MONTRÉAL INVIVO

Scientific watch for new therapies indicated in the treatment of rare conditions as well as cell and gene technologies

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Note to readers

Context

The challenges of **evaluating** and **implementing cutting-edge innovations** in the health and social services network can lead to sometimes critical **access delays** for patients with rare conditions. The importance of these issues is highlighted in the Quebec Life Sciences Strategy 2022-2025 and the Quebec Action Plan on Rare Diseases 2023-2027.

Objectives

1. Promote the alignment of necessary expertise and optimal integration into the healthcare network for the benefit of rare disease patients, the health and social services network and Quebec society.
2. Support the rare community's monitoring activities by offering enhanced information (fields of information, time horizon)

This tool is intended to provide information to the rare disease community in a context of limited resources, with more and more therapeutic options presenting significant potential benefits for patients. A history of our monitoring work can be consulted in the appendix.

Executive summary

- Nearly 25% of the 96 new therapies in development are for cancer.
- Targeted therapies and cell and gene therapies make up 52% and 23% respectively of the total 96 new treatments.
  - Viral-based gene therapies account for a predominant proportion of new cell and gene therapies in development.
  - Among targeted therapies, monoclonal antibodies predominate at 40%.
  - New cell and gene therapies are being developed for 12 rare and ultra-rare indications (excluding cancer).
  - New cell and gene therapies in development for 12 rare and ultra-rare cancers
  - There are 7 gene and cell therapies in development for cancer.
- The routes of administration of new therapies under development are predominantly non-oral, but 51% of new therapies under development are indicated for subcutaneous or oral injection: they can be obtained from community pharmacies and administered at home.
- The majority (65%) of therapies in development for cancer are in phase 3, and the majority of clinical trials are carried out in adults.

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Analysis of new treatments in development for rare conditions

Analysis period: 10/2022 - 06/2023

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Common definitions

- Orphan drugs: used to treat rare diseases or conditions.
- *Targeted therapy is* one of the main medical treatment modalities used in oncology and other rare diseases.
- For the purposes of this analysis, we have separated the categories of gene therapy into *viral-based gene therapy* and *cell-based gene therapy, as* described in detail in the appendix.
- The term cell therapy has been used for cellular immunotherapies and autologous stem cell therapies indicated against cancer.

Highlights

- The gene and cell therapy pipeline is expanding rapidly, with over 600 gene and cell therapies in various stages of development worldwide by 2022.[1]
- In Canada
  - Orphan drugs account for **58% of all drugs approved in Canada in 2020.**
  - This upward trend continues: **49% of new specialty drugs in development are indicated for orphan conditions**.[2]

Sources:
1. Meds Entry Watch report, 6th edition
2. https://www.law.utoronto.ca/blog/faculty/pharmaceutical-industry-s-shift-towards-niche-markets-and-p

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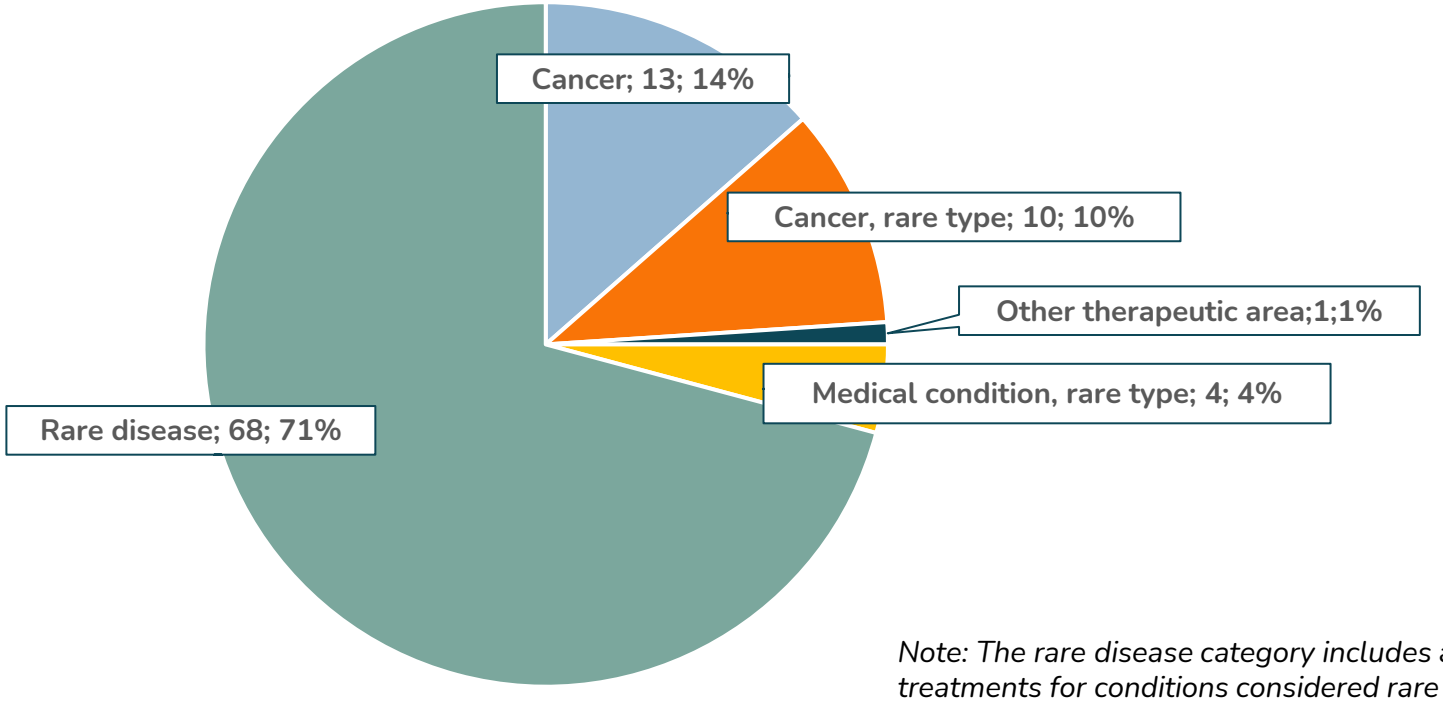
Breakdown of new therapies in development by therapeutic area (n=96)

Nearly a quarter of new therapies in development are for cancers



Note: The rare disease category includes all treatments for conditions considered rare and ultra-rare.

