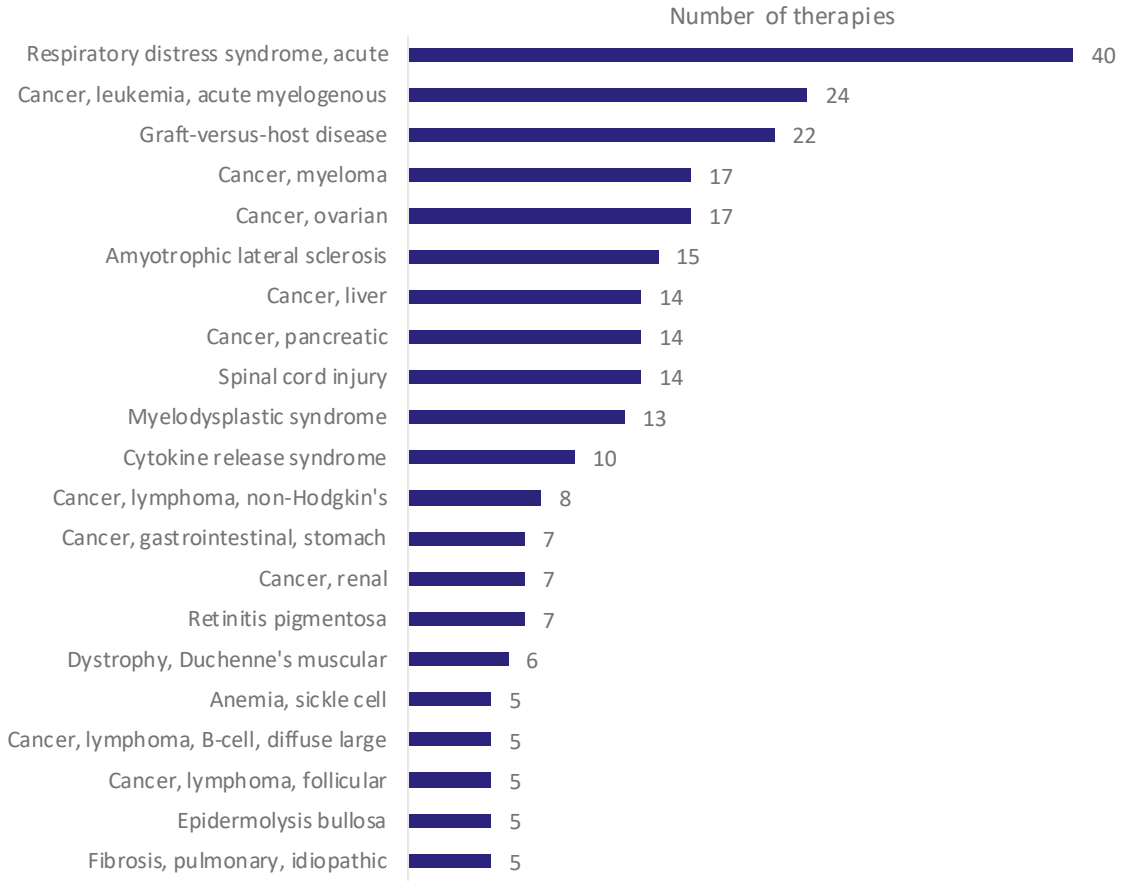
Non-genetically modified cell therapy pipeline: Most common rare diseases targeted

