Gene, Cell, & RNA Therapy Landscape

Q1 2023 Quarterly Data Report
About the authors

The American Society of Gene & Cell Therapy (ASGCT) is the primary professional membership organization for scientists, physicians, patient advocates, and other professionals with interest in gene and cell therapy.

Our members work in a wide range of settings including universities, hospitals, government agencies, foundations, biotechnology and pharmaceutical companies. ASGCT advances knowledge, awareness, and education leading to the discovery and clinical application of gene and cell therapies to alleviate human disease to benefit patients and society.

Citeline (formerly Pharma Intelligence) powers a full suite of complementary business intelligence offerings to meet the evolving needs of life science professionals to accelerate the connection of treatments to patients and patients to treatments. These patient-focused solutions and services deliver and analyze data used to drive clinical, commercial, and regulatory related-decisions and create real-world opportunities for growth.

Our global teams of analysts, journalists and consultants keep their fingers on the pulse of the pharmaceutical, biomedical and medtech industries, covering it all with expert insights: key diseases, clinical trials, drug R&D and approvals, market forecasts and more. For more information on one of the world’s most trusted life science partners, visit Citeline.
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Introduction

Welcome to the latest quarterly report from ASGCT and Citeline! In the first quarter of 2023, an mRNA vaccine was approved for COVID-19 prophylaxis in China, bringing the number of RNA therapy approvals to 22. In Japan, Vyznova was approved for corneal dystrophy, bringing the total non-genetically modified cell therapies to 61. No new gene therapies were approved in Q1, but Hemgenix was approved for hemophilia B in the EU and the UK.

The past quarter saw a decrease in gene therapy products in Phase I and II clinical trials, continuing a trend from Q4 2022. One therapy, exagamglogene autotemcel, or exa-cel, for people with transfusion-dependent beta thalassemia (TDT) or severe sickle cell disease (SCD), filed for approval in the first quarter. Also in the gene therapy pipeline, oncology and rare diseases remain the top areas of development both overall and in the clinic. Those two areas remain top areas of development in the pipeline of non-genetically modified cell therapies as well. In the RNA pipeline, rare diseases remain the top targeted therapeutic area, while anticancer therapies are the second most targeted area.

In Q1 2023, companies signed 110 deals — slightly fewer than the opening quarter of 2022 but similar compared to the previous two quarters. Series A and seed financings rebounded in Q1, reaching 17 transactions at a total of $615.2 million. This represents nearly double the volume and value of Q4 2022.
Key takeaways from Q1 2023

For the first time since Q2 2022, there were no new first approvals for gene therapies; however, Q1 2023 did see new RNA therapy and non-genetically modified cell therapy approvals

- CSPC Pharmaceutical's COVID-19 vaccine was granted emergency use authorization in China
- Aurion Biotech's Vyznova was approved for corneal dystrophy in Japan

Anticancer and rare diseases are the top two targeted therapeutic areas for pipeline gene, non-genetically modified, and RNA therapies

- Since Q4 2022, anticancer therapies overtook anti-infective therapies as the second most targeted therapy area for RNA therapies
- For all non-genetically modified cell therapies and RNA therapies, non-oncology indications dominate pipeline rare disease development; however, for gene therapies 54% of pipeline rare disease development occurs in oncology

Overall dealmaking by advanced molecule companies in Q1 2023 was virtually flat vs. Q4 2022, but start-up financing rebounded

- In Q1 2023, advanced molecular companies signed 110 total deals, just ahead of the 106 in Q4 2022, but slightly behind pace of the 123 done in the opening quarter of 2022
- Start-up financing saw big increases in Q1 compared with the previous quarter, doubling in volume and value to 17 Series A and seed financings together worth $615.2 million
- Active areas of investment for start-ups in Q1 were non-viral gene delivery via nanoparticles and lentiviral manufacturing
- Next-generation CAR-T developer Cargo had the top Series A round with $200 million
Key highlights in Q1 2023
Approved gene, cell, and RNA therapies

Globally, for clinical use:

- 24 gene therapies are approved (including genetically modified cell therapies)
  - There were no new gene therapy approvals in Q1 2023
- 22 RNA therapies are approved
  - In Q1 2023, an mRNA vaccine developed by CSPC Pharmaceutical was approved for COVID-19 prophylaxis in China
- 61 non-genetically modified cell therapies are approved
  - In Q1 2023, Vyznova was approved for corneal dystrophy in Japan

Source: Pharmaprojects | Citeline, April 2023
# Approved gene therapies as of Q1 2023 (1/2)

<table>
<thead>
<tr>
<th>Product name</th>
<th>Generic name</th>
<th>Year first approved</th>
<th>Disease(s)</th>
<th>Locations approved</th>
<th>Originator company</th>
</tr>
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<tbody>
<tr>
<td>Gendicine</td>
<td>recombinant p53 gene</td>
<td>2004</td>
<td>Head and neck cancer</td>
<td>China</td>
<td>Shenzhen SiBiono GeneTech</td>
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<td>Oncorine</td>
<td>E1B/E3 deficient adenovirus</td>
<td>2005</td>
<td>Head and neck cancer; nasopharyngeal cancer</td>
<td>China</td>
<td>Shanghai Sunway Biotech</td>
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<tr>
<td>Rexin-G</td>
<td>mutant cyclin-G1 gene</td>
<td>2006</td>
<td>Solid tumors</td>
<td>Philippines</td>
<td>Epeius Biotechnologies</td>
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<tr>
<td>Neovasculgen</td>
<td>vascular endothelial growth factor gene</td>
<td>2011</td>
<td>Peripheral vascular disease; limb ischemia</td>
<td>Russian Federation, Ukraine</td>
<td>Human Stem Cells Institute</td>
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<td>Imlygic</td>
<td>talimogene laherparepvec</td>
<td>2015</td>
<td>Melanoma</td>
<td>US, EU, UK, Australia</td>
<td>Amgen</td>
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<td>Strimvelis</td>
<td>autologous CD34+ enriched cells</td>
<td>2016</td>
<td>Adenosine deaminase deficiency</td>
<td>EU, UK</td>
<td>Orchard Therapeutics</td>
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<tr>
<td>Kymria</td>
<td>tisagenlecleucel-t</td>
<td>2017</td>
<td>Acute lymphocytic leukemia; diffuse large B-cell lymphoma; follicular lymphoma</td>
<td>US, EU, UK Japan, Australia, Canada, South Korea, Switzerland</td>
<td>Novartis</td>
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<td>Luxturna</td>
<td>voretigene neparvovec</td>
<td>2017</td>
<td>Leber’s congenital amaurosis; retinitis pigmentosa</td>
<td>US, EU, UK Australia, Canada, South Korea</td>
<td>Spark Therapeutics (Roche)</td>
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<td>Yescarta</td>
<td>axicabtagene ciloleucel</td>
<td>2017</td>
<td>Diffuse large B-cell lymphoma; non-Hodgkin’s lymphoma; follicular lymphoma</td>
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<td>Kite Pharma (Gilead)</td>
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<tr>
<td>Collategene</td>
<td>beperminogene perplasmid</td>
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<td>Critical limb ischemia</td>
<td>Japan</td>
<td>AnGes</td>
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<td>Zolgensma</td>
<td>onasemnogene abeparvovec</td>
<td>2019</td>
<td>Spinal muscular atrophy</td>
<td>US, EU, UK, Japan, Brazil, Israel, Taiwan, South Korea</td>
<td>Novartis</td>
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<td>Zynteglo</td>
<td>betibeglogene autotemcel</td>
<td>2019</td>
<td>Transfusion-dependent beta thalasemia</td>
<td>US</td>
<td>bluebird bio</td>
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Source: Pharmaprojects | Citeline, April 2023