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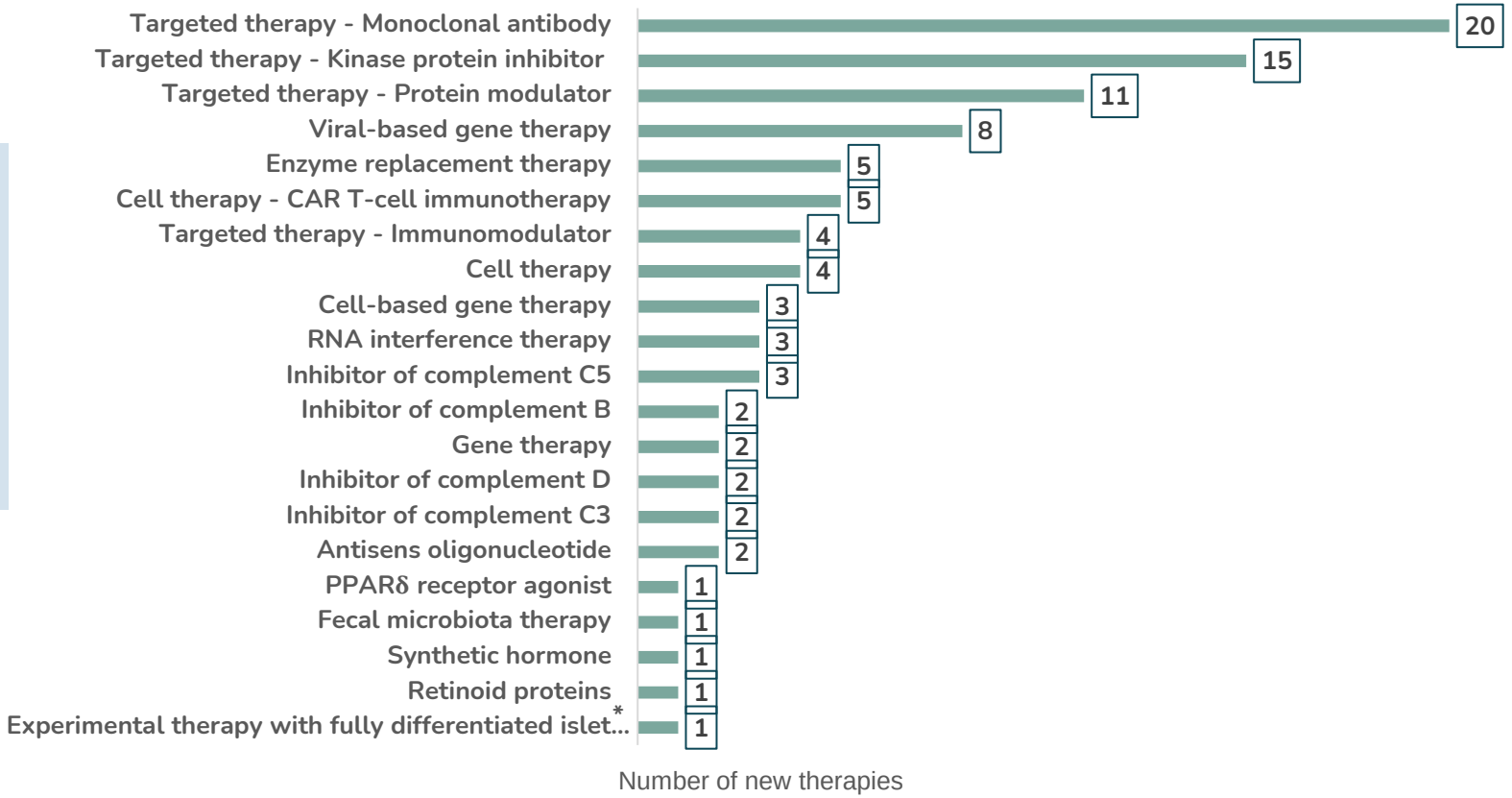
Breakdown of new therapies in development by type of treatment (n=96)

Targeted therapies account for 53% of all 94 new treatments.

Gene and cell therapies account for 23% of the total.



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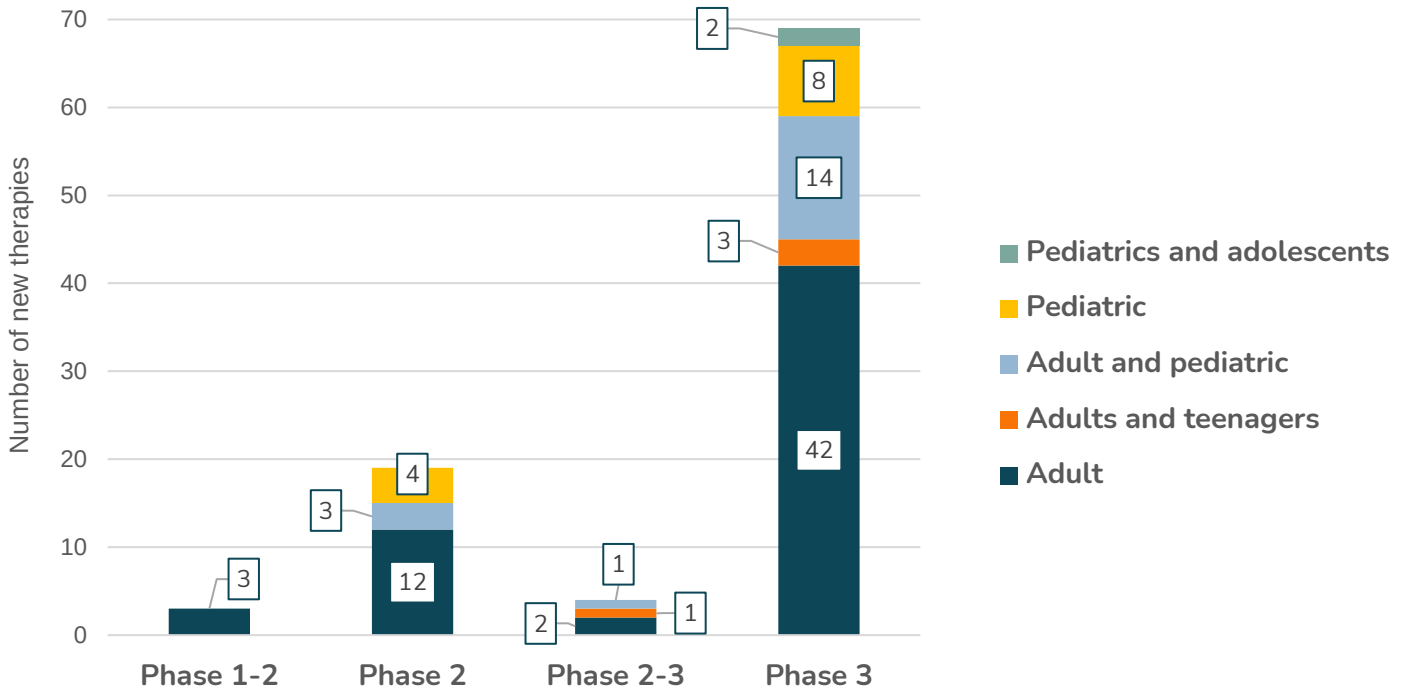
** Experimental therapy with fully differentiated islet cells derived from stem cells*

Breakdown of new therapies in development by phase of clinical research and target population (n=96)

The majority of clinical studies of treatments are carried out in the adult population.



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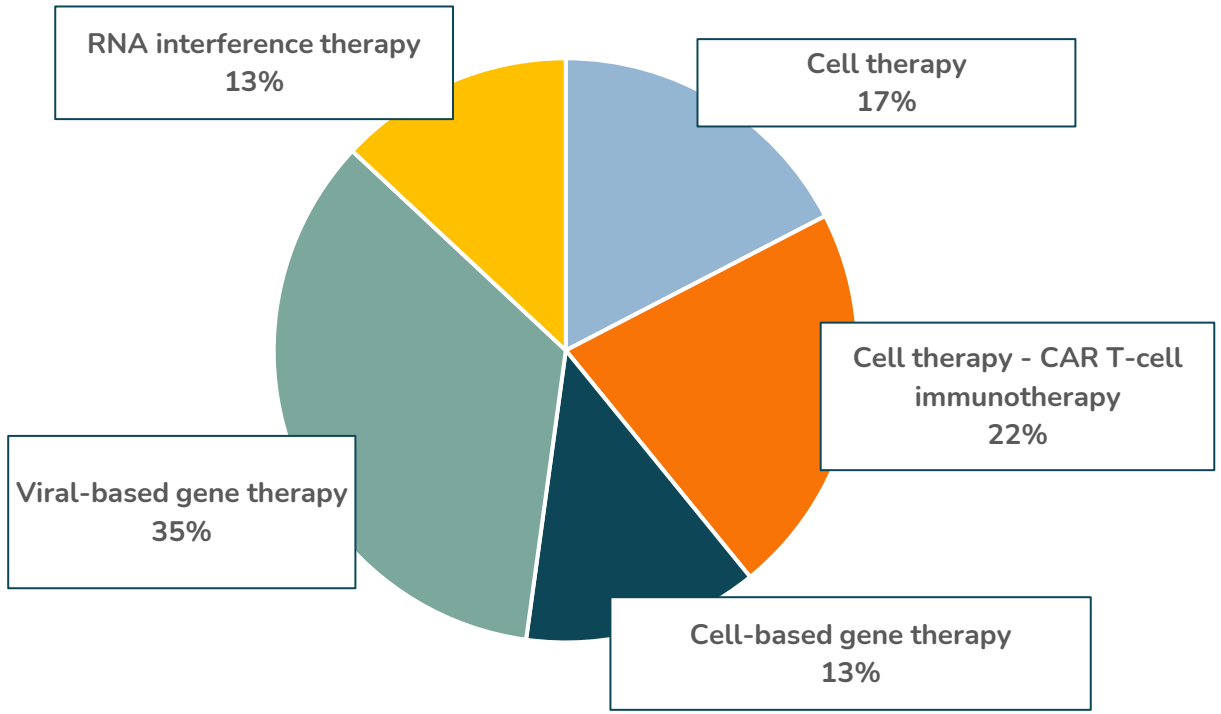
Breakdown of new cell and gene therapies in development by type of treatment (n=25)