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

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



Source: Pharmaprojects| Informa, April 2022

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

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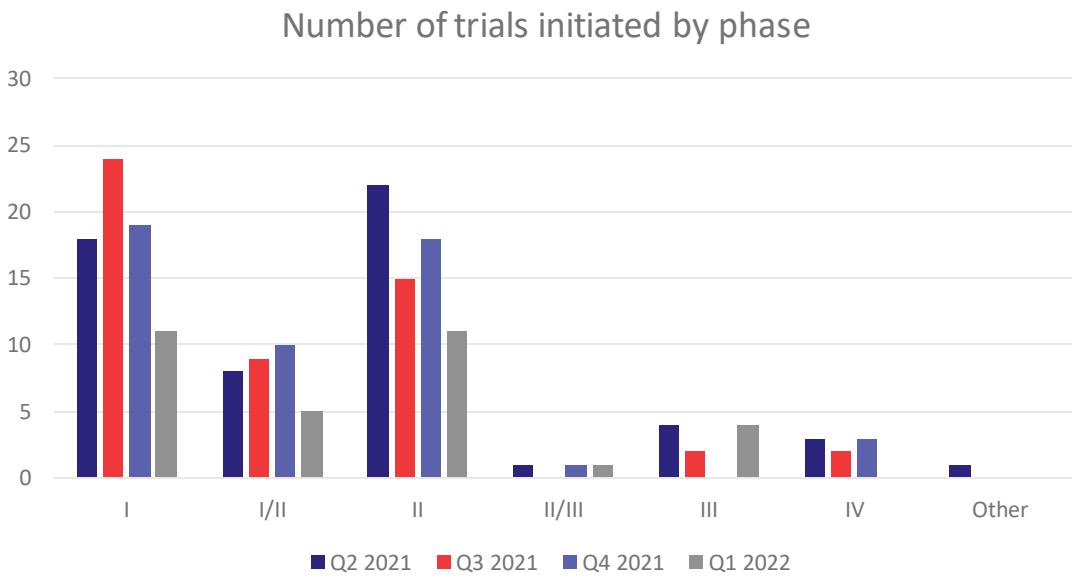
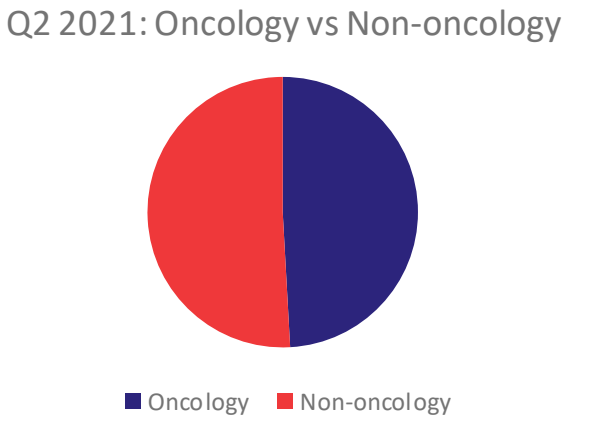
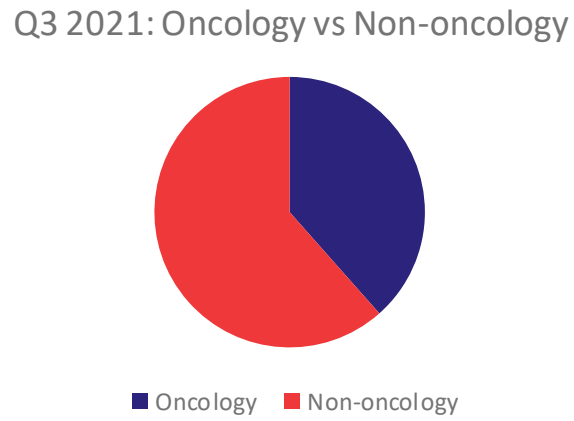
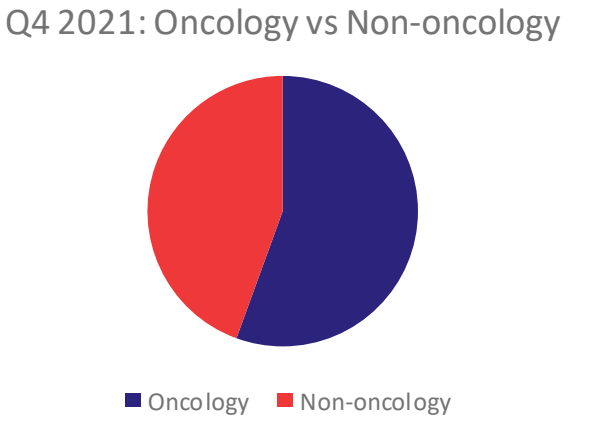
Non-genetically modified cell therapy trial activity

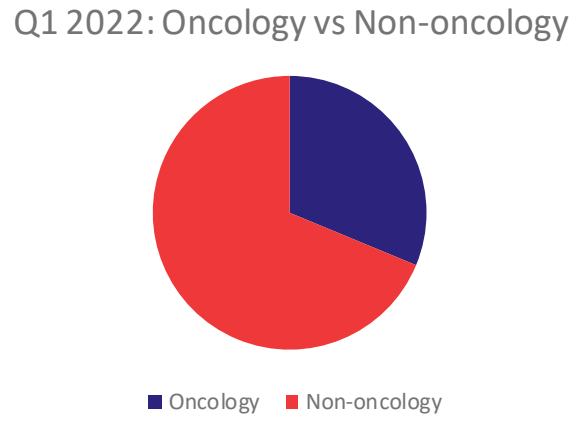
- 32 trials were initiated for non-genetically modified cell therapies in Q1 2022, and of these 69% are for non-oncology indications