*Text highlighted in yellow represents new approvals during Q1 2023*
## Approved gene therapies as of Q1 2023 (2/2)

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<tr>
<th>Product name</th>
<th>Generic name</th>
<th>Year first approved</th>
<th>Disease(s)</th>
<th>Locations approved</th>
<th>Originator company</th>
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<tr>
<td>Tecartus</td>
<td>brexucabtagene autoleucel</td>
<td>2020</td>
<td>Mantle cell lymphoma; acute lymphocytic leukemia</td>
<td>US, EU, UK</td>
<td>Kite Pharma (Gilead)</td>
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<td>Libmeldy</td>
<td>atidarsagene autotemcel</td>
<td>2020</td>
<td>Metachromatic leukodystrophy</td>
<td>EU, UK</td>
<td>Orchard Therapeutics</td>
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<tr>
<td>Breyanzi</td>
<td>lisocabtagene maraleucel</td>
<td>2021</td>
<td>Diffuse large B-cell lymphoma; follicular lymphoma</td>
<td>US, Japan, EU, Switzerland, UK, Canada</td>
<td>Celgene (Bristol Myers Squibb)</td>
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<tr>
<td>Abecma</td>
<td>idecabtagene vicleucel</td>
<td>2021</td>
<td>Multiple myeloma</td>
<td>US, Canada, EU, UK, Japan</td>
<td>bluebird bio</td>
</tr>
<tr>
<td>Delytact</td>
<td>teserpaturev</td>
<td>2021</td>
<td>Malignant glioma</td>
<td>Japan</td>
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<td>China</td>
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<td>Skysona</td>
<td>elivaldogene autotemcel</td>
<td>2021</td>
<td>Early cerebral adrenoleukodystrophy (CALD)</td>
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<td>bluebird bio</td>
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<td>BioMarin</td>
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<tr>
<td>Hemgenix</td>
<td>etranacogene dezaparvovec</td>
<td>2022</td>
<td>Hemophilia B</td>
<td>US, EU, UK</td>
<td>uniQure</td>
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<tr>
<td>Adstiladrin</td>
<td>nadofaragene firadenovec</td>
<td>2022</td>
<td>Bladder cancer</td>
<td>US</td>
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</table>

Source: Pharmaprojects | Citeline, April 2023

Text highlighted in yellow represents new approvals during Q1 2023
## Approved RNA therapies as of Q1 2023 (1/2)

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<th>Product name</th>
<th>Generic name</th>
<th>Year first approved</th>
<th>Disease(s)</th>
<th>Locations approved*</th>
<th>Originator company</th>
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<tbody>
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<td>Kynamro</td>
<td>mipomersen sodium</td>
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<td>Homozygous familial hypercholesterolemia</td>
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<td>Exondys 51</td>
<td>eteplirsen</td>
<td>2016</td>
<td>Dystrophy, Duchenne muscular</td>
<td>US</td>
<td>Sarepta Therapeutics</td>
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<td>Spinraza</td>
<td>nusinersen</td>
<td>2016</td>
<td>Muscular atrophy, spinal</td>
<td>US</td>
<td>Ionis Pharmaceuticals</td>
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<td></td>
<td></td>
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<td>EU, UK, Canada, South Korea, Australia, China, Argentina, Colombia, Taiwan, Turkey, Hong Kong, Israel</td>
<td>Ionis Pharmaceuticals</td>
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<td>Ampligen</td>
<td>rintatolimod</td>
<td>2016</td>
<td>Chronic fatigue syndrome</td>
<td>Argentina</td>
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<td>Tegsedi</td>
<td>inotersen</td>
<td>2018</td>
<td>Amyloidosis, transthyretin-related hereditary</td>
<td>EU, UK, Canada, US, Brazil</td>
<td>Ionis Pharmaceuticals</td>
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<tr>
<td>Onpattro</td>
<td>patisiran</td>
<td>2018</td>
<td>Amyloidosis, transthyretin-related hereditary</td>
<td>US, EU, UK, Japan, Canada, Switzerland, Brazil, Taiwan, Israel, Turkey</td>
<td>Ionis Pharmaceuticals</td>
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<tr>
<td>Vyondys 53</td>
<td>golodirsen</td>
<td>2019</td>
<td>Dystrophy, Duchenne muscular</td>
<td>US</td>
<td>Sarepta Therapeutics</td>
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<td>Waylivra</td>
<td>volanesorsen</td>
<td>2019</td>
<td>Hypertriglyceridemia; Lipoprotein lipase deficiency</td>
<td>EU, UK, Brazil, Canada</td>
<td>Ionis Pharmaceuticals</td>
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<tr>
<td>Comirnaty</td>
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<td>2020</td>
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<td>COVID-19 vaccine, Moderna</td>
<td>2020</td>
<td>Infection, coronavirus, novel coronavirus prophylaxis</td>
<td>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</td>
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*Text highlighted in yellow represents new approvals during Q1 2023*
## Approved RNA therapies as of Q1 2023 (2/2)