Viral-based gene therapies account for a predominant proportion of new cell and gene therapies in development



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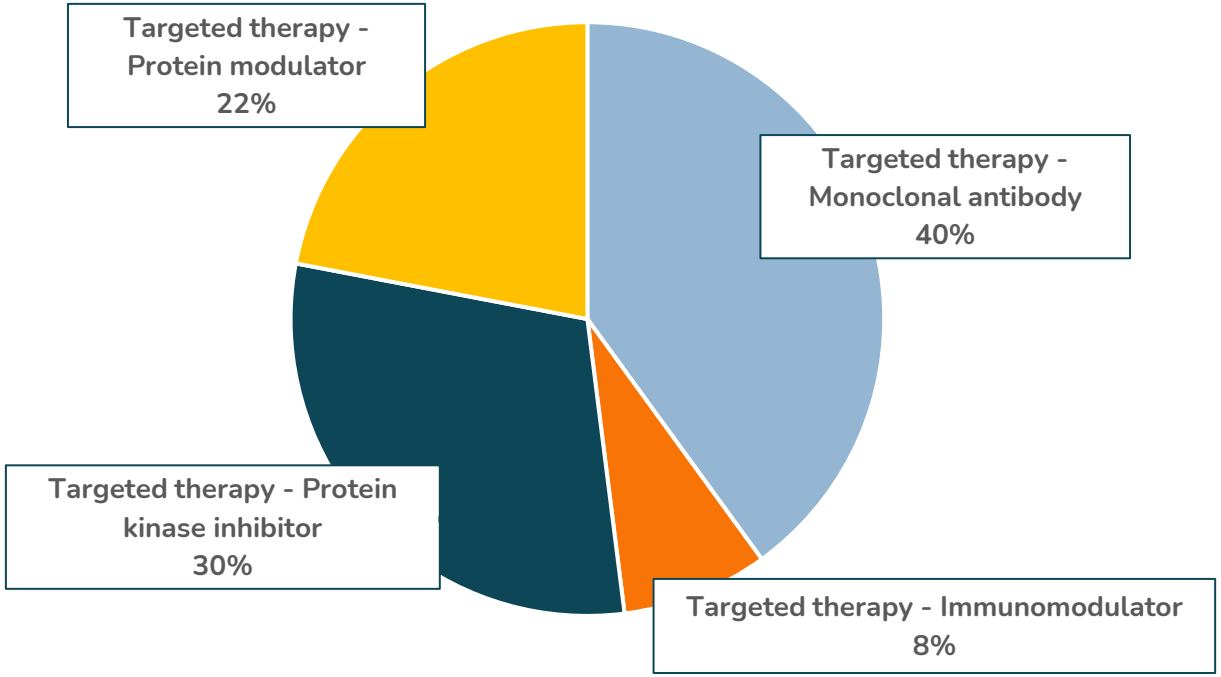
Breakdown of new targeted therapies in development by type of treatment (n=50)

Among targeted therapies, monoclonal antibodies predominate at 40%.



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Prevalence of rare and ultra-rare diseases

- Quebec's Ministry of Health and Social Services recognizes a rare disease as one that affects no more than one person in 2,000 or 5 people in 10,000.
- For the purposes of in-depth analysis of new therapies in development, an ultra-rare condition was defined as one affecting no more than one in 50,000 people.
- These definitions are also recognized by the Regroupement québécois des maladies orphelines (RQMO) and are used throughout this analysis report.

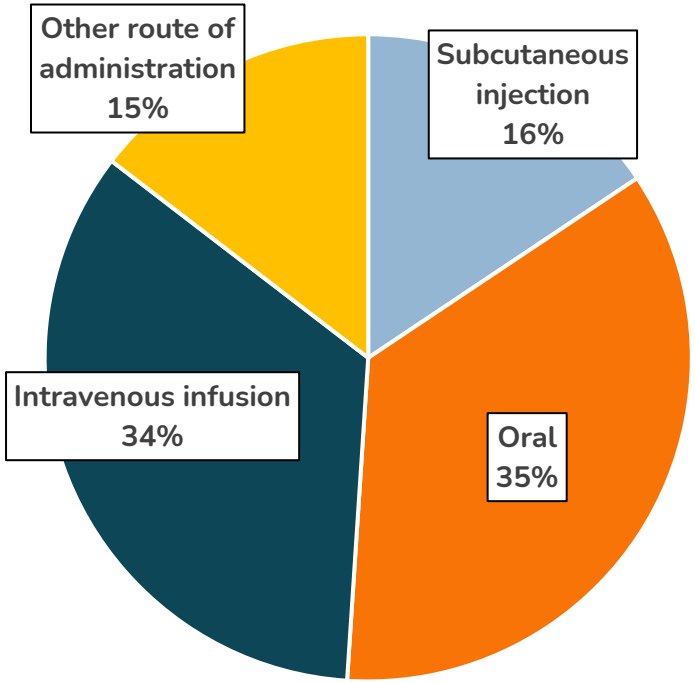
Impact of routes of administration on patient management in the Quebec healthcare system

- The complexity of new therapies brings challenges for implementation in the health and social services network
- One of Quebec's priorities is to relieve the healthcare system of the need for hospital care, and to increase the capacity and care of patients in outpatient clinics, community pharmacies or at home.
- Consequently, routes of administration such as oral intake or subcutaneous injection of the new therapies under development can support this initiative and facilitate patient management outside the hospital environment.

Breakdown of new therapies in development by route of administration (n=96)

51% of new therapies in development will be administered by subcutaneous injection or orally.

These treatments can be obtained from community pharmacies and administered at home - a major change in the patient care pathway.