Source: Trialtrove| Informa, April 2022

American Society of Gene + Cell Therapy

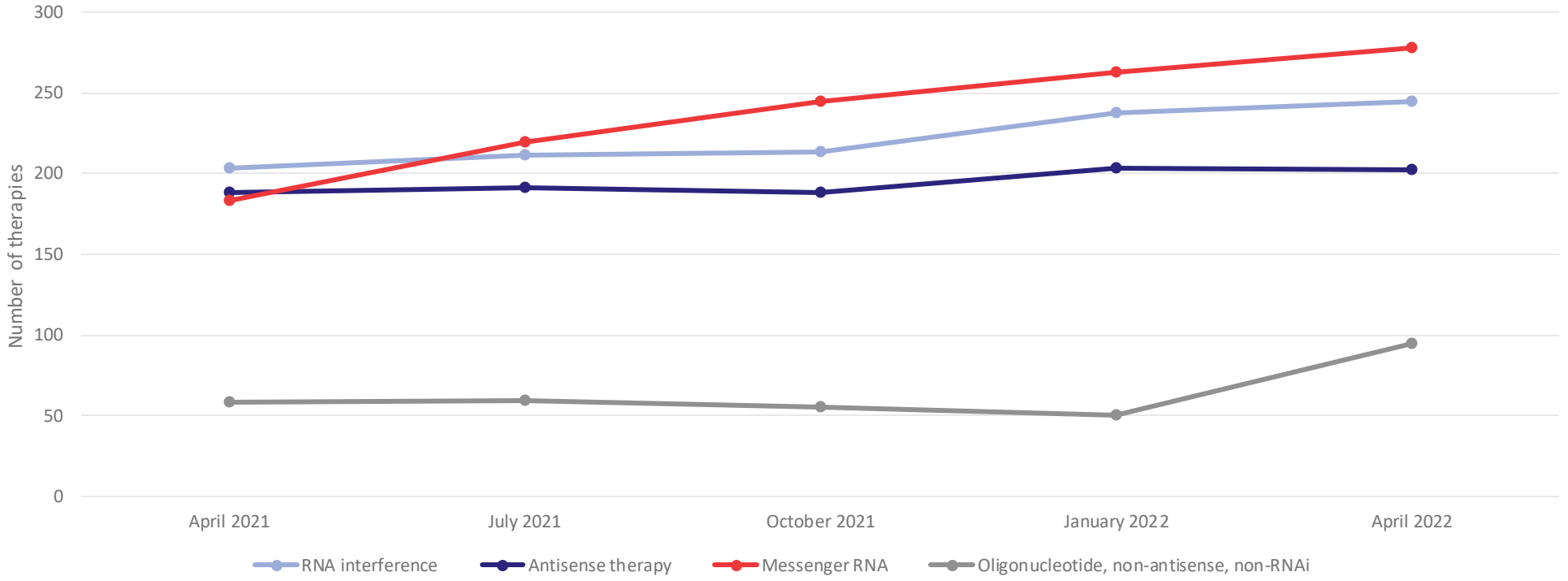
RNA therapy pipeline

Q1 2022

American Society of Gene + Cell Therapy

RNA therapy pipeline: Most common modalities

- Q1 2022 has continued the trends established in 2021 of an overall increase in messenger RNA and RNA interference therapies in pipeline (preclinical to pre-registration) development, rising to 278 and 245, respectively

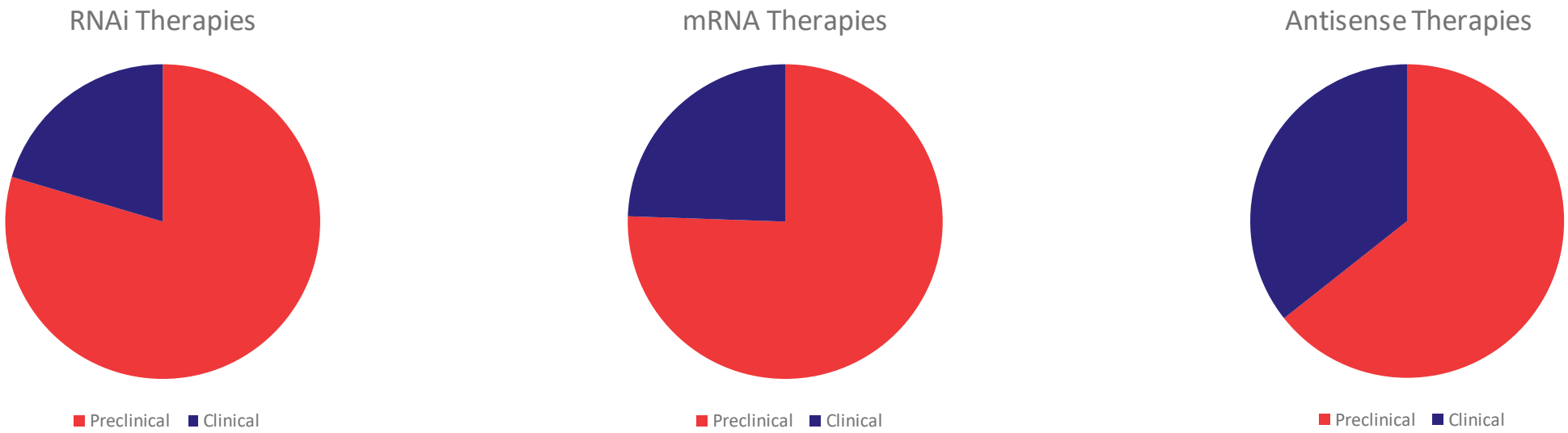


Source: Pharmaprojects| Informa, April 2022

American Society of Gene + Cell Therapy

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

- Preclinical development continues to dominate RNAi, mRNA, and antisense therapeutic development, representing 80%, 76%, and 64% of development respectively