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<th>Product name</th>
<th>Generic name</th>
<th>Year first approved</th>
<th>Disease(s)</th>
<th>Locations approved*</th>
<th>Originator company</th>
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<tbody>
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<td>givosiran</td>
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<td>Oxlumo</td>
<td>lumasiran</td>
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<td>Alnylam</td>
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<tr>
<td>Viltepso</td>
<td>viltolarsen</td>
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<td>Dystrophy, Duchenne muscular</td>
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<td>NS Pharma</td>
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<td>Leqvio</td>
<td>inclisiran</td>
<td>2020</td>
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<td>Nulibry</td>
<td>fosdenopterin</td>
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<td>Molybdenum cofactor deficiency</td>
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<td>2022</td>
<td>Infection, coronavirus, novel coronavirus prophylaxis</td>
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<td>Indonesia</td>
<td>Suzhou Abogen Biosciences</td>
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*For COVID-19 vaccines, this includes emergency use authorization and full approvals
Note that molnupiravir was previously included in this list; however, it has now been removed as it is no longer considered to fall under the category of RNA therapeutics

Source: Pharmaprojects | Citeline, April 2023

Text highlighted in yellow represents new approvals during Q1 2023
# Noteworthy events that happened in Q1 2023

<table>
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<tr>
<th>Drug</th>
<th>Event Type</th>
<th>Indication</th>
<th>Molecule</th>
<th>Event Date</th>
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<tbody>
<tr>
<td>Carvykti</td>
<td>Filing for Approval (China)</td>
<td>Multiple Myeloma (MM)</td>
<td>Cellular</td>
<td>02 January 2023</td>
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<tr>
<td>VX-522</td>
<td>Fast Track Status</td>
<td>Cystic Fibrosis (CF)</td>
<td>mRNA (messenger RNA)</td>
<td>09 January 2023</td>
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<tr>
<td>FBX-101</td>
<td>PRIME Designation (Europe)</td>
<td>Krabbe Disease (Globoid Cell Leukodystrophy)</td>
<td>Viral Gene Therapy</td>
<td>17 January 2023</td>
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<td>KB407</td>
<td>Orphan Drug Designation (Europe)</td>
<td>Cystic Fibrosis (CF)</td>
<td>Viral Gene Therapy</td>
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<td>AOC-1020</td>
<td>Fast Track Status</td>
<td>Muscular Dystrophy</td>
<td>siRNA/RNAi</td>
<td>18 January 2023</td>
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<tr>
<td>Exa-cell</td>
<td>EMA Validation of Approval Application</td>
<td>Sickle Cell Anemia and Transfusion-Dependent Beta Thalassemia</td>
<td>Non-Viral Gene Therapy</td>
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<td>Injectable Discogenic Cell Therapy</td>
<td>Regenerative Medicine Advanced Therapy (RMAT) Designation</td>
<td>Musculoskeletal Conditions</td>
<td>Cellular</td>
<td>26 January 2023</td>
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<tr>
<td>Ryoncil</td>
<td>Response Submitted to Complete Response Letter (CRL)</td>
<td>Graft vs. Host Disease (GVHD) - Treatment</td>
<td>Cellular</td>
<td>31 January 2023</td>
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<td>Leqvio</td>
<td>Filing for Approval (China) and J-NDA Filing (Japan)</td>
<td>Dyslipidemia / Hypercholesterolemia</td>
<td>siRNA/RNAi</td>
<td>01 February 2023</td>
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<td>RP-A501</td>
<td>Regenerative Medicine Advanced Therapy (RMAT) Designation</td>
<td>Glycogen Storage Disease (GSD)</td>
<td>Viral Gene Therapy</td>
<td>07 February 2023</td>
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<tr>
<td>MPC-06-ID</td>
<td>Regenerative Medicine Advanced Therapy (RMAT) Designation</td>
<td>Chronic Low Back Pain (CLBP)</td>
<td>Cellular</td>
<td>08 February 2023</td>
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<td>Fast Track Status and Regenerative Medicine Advanced Therapy (RMAT) Designation</td>
<td>Multiple Myeloma (MM)</td>
<td>Cellular</td>
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<td>Viral Gene Therapy</td>
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<td>GM1 Gangliosidosis</td>
<td>Viral Gene Therapy</td>
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<td>PRIME Designation (Europe)</td>
<td>Crigler-Najjar Syndrome</td>
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<td>07 March 2023</td>
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<td>Eplontersen</td>
<td>NDA/BLA Accepted</td>
<td>Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy (Familial Amyloid Polyneuropathy)</td>
<td>Antisense</td>
<td>07 March 2023</td>
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<td>ARO-APOC3</td>
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<td>NTLA-2002</td>
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<td>Non-Viral Gene Therapy</td>
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<td>Antisense</td>
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<td>COVID-19 Prophylaxis</td>
<td>mRNA vaccine</td>
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Source: Biomedtracker | Citeline, April 2023
Pipeline overview
Pipeline of gene, cell, and RNA therapies

3,689 therapies are in development, ranging from preclinical through pre-registration

- 2,022 gene therapies (including genetically modified cell therapies such as CAR T-cell therapies) are in development, accounting for 54% of gene, cell, and RNA therapies
- 813 non-genetically modified cell therapies are in development, accounting for 22% of gene, cell, and RNA therapies

Source: Pharmaprojects | Citeline, April 2023
Gene therapy pipeline

Gene therapy and genetically modified cell therapies
Gene therapy pipeline: Quarterly comparison

- Q1 2023 has continued last quarter’s trend of seeing a decrease in Phase I and II gene therapy products, and also sees a decrease in preclinical stage programs.
- One new therapy, exagamglogene autotemcel in sickle cell anemia and transfusion-dependent beta thalassemia, filed for approval in Q1 2023. Therapies currently in pre-registration are:
  - lenadogene nolparvovec (Genethon, GenSight Biologics)
    - In the EU and UK
  - beremagene geeperpavec (Krystal Biotech)
    - In the US, EU, and UK
  - equecabtagene autoleucel (Nanjing IASO Biotherapeutics, Innovent)
    - In China
  - delandistrogene moxeparvovec (Sarepta Therapeutics)
    - In China
  - zevor-cel (CARsgen Therapeutics)
    - In China
  - inaticabtagene autoleucel (CASI Pharmaceuticals, Juventas Cell Therapy)
    - In China
  - exagamglogene autotemcel (CRISPR Therapeutics, Vertex Pharmaceuticals)
    - In the EU and UK