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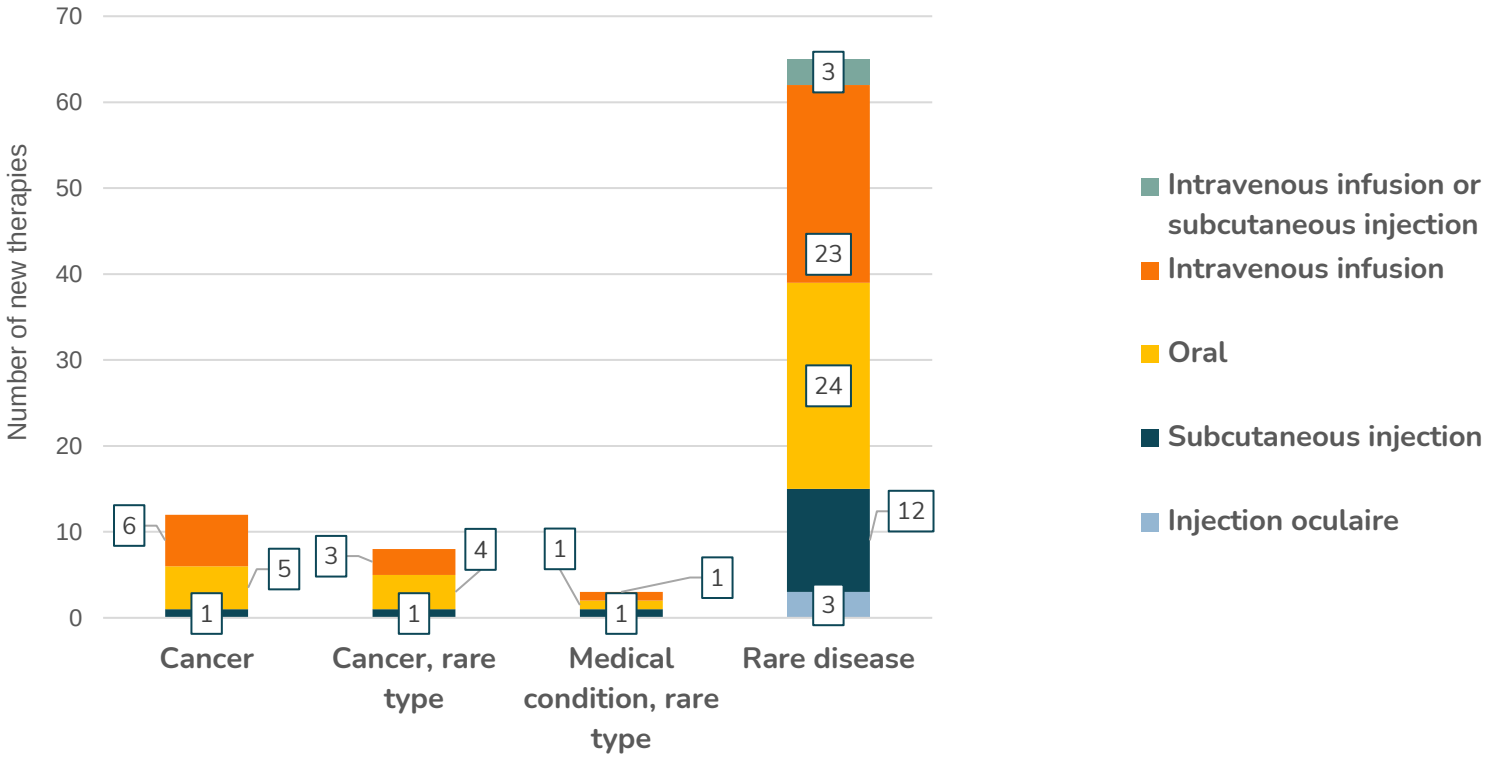
New therapies in development by route of administration and therapeutic area (n=90)

The routes of administration of new therapies under development are predominantly non-oral



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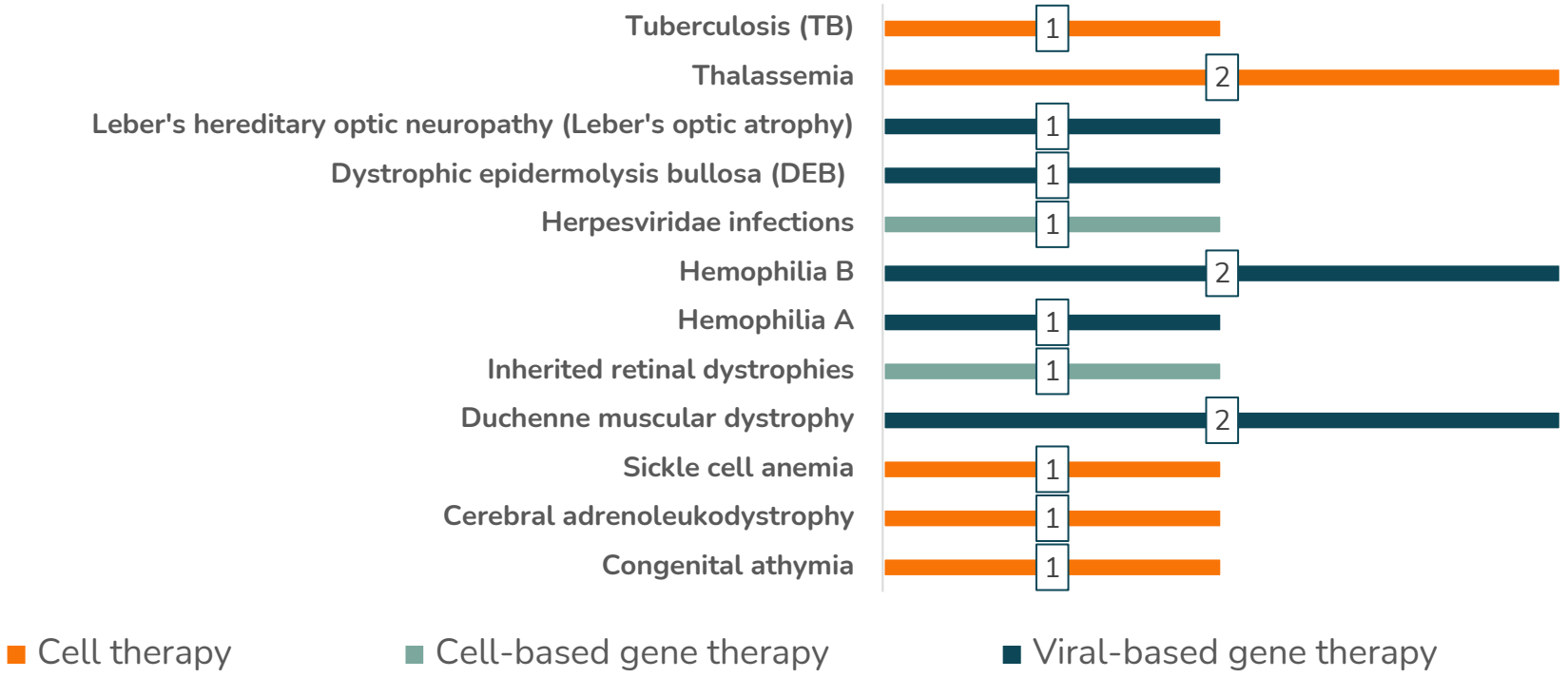
New cell and gene therapies used in rare and ultra-rare diseases (excluding cancers) by medical condition (n=15)

New cell and gene therapies in development for 12 rare and ultra-rare indications (excluding cancer)