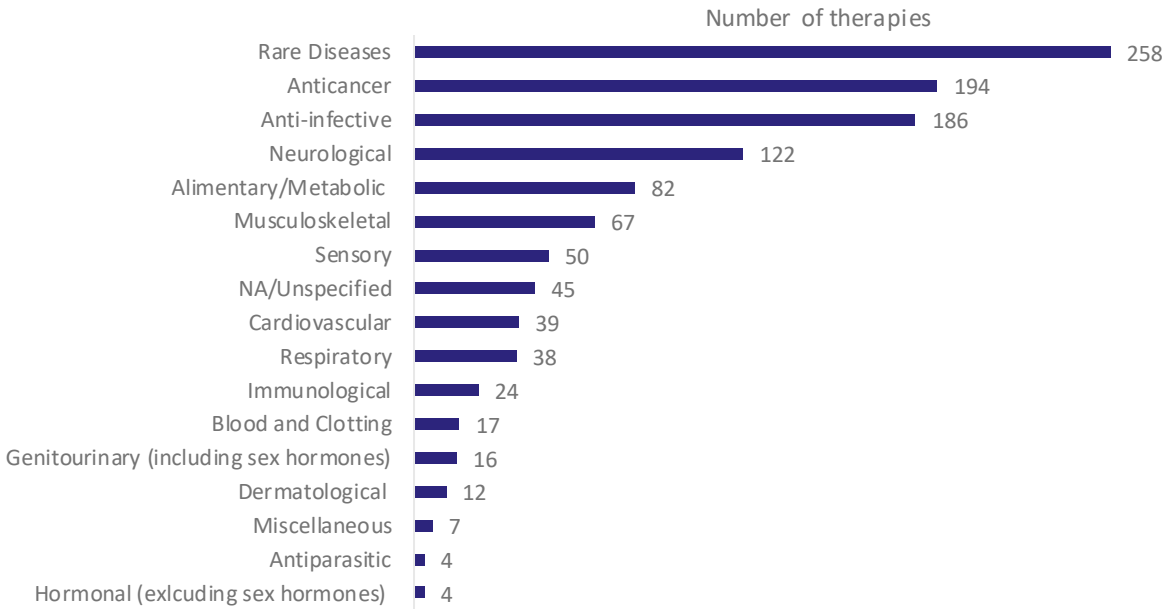


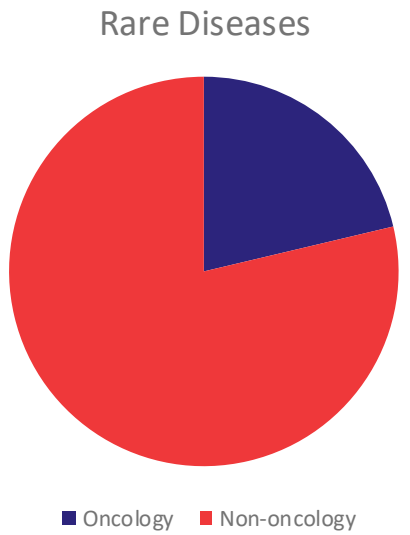
Source: Pharmaprojects| Informa, April 2022

RNA therapies: Most commonly targeted therapeutic areas

Of the 823 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Rare diseases remain the top therapeutic area being targeted by RNA therapies, while anticancer therapies have regained their position as the second most common RNA therapy type, overtaking anti-infective therapies
- As found in Q4 2021, of all the RNA therapies in preclinical to pre-registration development for rare diseases, 80% are in development for non-oncology rare diseases