<table>
<thead>
<tr>
<th>Global Status</th>
<th>Q1 2022</th>
<th>Q2 2022</th>
<th>Q3 2022</th>
<th>Q4 2022</th>
<th>Q1 2023</th>
</tr>
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<tbody>
<tr>
<td>Preclinical</td>
<td>1,451</td>
<td>1,482</td>
<td>1,480</td>
<td>1,515</td>
<td>1,493</td>
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<tr>
<td>Phase I</td>
<td>248</td>
<td>258</td>
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<tr>
<td>Phase II</td>
<td>250</td>
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<td>249</td>
<td>248</td>
<td>247</td>
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<tr>
<td>Phase III</td>
<td>31</td>
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<td>32</td>
<td>30</td>
<td>30</td>
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<tr>
<td>Pre-registration</td>
<td>6</td>
<td>8</td>
<td>6</td>
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<td>7</td>
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<tr>
<td>Total</td>
<td>1,986</td>
<td>2,024</td>
<td>2,031</td>
<td>2,053</td>
<td>2,022</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects | Citeline, April 2023
Genetic modification: *In vivo* vs. *Ex vivo*

- *Ex vivo* genetic modification is more widely used for gene therapies in pipeline development.
- In Q1 2023, *in vivo* delivery techniques were used in 28% of gene therapies, 1% higher than the proportion has been for over 1 year.

Source: Cell and Gene Therapy dashboard | Citeline, April 2023
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 at 34%, which includes a list of less commonly used technologies including TCR-NK, CAR-M, and TAC-T.

- 95% 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 | Citeline, April 2023
Gene therapy pipeline: Most commonly targeted therapeutic areas

- Oncology and rare diseases remain the top areas of gene therapy development in both the overall pipeline (preclinical to pre-registration) and in the clinic (Phase I to pre-registration)
- Development for rare diseases most commonly occurs in oncology, representing a majority of 54% compared to non-oncology rare disease gene therapy pipeline development

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Number of Therapies</th>
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</thead>
<tbody>
<tr>
<td>Anticancer</td>
<td>983</td>
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<tr>
<td>Rare Diseases</td>
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<tr>
<td>Neurological</td>
<td>192</td>
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<tr>
<td>Sensory</td>
<td>162</td>
</tr>
<tr>
<td>Alimentary/Metabolic</td>
<td>13</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>81</td>
</tr>
<tr>
<td>Blood and Clotting</td>
<td>71</td>
</tr>
<tr>
<td>NA/Unspecified</td>
<td>66</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>54</td>
</tr>
<tr>
<td>Immunological</td>
<td>52</td>
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<tr>
<td>Anti-infective</td>
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<tr>
<td>Respiratory</td>
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<tr>
<td>Dermatological</td>
<td>17</td>
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<tr>
<td>Genitourinary (including sex hormones)</td>
<td>12</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4</td>
</tr>
<tr>
<td>Hormonal (excluding sex hormones)</td>
<td>2</td>
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</table>

<table>
<thead>
<tr>
<th>Rare Diseases</th>
<th>Oncology</th>
<th>Non-oncology</th>
</tr>
</thead>
<tbody>
<tr>
<td>54%</td>
<td>46%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Therapies in the clinic (excludes preclinical development)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare Diseases</td>
</tr>
<tr>
<td>Anticancer</td>
</tr>
<tr>
<td>Alimentary/Metabolic</td>
</tr>
<tr>
<td>Neurological</td>
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<tr>
<td>Sensory</td>
</tr>
<tr>
<td>Blood and Clotting</td>
</tr>
<tr>
<td>Musculoskeletal</td>
</tr>
<tr>
<td>Anti-infective</td>
</tr>
<tr>
<td>Immunological</td>
</tr>
<tr>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Dermatological</td>
</tr>
<tr>
<td>Respiratory</td>
</tr>
<tr>
<td>Genitourinary (including sex hormones)</td>
</tr>
<tr>
<td>Hormonal (excluding sex hormones)</td>
</tr>
<tr>
<td>Miscellaneous</td>
</tr>
<tr>
<td>NA/Unspecified</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects | Citeline, April 2023

Note: figures based on indications in pipeline development only for each therapy
Gene therapy pipeline: Most common rare diseases targeted

- For the 983 pipeline (preclinical to pre-registration) gene therapies which are being developed for rare diseases, eight out of the top 10 rare diseases are oncological, as seen all throughout 2022.
- In the same order as the previous six quarters, the top five rare diseases for which gene therapies are being developed are:
  1. Myeloma
  2. Non-Hodgkin’s lymphoma
  3. Acute myelogenous leukemia
  4. B-cell lymphoma
  5. Ovarian cancer

Source: Pharmaprojects | Citeline, April 2023

Note: figures based on indications in pipeline development only for each therapy
Gene therapy pipeline: Most common targets

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

- CD19, B-cell maturation antigen (BCMA), also known as TNF receptor superfamily member 17, and CD22 molecule continue to be the top three most common targets for oncology indications.
- Coagulation factor VIII remains the most common target for non-oncology indications, while vascular endothelial growth factor A becomes the second most common in Q1 2023.