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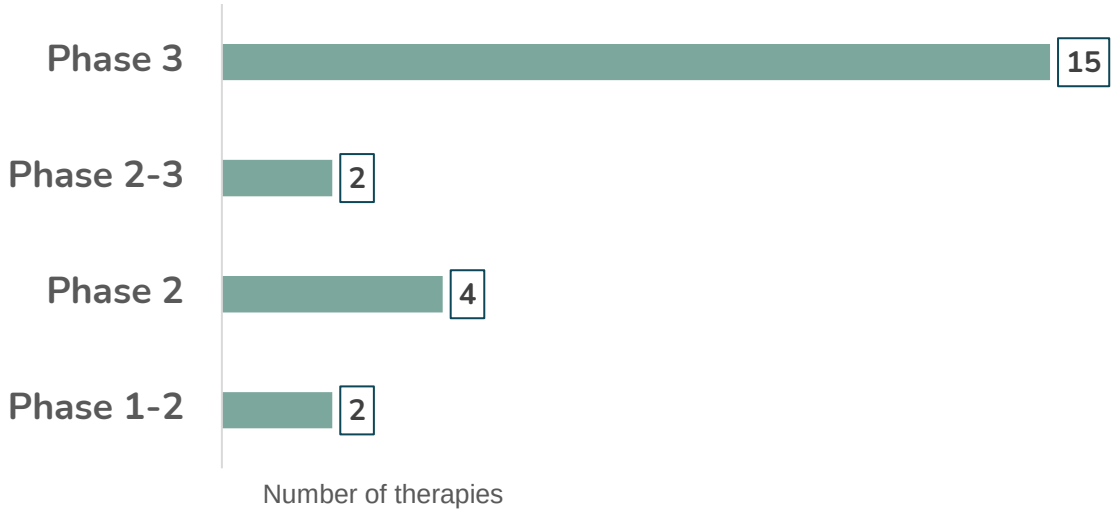
Breakdown of cancer therapies in development by clinical phase in adults (n=23)

The majority (65%) of therapies in development for cancer are in phase 3 clinical trials.



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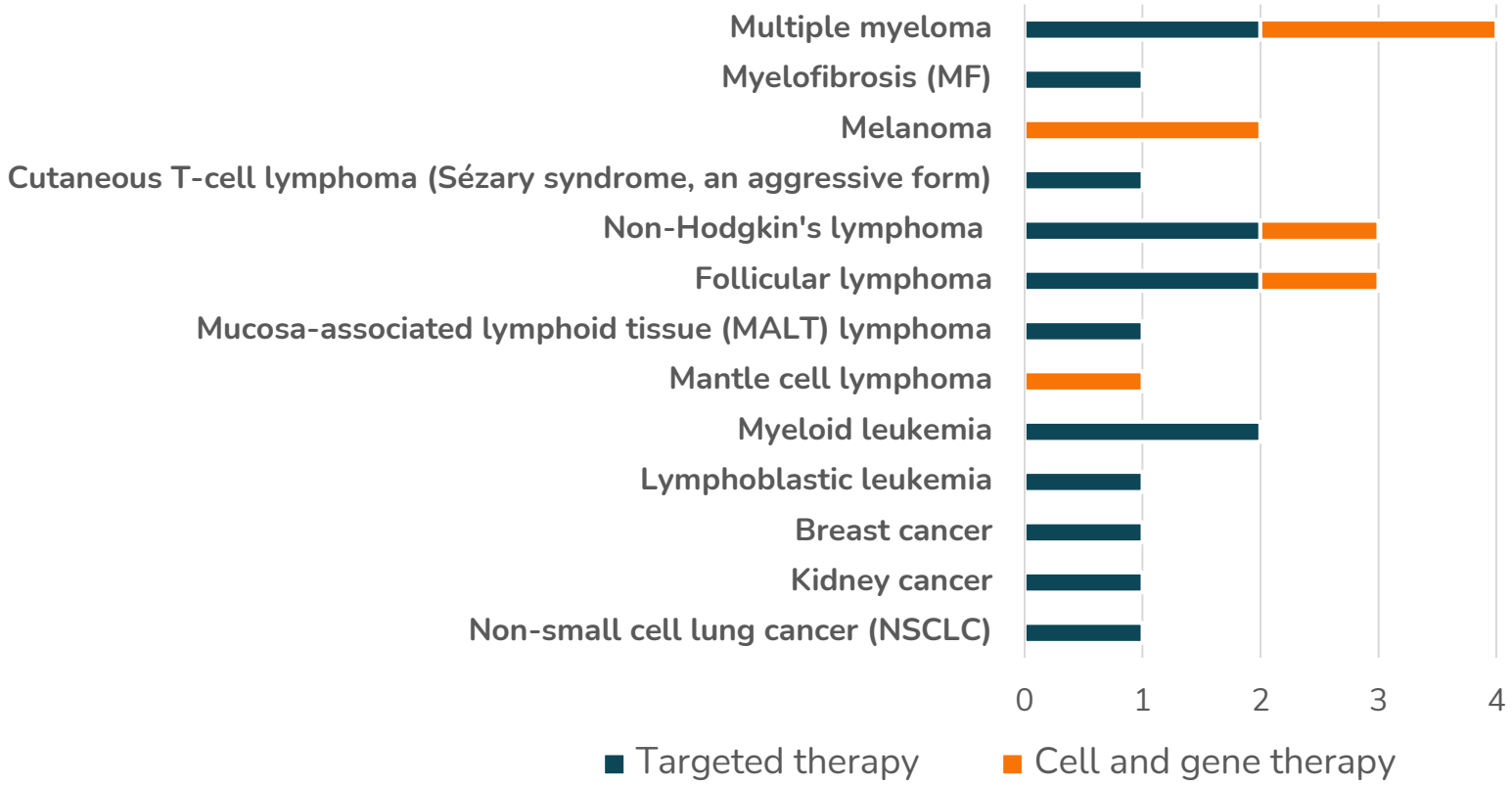
Breakdown of new oncology therapies by type of treatment (n=13)

New cell and gene therapies in development for 12 rare and ultra-rare cancers



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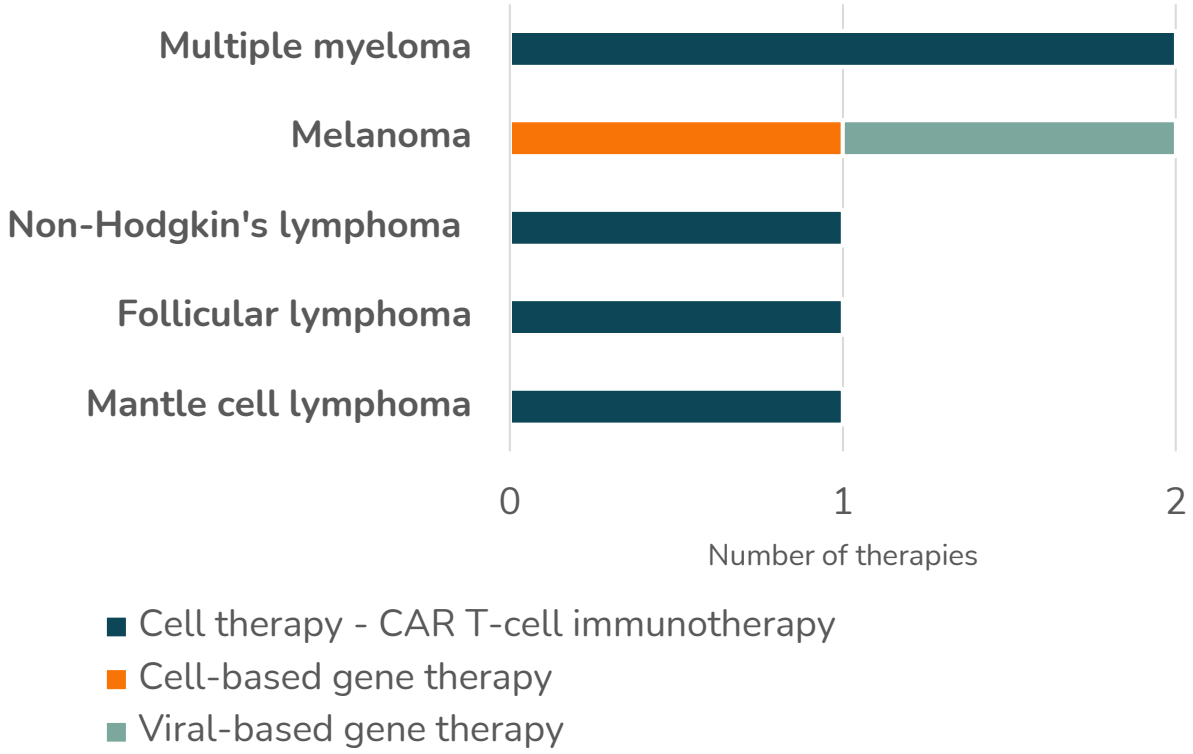
Distribution of gene and cell therapies used to treat cancer (n=7)

7 gene and cell therapies in development for cancer



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Future prospects

Strategic alignment to consider

- This scientific watch is part of a short-to-medium-term vision of the objectives of Montreal InVivo's specialized rare disease project committee, namely to:
  1. Enable Quebec patients with rare diseases to have rapid and optimal access to therapeutic and diagnostic innovations;
  2. Improve the competitiveness of Quebec's innovation ecosystem to attract investment and develop our skills, drawing on international best practices.