Source: Pharmaprojects| Informa, April 2022

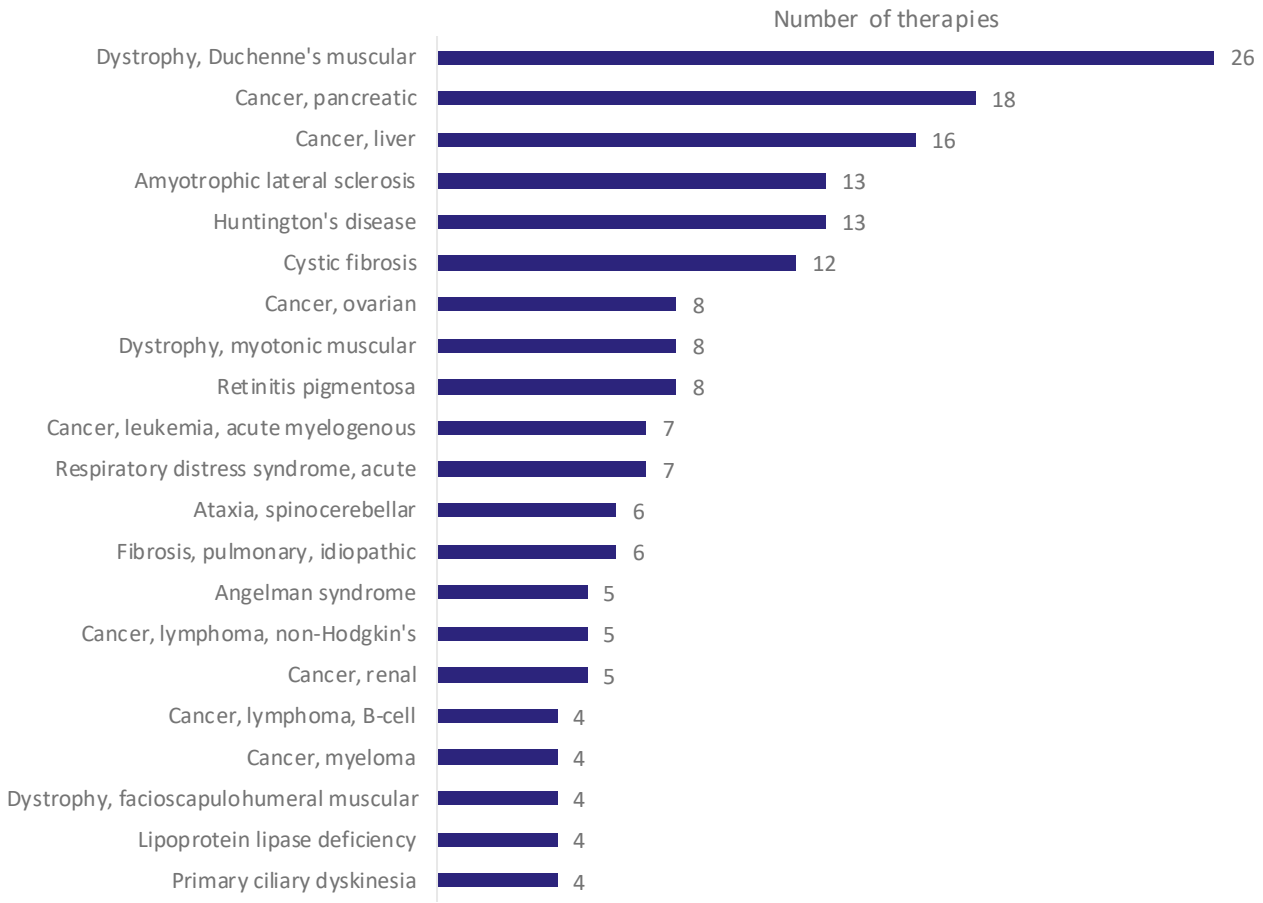
*figures based on indications in pipeline development only for each therapy

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



Source: Pharmaprojects| Informa, April 2022

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

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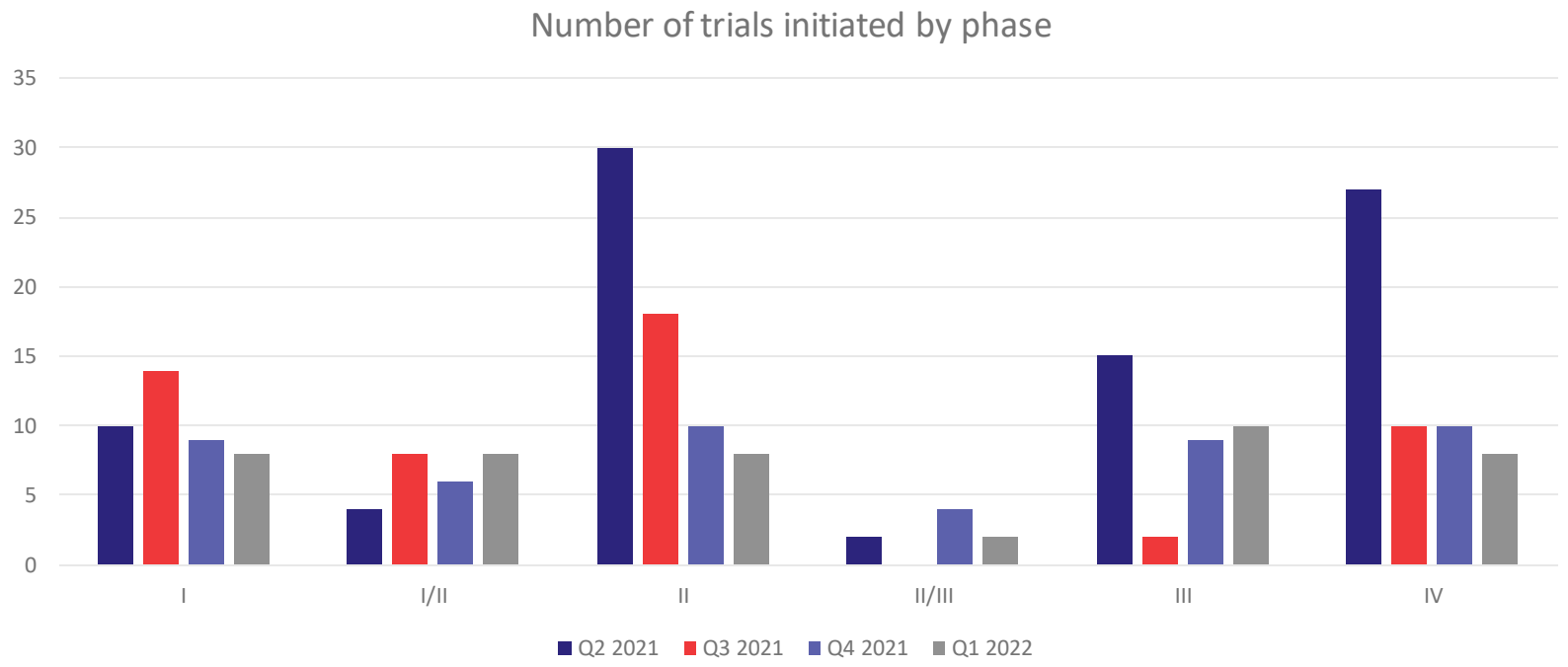
RNA therapy pipeline: Clinical trial activity