**Oncology**

<table>
<thead>
<tr>
<th>Target</th>
<th>Number of Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD19 molecule</td>
<td>52</td>
</tr>
<tr>
<td>TNF receptor superfamily member 17</td>
<td>33</td>
</tr>
<tr>
<td>CD22 molecule</td>
<td>24</td>
</tr>
<tr>
<td>membrane spanning 4-domains A1</td>
<td>23</td>
</tr>
<tr>
<td>glypican 3</td>
<td>22</td>
</tr>
<tr>
<td>erb-b2 receptor tyrosine kinase 2</td>
<td>19</td>
</tr>
<tr>
<td>mesothelin</td>
<td>18</td>
</tr>
<tr>
<td>claudin 18</td>
<td>15</td>
</tr>
<tr>
<td>cancer/testis antigen 1B</td>
<td>15</td>
</tr>
<tr>
<td>CD33 molecule</td>
<td>14</td>
</tr>
<tr>
<td>programmed cell death 1</td>
<td>14</td>
</tr>
<tr>
<td>CD276 molecule</td>
<td>11</td>
</tr>
<tr>
<td>CD7 molecule</td>
<td>11</td>
</tr>
<tr>
<td>CD70 molecule</td>
<td>10</td>
</tr>
<tr>
<td>C-type lectin domain family 12 member A</td>
<td>10</td>
</tr>
<tr>
<td>epidermal growth factor receptor</td>
<td>9</td>
</tr>
<tr>
<td>folate hydrolase 1</td>
<td>9</td>
</tr>
<tr>
<td>interleukin 3 receptor subunit alpha</td>
<td>9</td>
</tr>
<tr>
<td>KRAS proto-oncogene, GTPase</td>
<td>9</td>
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<tr>
<td>MAGE family member A4</td>
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**Non-oncology targets**

<table>
<thead>
<tr>
<th>Target</th>
<th>Number of Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>coagulation factor VIII</td>
<td>11</td>
</tr>
<tr>
<td>vascular endothelial growth factor A</td>
<td>9</td>
</tr>
<tr>
<td>CD19 molecule</td>
<td>9</td>
</tr>
<tr>
<td>dystrophin</td>
<td>8</td>
</tr>
<tr>
<td>glucosylceramide beta</td>
<td>7</td>
</tr>
<tr>
<td>coagulation factor IX</td>
<td>7</td>
</tr>
<tr>
<td>ATP binding cassette subfamily A member 4</td>
<td>6</td>
</tr>
<tr>
<td>serpin family A member 1</td>
<td>6</td>
</tr>
<tr>
<td>TNF receptor superfamily member 17</td>
<td>6</td>
</tr>
<tr>
<td>apolipoprotein E</td>
<td>5</td>
</tr>
<tr>
<td>C9orf72-SMC8 complex subunit</td>
<td>5</td>
</tr>
<tr>
<td>collagen type VII alpha 1 chain</td>
<td>5</td>
</tr>
<tr>
<td>granulin precursor</td>
<td>5</td>
</tr>
<tr>
<td>synuclein alpha</td>
<td>5</td>
</tr>
<tr>
<td>CF transmembrane conductance regulator</td>
<td>4</td>
</tr>
<tr>
<td>galactosylceramidase</td>
<td>4</td>
</tr>
<tr>
<td>gap junction protein beta 2</td>
<td>4</td>
</tr>
<tr>
<td>glucosidase alpha, acid</td>
<td>4</td>
</tr>
<tr>
<td>hemoglobin subunit beta</td>
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</tr>
<tr>
<td>retinoid isomerohydrolase RPE65</td>
<td>4</td>
</tr>
<tr>
<td>rhodopsin</td>
<td>4</td>
</tr>
<tr>
<td>TAR DNA binding protein</td>
<td>4</td>
</tr>
<tr>
<td>tripeptidyl peptidase 1</td>
<td>4</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects | Citeline, April 2023
Gene therapy clinical trial activity

- 52 trials were initiated in Q1 2023 for gene therapies
- The proportion of gene therapy trials for non-oncology indications has increased by 12 percentage points since the previous quarter, to 27%, matching the proportion seen in Q3 2022

Source: Trialtrove | Citeline, April 2023
Non-genetically modified cell therapy pipeline
Non-genetically modified cell therapy pipeline: Most common therapeutic areas targeted

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

- Oncology and rare diseases remain the top areas of non-genetically modified cell therapy development
- Of the non-genetically modified cell therapies in preclinical to pre-registration stages for rare diseases, 65% are in development for non-oncology rare diseases, a decrease of one percentage point from the previous quarter

Note: figures based on indications in pipeline development only for each therapy
Non-genetically modified cell therapy pipeline: Most common diseases targeted

Of the therapies for which indications are specified, the top three indications remain the same as in Q4 2021 and throughout 2022:

1. Acute respiratory distress syndrome
2. COVID-19 complications
3. Osteoarthritis

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

Source: Pharmaprojects | Citeline, April 2023
Non-genetically modified cell therapy pipeline: Most common rare diseases targeted

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

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

Source: Pharmaprojects| Citeline, April 2023

Note: figures based on indications in pipeline development only for each therapy
Non-genetically modified cell therapy trial activity

- 38 trials were initiated for non-genetically modified cell therapies in Q1 2023, 7 more than the previous quarter
- Of these 38, 53% are for non-oncology indications, a decrease of 2 percentage points from Q4 2022

Source: Trialtrove | Citeline, April 2023
RNA therapy pipeline
RNA therapy pipeline: Most common modalities

- Of RNA therapies in the pipeline, messenger RNA (mRNA) and RNA interference (RNAi) continue to be the preferred RNA modalities for research.

Source: Pharmaprojects | Citeline, April 2023
RNAi, mRNA, and antisense oligonucleotides: Preclinical vs. clinical

- The majority of RNAi, mRNA, and antisense therapeutics in development are in preclinical development, representing 78%, 69%, and 62% of their respective pipelines.
RNA therapies: Most commonly targeted therapeutic areas

Of the 897 RNA therapies currently in the pipeline (from preclinical through pre-registration):

- Rare diseases remains the top targeted therapeutic area by RNA therapies, while anticancer therapies replace anti-infective therapies as the second most targeted since Q4 2022
- Non-oncology indications continue to be the most targeted rare diseases by RNA therapies, representing a majority of 83%

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

Source: Pharmaprojects | Citeline, April 2023
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 cystic fibrosis are the most commonly targeted indications

Source: Pharmaprojects | Citeline, April 2023

Note: figures based on indications in pipeline development only for each therapy
RNA therapy pipeline: Clinical trial activity

- 31 RNA trials were initiated in Q1 2023, compared to 32 in Q4 2022, 87% of which were for non-oncology indications

Source: Trialtrove | Citeline, April 2023
Overview of dealmaking for gene, cell, and RNA therapy companies
Alliance, acquisition, and financing in gene, cell, and RNA therapy

- Advanced molecular therapy companies signed a total of 110 deals in Q1 2023, nearly flat compared with the previous two quarters.
- Slightly fewer deals were done in Q1 2023 compared with the opening quarter of 2022, which featured 123 transactions.
- The biggest increase in Q1 2023 was seen with alliances, which rose by 54% from 35 to 54 partnerships in Q4 2022 vs Q1 2023.