- Opportunities to support the MSSS's Quebec Action Plan for Rare Diseases 2023-2027 and the SQSV through the actions of Montreal InVivo and its partners:
  - Training and awareness: data science education programs
  - Better access to care: value-based agreements project committee, public-private collaborations to develop and commercialize innovations
  - Better use of healthcare data for research and innovation: Innovation hub on AI in healthcare

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Appendix

Methodology and approach

Methodology

- Methodology
  - Secondary research via Internet sites, databases, grey literature, third-party research reports.
  - Primary research: interviews with innovative companies and patient groups *(to come)*

- Research period: October 2022 to July 2023
- It should be noted that the information included in this work comes solely from publicly available sources. It has also been enhanced with data from feedback obtained from various stakeholders.
- Any information not found or insufficient to establish a link as to the rigor of its source has not been retained in the database and therefore has not been included in this analysis.

Information sources

- Pipeline of new treatments
  - Patented Medicine Prices Review Board (PMPRB) - https://www.canada.ca/content/dam/pmprb-cepmb/documents/npduis/analytical-studies/meds-pipeline-monitor-2022/NPDUIS-Meds-Pipeline-Monitor-2022_en.pdf
  - Targeted search in the PubMed database
  - Biopharmaceutical company websites: presentations on "pipelines" of therapies in development for rare conditions and diseases, such as BIOTECanada, Innovative Medicines Canada, Pharmaceutical Research and Manufacturers of America (PhRMA).
  - Presentations by biopharmaceutical companies at the 41e J.P. Morgan Annual Healthcare Conference, January 9-12, 2023, San Francisco, California, USA.
  - Health technology assessment organizations such as the Canadian Agency for Drugs and Technologies in Health (CADTH), Haute autorité de la santé (HAS), National Institute for Clinical Excellence (NICE), Scottish Medicines Consortium (SMC).
  - Data based on feedback from various stakeholders.

- Prevalence of rare conditions and diseases
  - Orphanet database (when information was not available on Orphanet, a literature search was performed).

Research approach and time horizon

- The decision to market a new therapy in Canada, and in Quebec, is usually taken by the pharmaceutical company itself, and often depends on a number of internal factors. It is therefore impossible to obtain precise timelines.
- Despite the FDA's approval of a new therapy, it is difficult to know whether it will be marketed in Canada and Quebec.
- The time horizon used in the present work is a simple estimate based on the dates of FDA product approval.
- Consequently, the new therapies in development selected and listed in this analysis are those most likely to come to market between 2023 and 2025.

Detailed common definitions

- Designated orphan drugs: drugs used to treat rare diseases or conditions.
- *Targeted therapy is* one of the main medical treatment modalities used in oncology and other rare diseases.
- Cell and gene therapy:
  - Cell therapy: cell therapy products include cellular immunotherapies, cancer vaccines and other autologous and allogeneic cell types for certain therapeutic indications, including hematopoietic stem cells and adult and embryonic stem cells.
  - Gene therapy: human gene therapy aims to modify or manipulate gene expression or alter the biological properties of living cells for therapeutic purposes. Delivery of DNA into cells can be accomplished by multiple methods.
    - The two main classes of gene therapy are recombinant virus-based vectors (sometimes called biological nanoparticles or viral vectors) and naked DNA or DNA complexes (non-viral methods), i.e. cell-based.
- For the purposes of this analysis, we have separated the categories of gene therapies according to their approach: *viral-based gene therapy* or *cell-based gene therapy*.
- The term cell therapy has been used for cellular immunotherapies and autologous stem cell therapies indicated against cancer.

Source: 1. 2022 Med Pipeline Monitor. - NPDUIS 2. GlobalData Healthcare

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History of work carried out

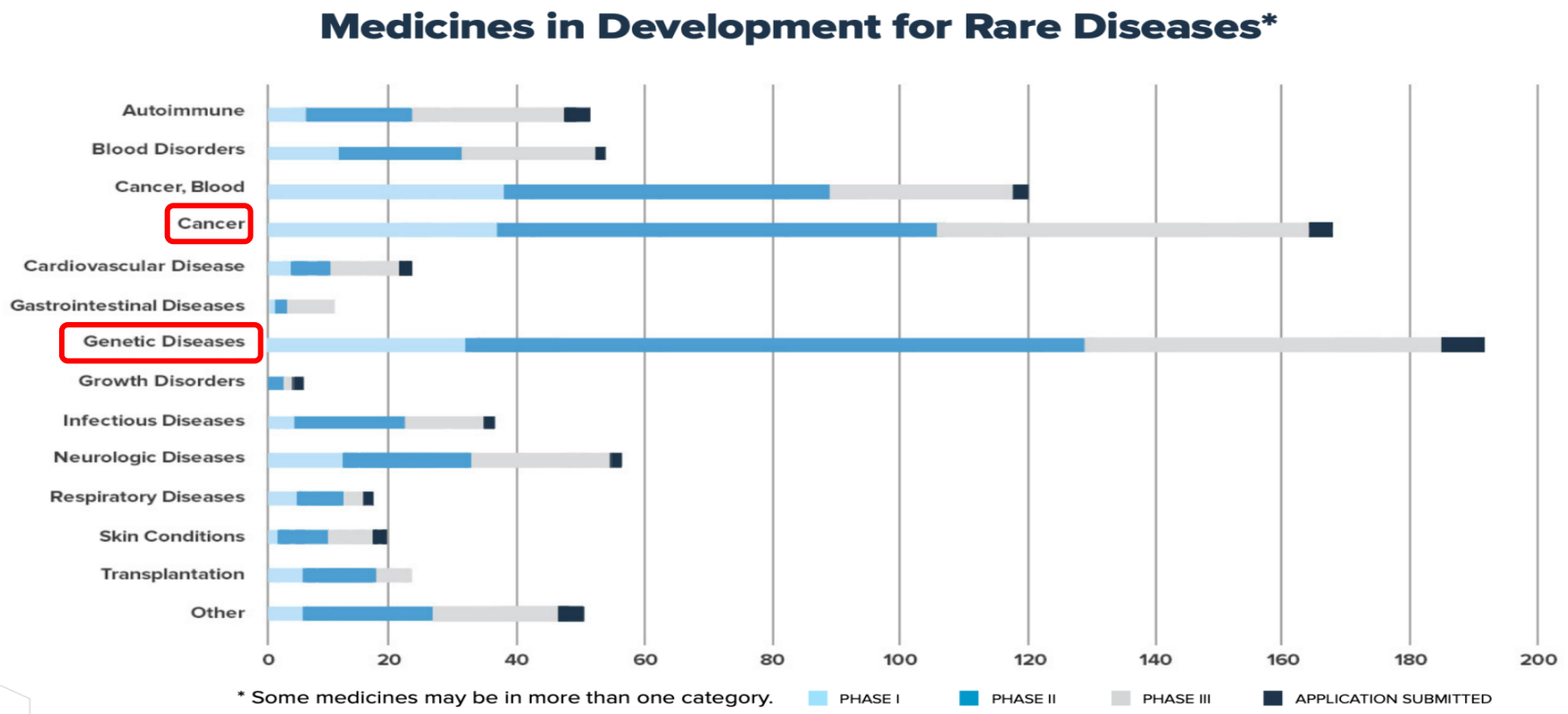
Version	Date
1	December 2022 - First scientific watch of the 45 new therapies in an Excel document.
	Spring 2023 - Presentation of the tool and collection of feedback from various stakeholders.
2	July 2023 - Addition of 51 new therapies for a total of 94 new therapies (data improved in November 2023 following feedback). Drafting of in-depth analysis report on all therapies.