- 44 RNA trials were initiated in Q1 2022, compared to 49 in Q4 2021, 93% of which were for oncology indications



Source: Trialtrove| Informa, April 2022

American Society of Gene + Cell Therapy

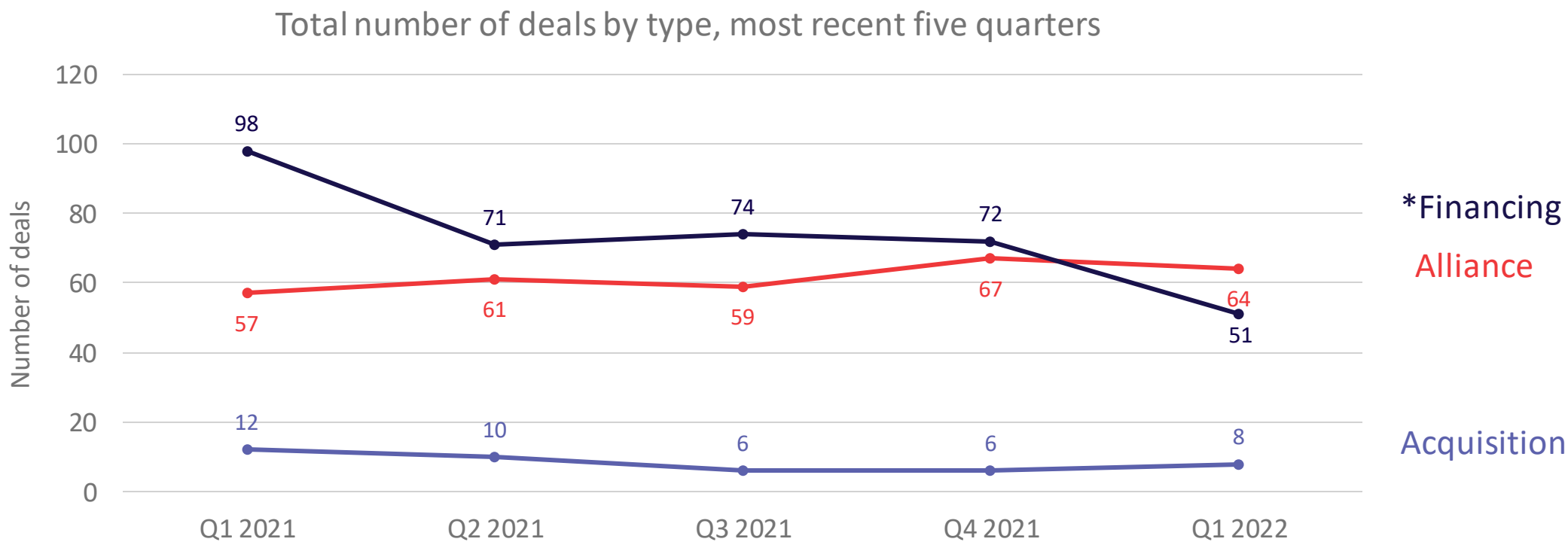
Overview of dealmaking for gene, cell, and RNA therapy companies

Q1 2022

American Society of Gene + Cell Therapy

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

- In Q1 2022, a total of 123 deals were signed, a 15% decrease in volume from Q4 2021
- Q1 2022 also featured the lowest quarter total within the last year, and represented a 26% decrease from the 167 deals done in the opening quarter of 2021
- Acquisition and alliance volume quarter by quarter remains flat, while financings continue to trend down



Source: Biomedtracker| Informa, April 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

Q1 2022 acquisitions in gene, cell, & RNA therapy

- Acquisitions were the only deal type to see an increase in Q1 2022, where there were 8 transactions done compared with 6 in Q4 2021
- In the largest takeover, Intellia paid $200M to acquire Rewrite Therapeutics, which develops DNA writing technologies for genome editing
- Recipharm was responsible for 2 of the 8 acquisitions of the quarter, buying CDMOs GenIbet and Vibalogics