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

*Financings include public financings (IPOs and follow-ons) plus privately raised funding through venture rounds, debt offerings, or private investment in public equity.

**Total number of deals by type, most recent five quarters**

Source: Biomedtracker | Citeline, BioSciDB | Evaluate, April 2023
## Q1 2023 acquisitions in gene, cell, and RNA therapy

- Acquisition volume in Q1 2023 was at a quarterly low in the past year, with a total of 7 transactions signed, compared with the 12 done in Q4 2022, but closer to the 8–9 range seen during previous quarters.
- Q1 2023 featured two billion-dollar takeovers: Chiesi’s acquisition of Amryt, worth up to $1.5 billion, includes a preclinical non-viral gene therapy for epidermolysis bullosa; and Sartorius paid €2.4 billion for Polypus, which makes transfection agents and plasmid DNA for viral vector manufacturing.

<table>
<thead>
<tr>
<th>Deal Date</th>
<th>Deal Title</th>
<th>Potential Deal Value (USD $)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/04/2023</td>
<td>Moderna to Acquire OriCiro Genomics for $85M</td>
<td>85,000,000</td>
</tr>
<tr>
<td>01/05/2023</td>
<td>Ensoma to Acquire Twelve Bio; Acquisition Closed</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>01/08/2023</td>
<td>Chiesi Farmaceutici to Acquire Amryt Pharma for up to $1.48B</td>
<td>1,475,000,000</td>
</tr>
<tr>
<td>01/17/2023</td>
<td>Elicio Therapeutics and Angion Enter into Definitive Merger Agreement</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>03/02/2023</td>
<td>Flamingo Therapeutics and Dynacure Merge to Develop RNA-Targeting Cancer Therapies</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>03/06/2023</td>
<td>Adaptimmune and TCR² Therapeutics Announce Strategic Combination</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>3/31/2023</td>
<td>Sartorius Acquires Viral Vector Manufacturing Company Polypus for €2.4B</td>
<td>2,600,000,000</td>
</tr>
</tbody>
</table>

Source: Biomedtracker | Citeline, BioSciDB | Evaluate, April 2023
Start-up funding for gene, cell, and RNA therapy companies
Start-up financing for gene, cell, and RNA therapy companies

- Series A and seed financings for advanced molecular companies rebounded in Q1 2023, reaching 17 transactions at an aggregate $615.2 million, representing nearly double the volume and value of Q4 2022.
- Among the fundraisers were several companies investigating non-viral gene delivery, including using nanoparticles, and two new CDMOs focused on lentiviral vector production.
- Note: The Q1 2023 totals include Aera Therapeutics’ combined Series A and B fundraise of $193 million.

Volume and dollar value of Series A and seed financings for gene, cell, & RNA therapy companies, most recent five quarters

Source: Biomedtracker | Citeline, April 2023
## Q1 2023 start-up financing for gene, cell, and RNA therapy companies (1/2)

<table>
<thead>
<tr>
<th>Deal Date</th>
<th>Deal Title</th>
<th>Modality Type</th>
<th>Company Location</th>
<th>Academic Source</th>
<th>Potential Deal Value (USD, $M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/11/2023</td>
<td>MPC Therapeutics Closes Seed Round</td>
<td>Small molecules that enhance performance and durability of CAR-T therapy</td>
<td>Switzerland, Plan-les-Ouates</td>
<td>University of Geneva</td>
<td>1.6</td>
</tr>
<tr>
<td>01/12/2023</td>
<td>Tiba Biotech Gets $2M in Seed Funding from CEPI</td>
<td>mRNA vaccines and therapeutics</td>
<td>United States, Massachusetts, Cambridge</td>
<td>MIT; Whitehead Institute</td>
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<tr>
<td>01/25/2023</td>
<td>Atomic AI Closes $35M Series A</td>
<td>AI platform to identify functional binders to RNA targets</td>
<td>United States, California, San Francisco</td>
<td>Stanford University</td>
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<tr>
<td>01/25/2023</td>
<td>Myosana Gets $5M in Seed Funding</td>
<td>Non-viral gene therapy</td>
<td>United States, Washington, Seattle</td>
<td>University of Washington</td>
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</tr>
<tr>
<td>01/26/2023</td>
<td>iVexSol Raises $23.8M in Series A-3 Financing</td>
<td>CMDO producer of lentiviral vectors</td>
<td>United States, Massachusetts, Lexington</td>
<td>Undisclosed</td>
<td>23.8</td>
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<tr>
<td>01/31/2023</td>
<td>Vector Biomed Raises $15M in Series A Financing</td>
<td>CMDO producer of lentiviral vectors</td>
<td>United States, Maryland, Gaithersburg</td>
<td>Undisclosed</td>
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<tr>
<td>01/31/2023</td>
<td>Sichuan Zhishanweixin Biotechnology (Zhi Shan Wei Xin) Raises $29.61 Million in Series A+ Financing</td>
<td>AAV gene therapy</td>
<td>China, Sichuan</td>
<td>Undisclosed</td>
<td>29.61</td>
</tr>
<tr>
<td>02/15/2023</td>
<td>Nanite Raises $6M in Seed Round; Adds $2M</td>
<td>Programmable polymer nanoparticles for non-viral gene therapy</td>
<td>United States, Massachusetts, Boston</td>
<td>University of Minnesota</td>
<td>8</td>
</tr>
</tbody>
</table>

Source: Biomedtracker| Citeline, April 2023
## Q1 2023 start-up financing for gene, cell, and RNA therapy companies (2/2)