Global overview of the rare disease environment and new therapies in development

Overview of new therapies in development

- Several treatments in development in the cell and gene therapy sector are for rare medical conditions, but also for cancer. It was therefore deemed appropriate to include CAR-T immunocellular therapies in the scope of the present work.
- Many of the therapies listed are already available on the Canadian market. However, new clinical indications and the approval of a new target population may be a reason to include this drug in the analysis.
- One of the weaknesses of this analysis is that it was difficult to identify all new indications or populations, as this information is sometimes not publicly available.
- It is therefore recommended that each organization add additional information to the list of medicines in the Excel document if this is deemed relevant to more specific work.

Drugs in development for rare diseases



Source: PhMRA https://catalyst.phrma.org/new-report-nearly-800-new-medicines-in-development-to-treat-rare-diseases (2021)

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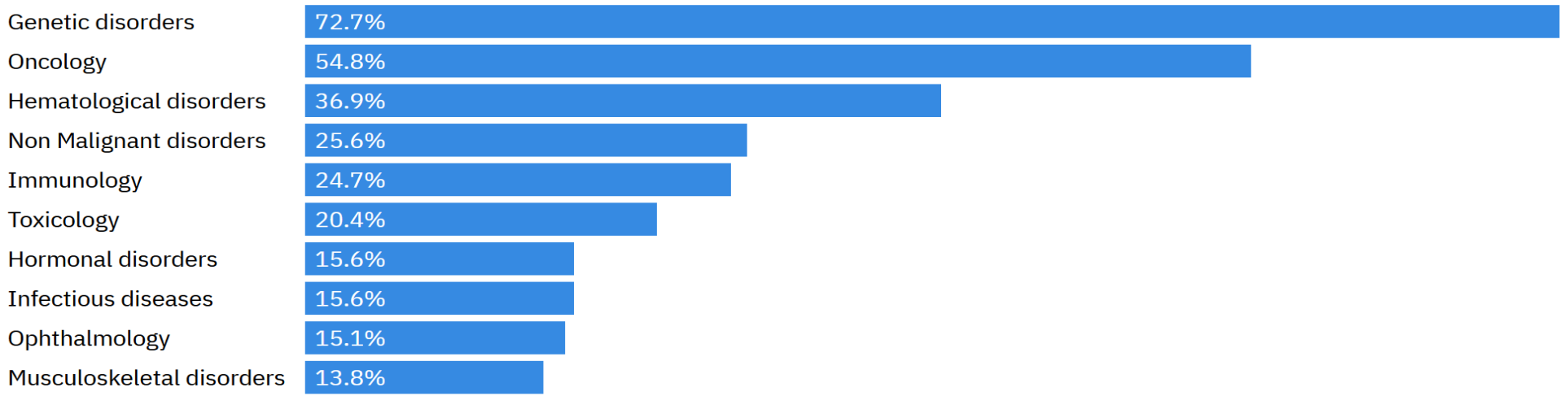
The top 10 therapeutic areas designated as rare diseases in the United States.



*The % of orphan therapies is calculated based on the total number of drugs in each therapy area in GlobalData's Pharma Intelligence Center

Source: GlobalData

PHARMACEUTICAL TECHNOLOGY

Source: https://www.pharmaceutical-technology.com/analysis/rare-disease-spotlight-ii-tracking-orphan-drugs-across-therapy-areas/ (2022)

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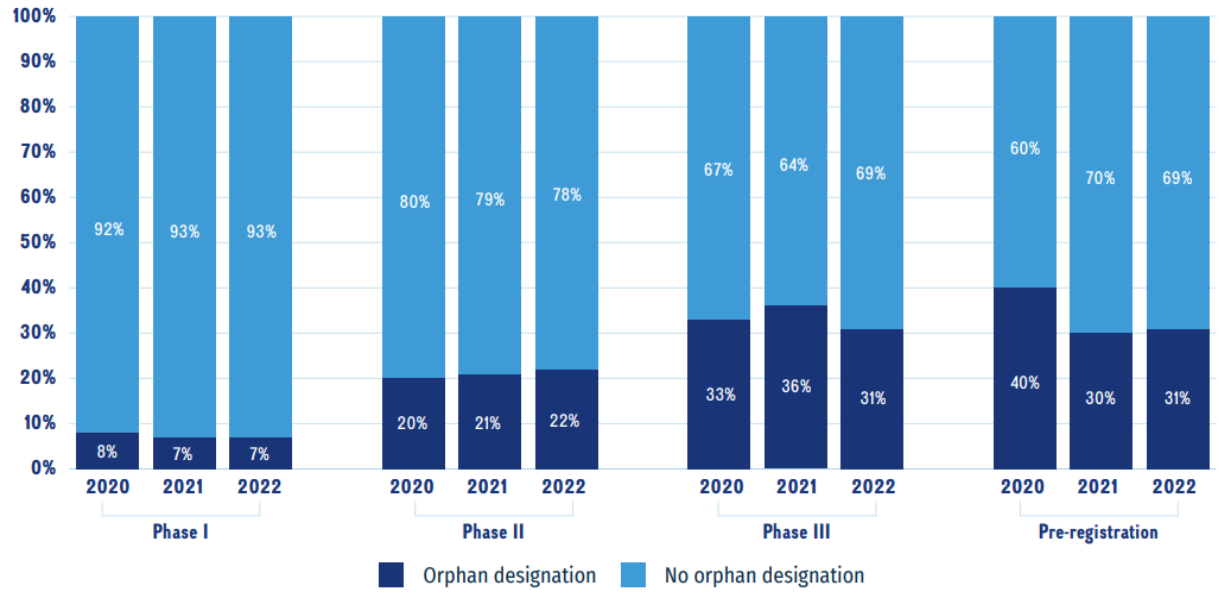
Share of orphan drugs in the pipeline by highest clinical evaluation phase, 2020-2022



Note: Includes all pipeline medicines with a highest development stage of Phase I to pre-registration that are being developed for market in Canada, the United States, or geographic Europe (excluding Russia and Turkey). Orphan medicines were defined as pipeline medicines that have been granted an orphan designation by the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA).

Data source: GlobalData Healthcare database (accessed September 2022).

Designated orphan drugs account for a larger share in the later stages of the pipeline, rising from 7% in Phase I to 31% in pre-registration by 2022. This has been a constant trend since 2020.