Deal Date	Deal Title	Potential Deal Value (USD)
01/07/2022	Kriya Expands Gene Therapy Pipeline and Establishes Rare Disease Therapeutic Area Division With the Acquisition of Warden Bio	Undisclosed
01/10/2022	Castle Creek Biosciences Acquires Novavita Thera to Expand Innovative Cell and Gene Therapy Platform	Undisclosed
01/18/2022	ProKidney to Become Publicly Traded via Business Combination with Social Capital Suvretta Holdings Corp. III	Undisclosed
01/28/2022	Oxford Biomedica Pays $175M for Homology Medicine's 80% Stake in AAV Manufacturing Business Oxford Biomedica Solutions LLC	175,000,000
02/01/2022	Polyplus Acquires Plasmid DNA Vector Company e-Zyvec	Undisclosed
02/01/2022	Recipharm Buys GenIbet, a Portuguese CDMO	Undisclosed
02/03/2022	Intellia Therapeutics Acquires Rewrite Therapeutics	200,000,000
02/18/2022	Recipharm Buys CDMO Vibalogics	Undisclosed

Source: Biomedtracker| Informa, April 2022

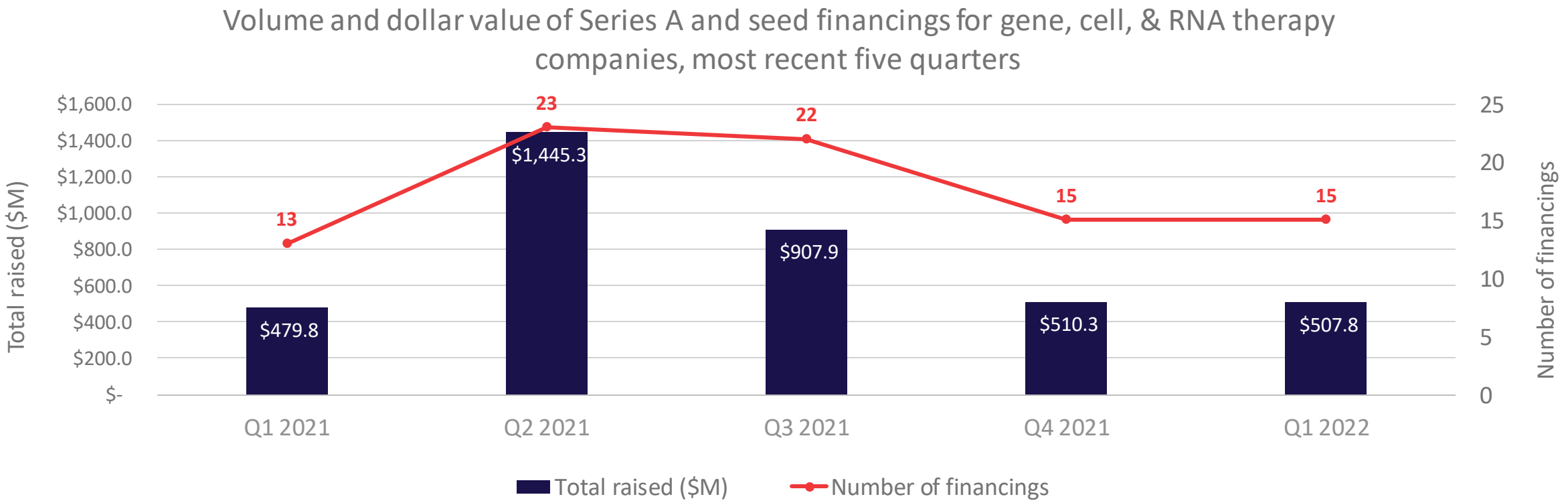
Start-up funding for gene, cell, & RNA therapy companies

Q1 2022

American Society of Gene + Cell Therapy

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

- 15 companies raised seed or Series A financing in Q1 2022, together totaling $507.8M; the number of companies and aggregate raised was virtually flat compared with Q4 2021, when 15 companies brought in $510.3M
- Q1 2022 was stronger than the opening quarter of 2021, when 13 companies amassed $479.8M in seed or Series A financing
- Cellino Biotech, an autologous and allogeneic cell manufacturing company, raised the largest financing with an $80M Series A round
- Note: The Q1 2022 totals do not include Affini-T Therapeutics' $175M financing, which the CEO said combined seed, Series A, and Series B cash



Source: Biomedtracker| Informa, April 2022; Scrip| Informa, March 2022

American Society of Gene + Cell Therapy

Q1 2022 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)
01/04/2022	Ray Therapeutics Closes $6M Seed Financing	Gene therapy (optogenetics)	United States, California, San Diego	Undisclosed	6
01/06/2022	ONK Therapeutics Raises $21.5M Series A Financing	Cell therapy (NK cells)	Ireland, Galway	National University of Ireland, Galway, and Australia's Walter and Eliza Hall Institute of Medical Research	21.5
01/19/2022	Ceptur Therapeutics Launches with $75M Series A Financing to Advance RNA Therapeutics Based on Proprietary U1 Adaptor Technology	Oligonucleotides	United States, New Jersey, Hillsborough	Rafal Goraczniak (inventor; currently Ceptur's director of platform development)	75
01/19/2022	64x Bio Closes $55M Series A Round to Fund Expansion of VectorSelect Platform	Cell line engineering for gene therapies	United States, California, San Francisco	Harvard Department of Genetics	55
01/25/2022	Cellino Biotech Raises $80M Series A Financing	Cell therapy (manufacturing, autologous and allogeneic)	United States, Massachusetts, Cambridge	Harvard University	80
02/10/2022	Indapta Therapeutics Raises $50M in Series A Financing	Cell therapy (NK cells)	United States, California, San Francisco	University of California, Davis	50
02/10/2022	Ucello Therapeutics Completes $25M Series A Financing	Cell therapy (CAR-T)	China	Undisclosed	25
02/16/2022	SpliceBio Raises $56.7M in an Oversubscribed Series A Financing	Gene therapy (improved delivery using protein splicing platform)	Spain, Barcelona	Muir Lab at Princeton University	56.8
02/23/2022	hC Bioscience Closes $24M Series A Financing	tRNA therapeutics	United States, Massachusetts, Cambridge	University of Iowa	24