<table>
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<tr>
<th>Deal Date</th>
<th>Deal Title</th>
<th>Modality Type</th>
<th>Company Location</th>
<th>Academic Source</th>
<th>Potential Deal Value (USD, $M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/16/2023</td>
<td>Aera Therapeutics Launches with $193M Combined Series A and B Financings</td>
<td>Proprietary protein nanoparticle delivery system for genetic medicine</td>
<td>United States, Massachusetts, Boston</td>
<td>Broad Institute of MIT and Harvard University; University of Utah</td>
<td>193</td>
</tr>
<tr>
<td>02/22/2023</td>
<td>Resalis Therapeutics Announces Seed Financing of €10M</td>
<td>Non-coding RNA therapy</td>
<td>Italy, Torino</td>
<td>Aalborg University's Center for RNA Medicine</td>
<td>10.7</td>
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<tr>
<td>02/28/2023</td>
<td>Verismo Therapeutics Raises $7M in Pre-Series A Round</td>
<td>KIR (killer immunoglobulin-like receptor)-CAR T therapy</td>
<td>United States, Pennsylvania, Philadelphia</td>
<td>University of Pennsylvania</td>
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<tr>
<td>03/01/2023</td>
<td>CARGO Therapeutics Raises $200M in Oversubscribed Series A Round</td>
<td>CAR-T therapy</td>
<td>United States, California, San Mateo</td>
<td>Stanford University's Center for Cancer Cell Therapy</td>
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<tr>
<td>03/01/2023</td>
<td>Thymmune Gets $7M in Seed Funding</td>
<td>Thymic cell therapy</td>
<td>United States, Massachusetts, Cambridge</td>
<td>Harvard University</td>
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<tr>
<td>03/13/2023</td>
<td>Shennon Biotechnologies Closes $13M Seed Round</td>
<td>Immune cell profiling to create cell therapy</td>
<td>United States, California, San Francisco</td>
<td>Undisclosed</td>
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<tr>
<td>03/14/2023</td>
<td>Switch Therapeutics Raises $52M in Series A Funding</td>
<td>siRNAtherapy</td>
<td>United States, California, San Francisco</td>
<td>Caltech; Harvard University; City of Hope</td>
<td>52</td>
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<tr>
<td>03/15/2023</td>
<td>Inspire Biotherapeutics Launches with Pre-seed Investment</td>
<td>Gene therapy</td>
<td>Canada, Toronto</td>
<td>Ottawa Hospital Research Institute</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>03/16/2023</td>
<td>Seamless Therapeutics Launches with $12.5M Seed Round</td>
<td>Gene editing</td>
<td>Germany, Dresden</td>
<td>Technische Universität Dresden's University Cancer Center</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Source: Biomedtracker | Citeline, April 2023
### Notable Q1 2023 start-up gene, cell, and RNA therapy companies

<table>
<thead>
<tr>
<th>Company details</th>
<th>Academic source</th>
<th>Financing type/amount raised</th>
<th>Lead investor(s)</th>
<th>Therapy areas of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Next-generation CAR-T therapies using STASH/GAS technology addressing resistance and relapse with current CAR-T therapies</td>
<td>Stanford University's Center for Cancer Cell Therapy</td>
<td>Series A/$200M</td>
<td>Third Rock Ventures, RTW Investments, LP, Perceptive Xonto-geny Venture Fund</td>
<td>Cancer (hematological, including large B-cell lymphoma)</td>
</tr>
<tr>
<td>Protein nanoparticle for delivery of gene therapy and gene editing systems</td>
<td>Broad Institute of MIT and Harvard University; University of Utah</td>
<td>Series A + Series B/$193M</td>
<td>ARCH Venture Partners, GV, Lux Capital</td>
<td>Unspecified</td>
</tr>
<tr>
<td>Conditionally Activated siRNA (CASi) molecules for cell selective knockdown of targets</td>
<td>Caltech; Harvard University; City of Hope</td>
<td>Series A/$52M</td>
<td>Insight Partners, UCB Ventures</td>
<td>CNS and systemic indications</td>
</tr>
</tbody>
</table>
Upcoming catalysts
## Upcoming Catalysts

Below are noteworthy catalysts (forward-looking events) expected in Q2 2023

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Generic Name</th>
<th>Disease</th>
<th>Catalyst</th>
<th>Catalyst Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIIB-067</td>
<td>tofersen</td>
<td>Amyotrophic Lateral Sclerosis (ALS)</td>
<td>PDUFA for NDA - First Review</td>
<td>25 Apr 2023 - 25 Apr 2023</td>
</tr>
<tr>
<td>Libmeldy</td>
<td>atidarsagene autotemcel</td>
<td>Metachromatic Leukodystrophy</td>
<td>Meeting with FDA</td>
<td>10 Jan 2023 - 30 Apr 2023</td>
</tr>
<tr>
<td>Amvuttra</td>
<td>vutrisiran</td>
<td>Hereditary Transthyretin (hATTR) Amyloidosis With Polyneuropathy</td>
<td>Japanese Approval Decision</td>
<td>1 Oct 2022 - 30 Apr 2023</td>
</tr>
<tr>
<td>Tab-cell</td>
<td>tabelecleucel</td>
<td>Hematologic Cancer</td>
<td>Approval Decision (UK)</td>
<td>8 Feb 2023 - 30 Apr 2023</td>
</tr>
<tr>
<td>NiCord</td>
<td>omidubicel</td>
<td>Bone Marrow Transplant and Stem Cell Transplant</td>
<td>PDUFA for BLA - First Review</td>
<td>1 May 2023 - 1 May 2023</td>
</tr>
<tr>
<td>Vyjuvek</td>
<td>beremagene geperpavec</td>
<td>Epidermolysis Bullosa</td>
<td>PDUFA for BLA - First Review</td>
<td>19 May 2023 - 19 May 2023</td>
</tr>
<tr>
<td>SRP-9001</td>
<td>delandistrogene moxparvovec</td>
<td>Duchenne Muscular Dystrophy (DMD)</td>
<td>PDUFA for BLA - First Review</td>
<td>29 May 2023 - 29 May 2023</td>
</tr>
<tr>
<td>Roctavian</td>
<td>valoctocogene roxaparvovec</td>
<td>Duchenne Muscular Dystrophy (DMD)</td>
<td>FDA Advisory Panel Meeting and Brief</td>
<td>16 Mar 2023 - 29 May 2023</td>
</tr>
<tr>
<td>Libmeldy</td>
<td>atidarsagene autotemcel</td>
<td>Metachromatic Leukodystrophy</td>
<td>Approval Decision - Swissmedic</td>
<td>1 Jan 2023 - 30 Jun 2023</td>
</tr>
<tr>
<td>SB623</td>
<td>vandefitemcel</td>
<td>Traumatic Brain Injury (TBI)</td>
<td>Approval Decision (Japan)</td>
<td>1 Dec 2022 - 30 Jun 2023</td>
</tr>
<tr>
<td>Oxlumo</td>
<td>lumasiran</td>
<td>Hyperoxaluria</td>
<td>Supplemental Approval Europe (PH1)</td>
<td>31 Mar 2023 - 30 Jun 2023</td>
</tr>
<tr>
<td>Lantidra</td>
<td>allogeneic Islets of Langerhans</td>
<td>Diabetes Mellitus, Type I</td>
<td>PDUFA for BLA - First Review</td>
<td>21 Dec 2022 - 30 Jun 2023</td>
</tr>
<tr>
<td>Honedra</td>
<td>autologous CD34+ cells</td>
<td>Peripheral Arterial Disease (PAD)</td>
<td>Japanese Approval Decision</td>
<td>1 Jan 2023 - 30 Jun 2023</td>
</tr>
<tr>
<td>AT-132</td>
<td>resamirigene bilparvovec</td>
<td>X-linked Myotubular Myopathy</td>
<td>Meeting with FDA</td>
<td>29 Mar 2023 - 31 Jul 2023</td>
</tr>
<tr>
<td>Lumevoq</td>
<td>lenadogene nolparvovec</td>
<td>Leber’s Hereditary Optic Neuropathy (LHON) (Ophthalmology)</td>
<td>European Approval Decision</td>
<td>1 Dec 2022 - 30 Nov 2023</td>
</tr>
<tr>
<td>Exa-cell</td>
<td>exagamglogene autotemcel</td>
<td>Sickle Cell Anemia</td>
<td>Approval Decision (UK)</td>
<td>31 Dec 2022 - 31 Dec 2023</td>
</tr>
<tr>
<td>Exa-cell</td>
<td>exagamglogene autotemcel</td>
<td>Thalassemia</td>
<td>Approval Decision (UK)</td>
<td>31 Dec 2022 - 31 Dec 2023</td>
</tr>
<tr>
<td>HPC-Cord Blood Therapy</td>
<td>umbilical cord blood mononuclear stem cell therapy</td>
<td>Ischemic Stroke</td>
<td>PDUFA for BLA - First Review</td>
<td>1 Jan 2023 - 31 Dec 2023</td>
</tr>
</tbody>
</table>