Source: Med Pipeline Monitor 2022. - NPDUIS

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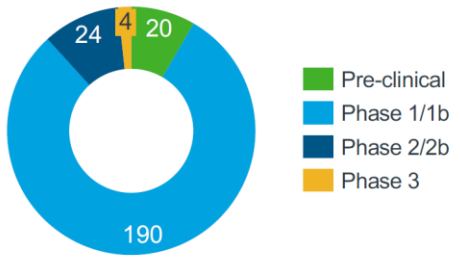
Cell and gene therapy

- According to a joint report by the European Federation of Pharmaceutical Industries and Associations (EFPIA) and IQVIA, 1,078 clinical trials on advanced therapies (*e.g. gene therapy, cell therapy and tissue engineering*) were conducted worldwide in 2020.
  - Of these 1,078 clinical trials, 204 involve cell therapy.
  - More than 50% of advanced therapy trials are developed for use in oncology
  - More than 200 CAR-Ts under study, including 28 in Phase 2-3 trials for hematological cancers

Chimeric antigen receptor T-cell therapy *(CAR T-cell therapy)*

CAR-T therapies (all active trials)

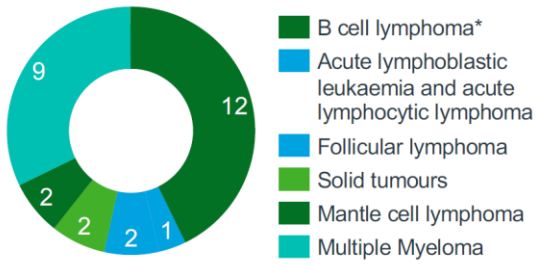
N=238



- There are multiple CAR-Ts currently in clinical development – with the majority in Phase 1 / 1b
- Many of these studies include research into the **novel applications of CAR-T's** e.g. for treatment of solid tumours, or in combination with CRISPR/CaS9

Indications studied in trials (Phase 2, 2b and 3 only)

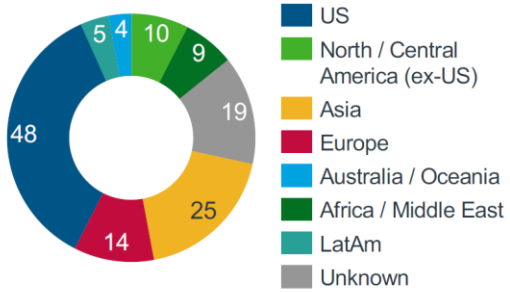
N=28



- Most CAR-Ts in the late development stage are being studied to treat **haematological cancers**, namely multiple myeloma, and acute lymphoblastic leukaemia
- There are also a few late stage trials for **solid tumours**

Active studies by geographic location

N=134



- CAR-T trials are happening globally, across **all continents,** however, the majority of trials are happening in the **US and Europe**

Source: IQVIA/EFPIA Pipeline Review 2021

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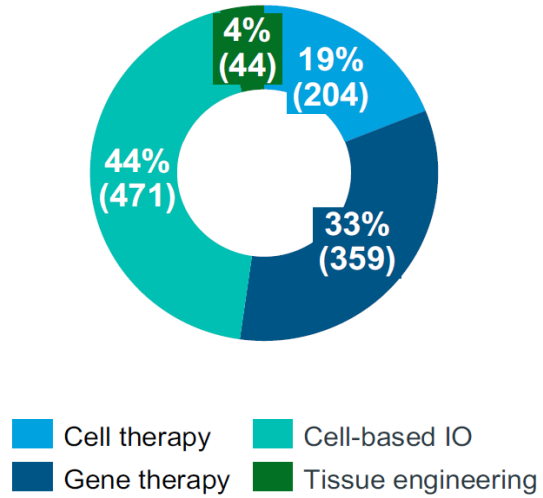
Advanced and gene therapies - Ongoing clinical trials

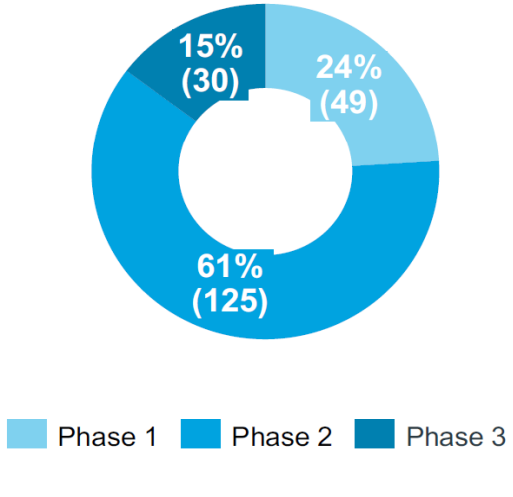
1.078 clinical trials are ongoing worldwide in advanced therapies*

Trails for advanced therapies by technology



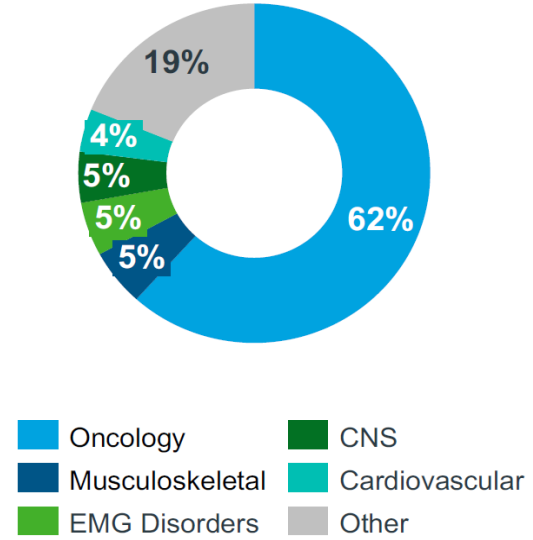
204 out of these trials are for cell therapies

Trials for cell therapy by phase



>50% of trials for advanced therapies* are in oncology

Trials for advanced therapies by indication



Source: IQVIA/EFPIA Pipeline Review 2021

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Advanced therapies in development

According to the EFPIA-IQVIA report, there were some 179 ongoing trials for gene therapies. The most extensive drug ranges concern hemophilia A and ophthalmological disorders.

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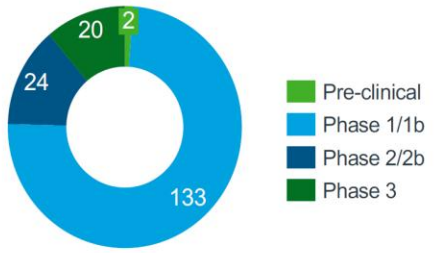
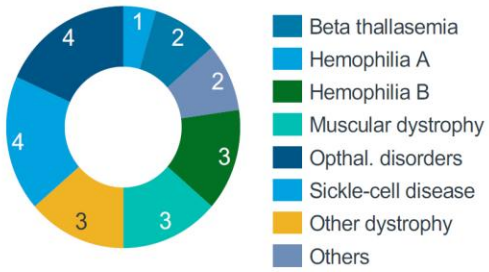


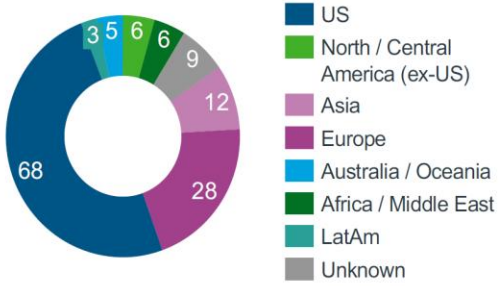
- There are currently **~179 ongoing trials** studying gene therapies
- As with other innovative areas, the majority of these trials are in **early development phases**

N=23



- Most of the Phase 2b and Phase 3 trials are being studied in Haemophilia
- **As opposed to** the 2019 update, where Haemophilia B was the key focus area, **Haemophilia A has also seen increased activity,** with 4 trials ongoing in 3 different therapies

N=137*



- The majority of trials are happening in the **US and Europe**
- Gene therapy trials are also happening globally, across all continents

Source: IQVIA/EFPIA Pipeline Review 2021

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