Source: Biomedtracker| Informa, April 2022

Q1 2022 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)
03/01/2022	NextRNA Secures $46.8M in a Series A Round	Small molecules that address protein interactions with non-coding RNA	United States, Massachusetts, Cambridge	Dana-Farber Cancer Institute	46.8
03/01/2022	NextRNA Launches with $9.3M in Seed Financing	Small molecules that address protein interactions with non-coding RNA	United States, Massachusetts, Cambridge	Dana-Farber Cancer Institute	9.3
03/17/2022	Zhongbo Ruikang Raises up to USD15.7 Million in Series A Financing	Cell and gene therapy tools and services	China, Beijing	Undisclosed	15.7
03/20/2022	CRISP-HR Therapeutics Raises Funds through Seed Financing	CRISPR gene editing	United States, California, San Carlos	Co-founders from NYU and Georgia Tech	Undisclosed
03/21/2022	Suzhou Qiheshengke Biotech Raises USD15.7 Million in Seed Financing	Gene editing	China, Suzhou	Undisclosed	15.7
03/29/2022	RNAimmune Raises $27M Series A Financing	mRNA vaccines and therapeutics	United States, Maryland, Gaithersburg	n/a - subsidiary of Sirnaomics	27

Source: Biomedtracker| Informa, April 2022

Notable Q1 2022 start-up gene, cell, & RNA therapy companies

Company details	Academic source	Financing type/amount raised	Lead investor(s)	Therapy areas of interest
Large-scale production of personalized cell therapies: automated cell reprogramming, expansion, and differentiation in a closed cassette format	Harvard University	Series A/$80M	Leaps by Bayer, 8VC, and Humboldt Fund	Undisclosed
U1 adapter therapeutics (bivalent oligonucleotides) that control gene expression at the pre-mRNA level	Rafal Goraczniak (inventor; currently Ceptur's director of platform development)	Series A/$75M	venBio Partners and Qiming Venture Partners USA	Oncology, CNS, nephrology, and immunology
Protein splicing platform (next-generation engineered split inteins) for development of gene therapies	Muir Lab at Princeton University	Series A/$56.8M	UCB Ventures and Ysios Capital	Ophthalmology

Source: Biomedtracker| Informa, April 2022

Upcoming catalysts

Q1 2022

American Society of Gene + Cell Therapy

Upcoming Catalysts

Below are noteworthy catalysts (forward looking events) expected in Q2 2022

Therapy	Generic Name	Disease	Catalyst	Catalyst Date
Kymriah	tisagenlecleucel-t	Indolent Non-Hodgkin's Lymphoma (Including Follicular Lymphoma) - NHL	PDUFA for sBLA - First Review	27 Apr 2022 – 27 Apr 2022
PTC-AADC	eladocagene exuparvovec	Neurology - Other	CHMP Opinion	1 Apr 2022 – 30 Apr 2022
Lantidra	Allogeneic Islets of Langerhans	Diabetes Mellitus, Type I	PDUFA for BLA - First Review	7 Mar 2022 – 31 May 2022
Zynteglo	betibeglogene autotemcel	Thalassemia	FDA Advisory Panel Brief	7 Jun 2022 – 8 Jun 2022
Zynteglo	betibeglogene autotemcel	Thalassemia	FDA Advisory Panel Meeting	9 Jun 2022 – 10 Jun 2022
Lenti-D	elivaldogene autotemcel	Adrenoleukodystrophy	FDA Advisory Panel Meeting	9 Jun 2022 – 10 Jun 2022
Breyanzi	lisocabtagene maraleucel	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	PDUFA for sBLA - 2L LBCL	24 Jun 2022 – 24 Jun 2022
Roctavian	valoctocogene roxaparvovec	Hemophilia A	CHMP Opinion	9 Jan 2022 – 30 Jun 2022
Yescarta	axicabtagene ciloleucel	Diffuse Large B-Cell Lymphoma (DLBCL) - NHL	Supplemental CHMP Opinion	1 May 2022 – 31 Oct 2022
Oxlumo	lumasiran	Hyperoxaluria	CHMP Supplemental Opinion	1 May 2022 – 31 Oct 2022
vutrisiran	vutrisiran	Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)	CHMP Opinion	1 Jun 2022 – 31 Dec 2022

Source: Biomedtracker | Informa, April 2022

Appendix

Methodology, sources, & glossary of key terms

Q1 2022

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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