Source: Biomedtracker | Citeline, April 2023
Appendix

Methodology, sources, and glossary of key terms
Methodology: Sources and scope of therapies

Sources for all data come from Citeline (formerly Pharma Intelligence)

Pipeline and trial data

- Data derived from Pharmaprojects and Trialtrove
- Therapeutic classes included in report categorizations:
  - Gene therapies: Gene therapy; cellular therapy, chimeric antigen receptor; cellular therapy, T cell receptor; lytic virus
  - Cell therapies: Cellular therapy, other; cellular therapy, stem cell; cellular therapy, tumor-infiltrating lymphocyte
  - RNA therapies: Messenger RNA; oligonucleotide, non-antisense, non-RNAi; RNA interference; antisense therapy

Deal, financing, and catalyst data

- Data derived from Biomedtracker. The following industry categorizations of deals are included: Gene therapy, cell therapy; antisense, oligonucleotides
- Additional alliance and acquisition deals data from BioSciDB, part of Evaluate Ltd. The following industry categorizations of deals are included: Cell Therapy - Stem Cells/Factors, oligonucleotides, antisense/triple helix, gene therapy, RNAi
## Glossary of Key Terms

### Therapy Type Definitions

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

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gene therapy</strong></td>
<td>Therapies containing an active ingredient synthesized following vector-mediated introduction of a genetic sequence into target cells (\text{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.</td>
</tr>
<tr>
<td><strong>Cellular therapy, chimeric antigen receptor</strong> <em>Falls under gene therapy in this report</em></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Cellular therapy, T cell receptor</strong> <em>Falls under gene therapy in this report</em></td>
<td>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).</td>
</tr>
<tr>
<td><strong>Lytic virus</strong> <em>Falls under gene therapy in this report</em></td>
<td>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.</td>
</tr>
</tbody>
</table>
### Glossary of Key Terms

**Therapy type definitions, cont.**

**Cell therapy** includes the following therapeutic classes:

<table>
<thead>
<tr>
<th>Cellular therapy, stem cell</th>
<th>Regenerative therapy which promotes the repair response of injured tissue using stem cells (cells from which all other specialized cells would originate).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular therapy, tumor infiltrating lymphocyte</td>
<td>Adoptive cellular transfer of tumor resident T cells from tumor material, their expansion <em>ex vivo</em>, and transfer back into the same patient after a lymphodepleting preparative regimen.</td>
</tr>
<tr>
<td>Cellular therapy, other</td>
<td>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.</td>
</tr>
</tbody>
</table>
Glossary of Key Terms

Therapy type definitions, cont.

**RNA therapy** includes the following therapeutic classes:

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Messenger RNA</td>
<td>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.</td>
</tr>
<tr>
<td>Oligonucleotide, non-antisense, non-RNAi</td>
<td>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.</td>
</tr>
<tr>
<td>RNA interference</td>
<td>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). <em>In vivo</em>, 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.</td>
</tr>
<tr>
<td>Antisense therapy</td>
<td>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 <em>in vivo</em> 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.</td>
</tr>
</tbody>
</table>
# Glossary of Key Terms

## Development status definitions

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

## Unspecified indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer, unspecified</td>
<td>Indications for which the specific tumor type is not specified</td>
</tr>
<tr>
<td>Cancer, hematological, unspecified</td>
<td>Indications for which the specific hematological cancer is not specified</td>
</tr>
<tr>
<td>Cancer, solid, unspecified</td>
<td>Indications for which the specific solid tumor is not specified</td>
</tr>
</tbody>
</table>

## Deal type categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alliances</td>
<td>Co-marketing, co-promotion, disease management, joint venture, manufacturing or supply, marketing-licensing, product or technology swap, product purchase, R&amp;D and marketing-licensing, reverse licensing, trial collaborations</td>
</tr>
<tr>
<td>Financing</td>
<td>Convertible debt, FOPO, IPO, nonconvertible debt, financing/other, private investment in public equity, private placement, royalty sale, special-purpose financing vehicle, spin-off</td>
</tr>
<tr>
<td>Acquisitions</td>
<td>Buy-out, divestiture, spin-out, full acquisition, partial acquisition, reverse acquisition</td>
</tr>
</tbody>
</table>
Report Contributors

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